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**Enteral nutrition in acute pancreatitis: A review of the current evidence**

Oláh A *et al* Enteral nutrition in acute pancreatitis

Attila Oláh, Laszlo Romics Jr

**Attila Oláh,** Department of Surgery, Petz Aladár Teaching Hospital, H-9023 Győr, Hungary

**Laszlo Romics Jr,** Department of Surgery, Glasgow Victoria Infirmary, Glasgow G42 9TY, United Kingdom

**Author contributions**: Olah A designed research; Olah A and Romics Jr L performed literature search, analyzed data and wrote the paper.

**Correspondence to:** **Attila Oláh, MD, PhD, MRCS,** Department of Surgery, Petz Aladár Teaching Hospital, P.O. Box 92, H-9023 Győr, Hungary. olaha@petz.gyor.hu

**Telephone:** +36–96–418244 **Fax:** +36–96–507907

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**Abstract**

The use of enteral feeding as part of the management of acute pancreatitis dates back almost two decades. This review describes the indications for and limitations of enteral feeding for the treatment of acute pancreatitis using up-to-date evidence-based data. A systematic review was carried out to analyse current data on the use of enteral nutrition in the management of acute pancreatitis. Relevant literature was analysed from the viewpoints of enteral *vs* parenteral feeding, early *vs* delayed enteral nutrition, nasogastric *vs* nasojejunal feeding, and early oral diet and immunonutrition, particularly glutamine and probiotic supplementation. Finally, current applicable guidelines and the effects of these guidelines on clinical practice are discussed. The latest meta-analyses suggest that enteral nutrition significantly reduces the mortality rate of severe acute pancreatitis compared to parenteral feeding. To maintain gut barrier function and prevent early bacterial translocation, enteral feeding should be commenced within the first 24 h of hospital admission. Also, the safety of nasogastric feeding, which eases the administration of enteral nutrients in the clinical setting, is likely equal to nasojejunal feeding. Furthermore, an early low-fat oral diet is potentially beneficial in patients with mild pancreatitis. Despite the initial encouraging results, the current evidence does not support the use of immunoenhanced nutrients or probiotics in patients with acute pancreatitis.

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**Key words:** Acute pancreatitis; Enteral nutrition; Immunonutrition; Probiotics

**Core tip****:** The application of enteral feeding in acute pancreatitis is much debated. This systematic review provides global insight for clinicians on how to incorporate enteral feeding in the management of acute pancreatitis. The timing, route and composition of enteral nutrition are discussed with up-to-date evidence-based data, and the latest relevant guidelines are also detailed. Importantly, enteral nutrition significantly reduces mortality in severe acute pancreatitis compared to parenteral nutrition. Furthermore, early commencement of enteral feeding (within the first 24 h) is beneficial, and the safety of the nasogastric route seems to be equal to that of the nasojejunal route.

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**Introduction**

The treatment of acute pancreatitis is purely symptomatic because there is no effective therapy to prevent the activation of inflammatory and proteolytic cascades. This vicious cycle of cell signalling is believed to be triggered by bacterial infection, predominately Gram-negative strains. The most likely hypothetical source of the bacterial infection is the gastrointestinal tract. Bacterial translocation is caused by increased permeability in the gut and a consequent migration of macromolecules such as bacteria, endotoxins and antigens from the gastrointestinal tract to the portal system, mesenteric lymph nodes, liver, spleen and pancreas. This process leads to the stimulation of macrophages, circulatory neutrophils and granulocytes, and then the release of pro-inflammatory cytokine causes an inflammatory response. If the inflammatory response, which is initially part of the defence mechanisms of the host, is over-activated, it may turn into a self-destructive process. The unbalanced production of inflammatory mediators might lead to the development of systemic inflammatory response syndrome (SIRS), infectious pancreatic necrosis and ultimately multi-organ failure (MOF)[1].

Severe acute pancreatitis (SAP) represents a typical model of septic syndrome due to a failure of the gut barrier. Hence, one of the main therapeutic goals in SAP is to maintain gut integrity to prevent bacterial and endotoxin translocation and improve the immune system of the gut. Recently, various clinical methods have aimed to prevent or decrease bacterial translocation. These methods include enteral feeding, with or without immunonutrition, as well as the use of probiotics during treatment. This paper provides a review of the available data in the evidence-based literature on the application of enteral feeding to acute pancreatitis. Furthermore, the authors discuss the evidence supporting early as opposed to delayed commencement of enteral feeding. The latest results on immunonutrition and probiotic use are also presented. In addition, the debate on the adequate route for enteral feeding is outlined. Finally, up-to-date guidelines and clinical practices are discussed.

**Enteral nutrition *vs* parenteral nutrition**

Prolonged parenteral feeding carries numerous unfavourable side-effects such as atrophy and increased permeability of the gut mucosa. Furthermore, the lack of peristaltic stimulation results in hypomotility of the gut, and the stagnant bowel contents also cause significant changes in the intestinal microflora. Conversely, enteral feeding prevents the aforementioned atrophic changes as the uptake of nutrients in intestinal epithelial cells comes directly from the intestinal lumen. In addition, enteral feeding facilitates gut motility due the hyperosmolarity of the nutrients. These pathophysiological mechanisms protect against the overgrowth of abnormal intestinal flora and increased gut permeability, hence, potentially alleviating subsequent bacterial translocation.

In the first two randomised prospective trials, McClave *et al*[2] and Nakad *et al*[3] demonstrated that nasojejunal feeding is feasible, safe and beneficial in mild to moderate pancreatitis, or even severe pancreatitis. Altogether, 16 randomised controlled trials involving 847 patients with acute pancreatitis compared enteral to parenteral feeding[2,4–18]. Eleven of these studies randomised patients with severe pancreatitis or predicted SAP. All meta-analyses demonstrated a statistically significant reduction of infectious complications with the use of enteral nutrition[19–21], except two studies which failed to confirm the beneficial effect of nasojejunal feeding[6,16]. Hence, enteral nutrition has been established as a key component in the management of SAP[22].

The meta-analyses published by Marik and Zaloga[21] as well as McClave *et al*[23] demonstrated that the use of enteral nutrition resulted in a significant reduction of infectious complications and length of hospital stay, as well as a trend toward reduced organ failure. However, these meta-analyses failed to confirm that enteral feeding could reduce mortality. In a meta-analysis published by Petrov *et al*[20], more homogenous subgroups were compared, and altogether 202 patients with predicted SAP were included. The mortality rate in the enteral nutrition group was 4% (4/95) *vs* 15.9% (17/107) in the parenteral nutrition group, a statistically significant difference (RR = 0.32; 95%CI: 0.11–0.98; *p =* 0.03). Furthermore, Cao *et al*[19] analysed six randomised controlled trials involving 224 patients and demonstrated a statistically significant decrease in mortality (OR = 0.251; 95%CI: 0.095–0.666, *p =* 0.005) and MOF (OR = 0.306; 95%CI: 0.128–10.736) in patients receiving enteral feeding. Finally, in a recent meta-analysis involving 381 patients from eight randomised controlled trials, Yi *et al*[24] found that total enteral nutrition is significantly superior to total parenteral nutrition in patients with SAP. A statistically significant difference was observed in mortality (*p =* 0.001; OR = 0.37; 95%CI: 0.21–0.68), infectious complications (*p =* 0.004; OR = 0.46; 95%CI: 0.27–0.78), organ failure (*p =* 0.02; OR = 0.44; 95%CI: 0.22–0.88) and surgical intervention (*p =* 0.003; OR = 0.41; 95%CI: 0.23–0.74). However, no difference was detected in terms of length of hospital stay and duration of nutrition administration.

In summary, the data accumulated so far provide strong evidence of the benefits of enteral over parenteral nutrition in patients with SAP, because the risk of mortality was statistically less in patients given enteral compared to parenteral nutrition. Importantly, in the clinical setting, there are no specific contraindications for enteral nutrition. It can be performed safely even when SAP is complicated by fistulas, ascites or pseudocysts. The role of parenteral nutrition is limited in conditions such as severe ileus, when enteral nutrition can be restricted by paralysis. Nevertheless, enteral feeding in reduced amounts is still suggested in these cases, which provides the physiological benefits discussed above[25] (Table 1).

# Early *vs* delayed enteral nutrition

Although the exact pathophysiological mechanisms of bacterial infection have not been determined, it seems unequivocal that it is a significant risk factor for pancreatic necrosis and the development of MOF during SAP. Importantly, bacterial translocation and pathogen overgrowth can be detected in the very early phase of acute pancreatitis. In a multicentre study, Besselink *et al*[26] demonstrated that bacteraemia can be detected as early as day 7 and that infected necrosis can be detected on average 26 d after hospital admission. Furthermore, early bacterial invasion may aggravate SIRS, which in turn makes the patient even more susceptible to organ failure. This can result in a vicious cycle, because the development of organ failure frequently precedes bacterial infection. Hence, if bacterial translocation can be reduced or prevented through the maintenance of the intestinal barrier with enteral feeding, then it is reasonable to begin enteral feeding as early as possible.

A systematic meta-analysis published by Petrov *et al*[27] involving 11 randomised controlled trials demonstrated that the risk of MOF, pancreatic infectious complications and mortality were significantly reduced in patients with acute pancreatitis who were enterally fed within the first 48 h of admission as opposed to parenteral feeding. Importantly, the differences were not statistically significant, if enteral nutrition was commenced 48 h after admission. In fact, a large amount of evidence-based data support the administration of enteral nutrition within 24 h of hospital admission[28].

 This has been further confirmed by Sun *et al*[29] in a recently published randomised controlled trial. The authors investigated the effects of early administration of enteral nutrition on the immune function and clinical outcomes of 60 patients with SAP. The incidences of multiple organ dysfunction syndrome, SIRS and pancreatic infection, as well as the duration of stay in the intensive care unit, were significantly lower in the early administration group (commenced within 48 h of hospital admission) than in patients whose enteral feeding began on the eighth day of hospital stay. However, the authors did not report a difference in mortality between the two groups, which could have been due to the relatively low number of patients in the study. In another recent randomised controlled trial involving 197 patients with SAP, Wereszczynska-Siemiatkowska *et al*[30] found that enteral feeding within 48 h of admission significantly decreased the incidence of infective necrosis/fluid collection, respiratory failure, intensive care treatment and mortality compared to enteral feeding started after 48 h of hospital admission. While a clear trend towards a reduction in the rate of multi-organ dysfunction and surgical interventions was observed in patients with early enteral feeding, these differences were not statistically significant. An interesting aspect of the pathophysiology of acute pancreatitis was investigated in a pilot study by Sun *et al*[31], which compared the incidence of intra-abdominal hypertension in 60 patients with early (within 48 h) or delayed (after day 8) administration of enteral nutrition. Intra-abdominal hypertension was more prevalent in patients with delayed administration of enteral nutrition. They also argued that higher intra-abdominal pressure (over 15 mmHg) may correlate with intolerance to feeding (Table 2).

 The above findings were confirmed by a recent meta-analysis on the benefits of early administration of enteral nutrition commenced within 48 h of hospital admission[32]. Based on 11 studies involving 775 patients, Li *et al*[33] concluded that early enteral feeding was associated with significant reductions in all infections (OR = 0.38; 95%CI: 0.21–0.68; *p <* 0.05), catheter-related septic complications (OR = 0.26; 95%CI: 0.11–0.58; *p <* 0.05), pancreatic infection (OR = 0.49; 95%CI: 0.31–0.78; *p <* 0.05), hyperglycaemia (OR = 0.24; 95%CI: 0.11–0.52; *p <* 0.05), length of hospitalisation (mean difference -2.18; 95%CI: -3.48-(-0.87); *p <* 0.05) and mortality (OR = 0.31; 95%CI: 0.14–0.71; *p <* 0.05). Importantly, a multi-centre randomised controlled trial that investigated 208 patients with predicted SAP has yet to report its results. The PYTHON trial, which was organised by the Dutch Pancreatitis Study Group, compared very early nasojejunal feeding (within 24 h of hospital admission) to standard practice (oral nutrition on demand, or if needed, enteral feeding after 72 h).

# Nasogastric *vs* nasojejunal feeding

While the placement of a nasogastric tube is a simple routine procedure that can facilitate the commencement of early enteral feeding, nasojejunal feeding requires an endoscopist or radiologist for tube placement, which may cause a delay in the start of early enteral feeding. Hence, nasogastric feeding seems to be the most feasible option in clinical practice. However, arguments against nasogastric feeding are based on the effects of stimulating pancreatic secretion and gastric emptying problems due to paralysis.

Eatock *et al*[34] were the first to investigate these concerns in a prospective pilot study and found that nasogastric feeding is safe and well-tolerated. Then, two randomised controlled trials that compared nasogastric and nasojejunal feeding[35,36] concluded that nasogastric nutrition at a slow rate of infusion was well tolerated, and there were no differences in the outcome measures (discharge, surgery and mortality rate) between the two groups. Another randomised controlled trial, which compared early nasogastric feeding to total parenteral nutrition in patients with predicted SAP[37], demonstrated that enterally fed patients had significantly more total complications and pulmonary complications within the first 3 d. Two meta-analyses based on the above studies involving a total of 131 patients[38,39] revealed no significant differences in mortality rate, length of hospital stay, infectious complications or MOF in SAP between nasogastric enteric feeding and conventional feeding. A recent meta-analysis based on three randomised trials involving 157 patients drew the same conclusion, that nasogastric feeding is not inferior to nasojejunal feeding[40]. Although nasogastric feeding seems safe and well tolerated compared to nasojejunal feeding, more high-quality randomised controlled trials are needed to provide strong evidence, because the sample sizes in the studies conducted to date have been relatively low.

**Early oral diet**

Regarding early oral feeding, a pilot study was the first to demonstrate the feasibility of administration of an oral diet an average of 3 d after hospital admission[41]. To determine if oral feeding is feasible for treating mild pancreatitis, Erckerwall *et al*[42] randomised 60 patients with mild acute pancreatitis to compare the efficacy and feasibility of immediate oral feeding and traditional fasting. No differences were found in amylase values or the systemic inflammatory response between the two groups. This trial proved that immediate oral feeding is feasible and safe for treating mild acute pancreatitis. Furthermore, two randomised controlled trials demonstrated that it is not necessary to keep the patient on a liquid diet after acute mild pancreatitis[43,44], as no detrimental effects were observed from a solid diet. In fact, a solid diet was associated with a shorter length of hospital stay[44]. Hence, patients with mild acute pancreatitis can be started on a low-fat oral diet, although an initial period of fasting is still reasonable[28].

# Immunonutrition: glutamine supplementation

Immunoenhanced nutrients involve substrates that modulate the activity of the host immune system and inflammatory response (Table 3). Immunonutrition formulas include glutamine, arginine, nucleotides and omega-3 fatty acids, as well as enteral nutrients supplemented by probiotics. Experimental studies have suggested that supplementation of enteral feed with glutamine or omega-3 fatty acids may reduce the severity of experimental acute pancreatitis[45]. However, results have been rather moderate in the clinical setting. The four randomised controlled trials on this subject[46–49] demonstrated that immunonutrition has some beneficial effects, such as a shortened length of hospital stay, reduced gut permeability and decreased plasma endotoxin levels, but no significant differences were found in terms of clinical outcomes. Furthermore, a meta-analysis published by Petrov *et al*[50] based on three randomised controlled trials[48–50] clearly demonstrated that immunonutrition, compared to standard enteral nutrition, was not associated with a significantly reduced risk of total infectious complications (RR = 0.82; 95%CI: 0.44–1.53; *p =* 0.53) or mortality (RR = 0.64; 95%CI: 0.20–2.07; *p =* 0.46).

As for glutamine supplementation, emerging evidence suggests that glutamine supplementation should be considered in patients with a critical illness associated with a catabolic response. A meta-analysis published by Asrani *et al*[51], which included 505 patients from 12 studies, demonstrated that glutamine supplementation resulted in a significantly reduced risk of mortality (RR = 0.30; 95%CI: 0.15–0.60; *p <* 0.001) and total infectious complications (RR = 0.58; 95%CI: 0.39–0.87; *p =* 0.009), but not the length of hospital stay (MD = -1.35; 95%CI: -3.25–0.56; *p =* 0.17). However, a clear advantage of glutamine supplementation was seen in patients who received total parenteral nutrition as opposed to enteral nutrition. We drew a similar conclusion when we investigated the effects of intravenous glutamine and early administration of enteral nutrition on SAP outcomes in a prospective randomised controlled trial with 45 patients[52]. This study demonstrated that enteral nutrition supplemented by intravenous glutamine reduced the rate of complications (infected acute and post-necrotic peripancreatic fluid collections, infected pseudocysts and walled-off pancreatic necrosis), but the extent of reduction was not statistically significant. However, the mean hospital stay of the group that received intravenous glutamine and enteral feeding was 10.6 days, significantly shorter than that of the control group, who received enteral feeding alone (15.9 d; *p =* 0.00104).

**Immunonutrition: probiotic supplementation**

Probiotics are live microorganisms that confer a health benefit to the host, are responsible for the maintenance of the natural balance among gut flora and possess an *in vivo* antagonist effect against pathogenic bacteria. The most widely used probiotic bacteria are *Lactobacillus* and *Bifidobacterium*, which can be isolated from human faeces or intestinal mucosa. Prebiotics are non-digestible food ingredients that are necessary for the propagation of probiotics. Prebiotics selectively stimulate the growth and activity of certain bacteria in the normal gut flora. Synbiotics are nutritional supplements containing both probiotics and prebiotics[53].

Physiologically, some probiotics have been shown to have significant anti-infective and immunomodulatory properties. In addition, they can also prevent pathogenic bacteria from adhering to the gut mucosa via their strong affinity for enterocytes. The complex bacteriostatic and bactericidal effects of probiotics are mainly due to the production of lactic acid and antimicrobial peptides.

Basic data from experimental pancreatitis models initially confirmed the beneficial effects of probiotics. Application of *Lactobacillus plantarum* (*L*. *plantarum*) reduced the rate of infective necrosis[54], while *Saccharomyces boulardii* with concomitant ciprofloxacin lowered the histopathologic scores of acute necrotizing pancreatitis[55]. Furthermore, probiotics reduced the severity of acute experimental pancreatitis, as well as bacterial translocation to extra-intestinal sites due to a reduction in duodenal bacterial overgrowth, the latter reducing late-phase mortality[56,57].

Similarly, prospective randomised controlled trials have demonstrated beneficial effects of probiotics in acute pancreatitis. Karakan *et al*[58] showed that probiotics reduced the length of hospital stay in enterally fed patients when prebiotics were also applied. Supplementation of enteral nutrients with *L*. *plantarum* improved clinical outcomes, although control group patients in this study were fed parenterally[17]. In clinical studies, the effects of lactic acid-producing bacteria in acute pancreatitis was investigated for the first time in our department[59]. We found that the rate of pancreatic infectious complications was significantly lower in patients who received live *L*. *plantarum*. However, mortality was not significantly different between the two groups. We also investigated the use of a combination formula called “Synbiotic 2000” in patients with predicted severe pancreatitis[60]. A decreasing trend in the rate of MOF and septic complications was detected, but these differences did not reach statistical significance. In a multicentre, double-blind, placebo-controlled trial called PROPATRIA organised by the Dutch Acute Pancreatitis Study Group[61], 298 patients with predicted SAP were randomised to receive fibre-enriched enteral nutrition for 28 d with a multispecies probiotic preparation (Ecologic 641) or a placebo. The rate of infectious complications was comparable in both groups, and the mortality rate was higher in the synbiotic group (16% *vs* 6%), which was mainly due to bowel ischemia. Furthermore, organ failure and MOF were more common in the probiotic group (13.2% *vs* 4.9% and 3.0% *vs* 0.7%, respectively), although these differences did not reach statistical significance. Certainly, the synbiotic composition used in the PROPATRIA trial should not be used in critically ill patients[62]. Interestingly, a recent retrospective analysis[63] revealed that probiotic treatment had no apparent negative effect on patients with predicted SAP without initial organ failure, although the authors could not demonstrate the beneficial effects of probiotics in this subgroup of patients. However, the latest randomised controlled trial by Cui *et al*[64] supported the use of probiotics in combination with enteral feeding. The authors compared 70 patients with SAP who received parenteral feeding, enteral feeding or enteral feeding supplemented with *Bifidobacterium*. They found that the incidence of upper gastrointestinal bleeding, infection and abscess were significantly lower in the probiotic group, and that the length of hospital stay was also significantly shortened in this group. Nevertheless, the results of this study, which was a single-centre study with a relatively low patient number, do not deny the conclusion of the PROPATRIA trial warranting the cautious application of probiotics in SAP. In fact, probiotics cannot be recommended for the management of acute pancreatitis based on the presently available evidence-based data[65,66].

# Latest guidelines

Recently, an International Consensus Guideline was published based on 11 previous guidelines of various societies, which was endorsed by the American Society for Parenteral and Enteral Nutrition (ASPEN)[67]. The committee established three categories for the level of evidence in their statements. Importantly, enteral nutrition is generally preferred over parenteral nutrition, and if feasible should be initiated first. Furthermore, continuous enteral nutrition infusion over bolus or cyclic administration is preferred. Similarly, the use of a nasogastric tube for administering enteral nutrition (and the lack of a need to position a postpyloric feeding tube) is also suggested by the committee. Finally, the committee recommends using enteral nutrition in the presence of pancreatic complications such as fistulas, ascites and pseudocysts.

Two other guidelines on the management of acute pancreatitis were published last year, which involved statements on nutritional support during acute pancreatitis. The American College of Gastroenterology guideline recommends enteral nutrition in SAP to prevent infectious complications, whereas parenteral nutrition should be avoided[68]. The most detailed guidelines are based on the collaboration of the International Association of Pancreatology and the American Pancreatic Association involving 121 expert authors, which suggest that enteral nutrition is the preferable method of nutritional support in acute pancreatitis[69]. As far as the composition of nutrients, either elemental or polymeric nutrition formulations can be used. In addition, nasogastric feeding is equally as effective as nasojejunal feeding, and the relevant evidence supports nasogastric feeding. However, a prospective randomised controlled trial called the Study on Nutrition in Acute Pancreatitis (SNAP) is currently underway, which will provide further evidence on nasogastric *vs* nasojejunal feeding (http://clinicaltrials.gov/ct2/show/NCT00580749).

Despite the relatively clear guidelines, everyday clinical practice does not necessarily follow these recommendations. In a recent study by Sun *et al*[70], 43.3% of United States physicians utilised total parenteral nutrition for the treatment of pancreatitis and 36.5% used nasojejunal feeding. Moreover, private physicians use nasojejunal tube feeding in only 19.9% of cases. In a transatlantic survey of nutrition practices in the United Kingdom, the Republic of Ireland and Canada, 54.2% favoured early feeding in SAP. There was a higher tendency towards enteral nutrition in university hospitals with the nasojejunal route being preferred[71]. In Sweden, enteral feeding is a routine practice in 60% of the hospitals[72]. The positive effects of a national consensus conference were demonstrated by Rebours *et al*[73] in a study involving 176 hospitals in France. While enteral feeding was applied in 25% of the hospitals in 2001, it increased to 58% after the consensus conference.

**Conclusion**

Current evidence confirms that the administration of enteral nutrition is beneficial for the treatment of SAP. Enteral feeding reduces mortality, infectious complications and MOF. As far as the route of enteral feeling is concerned, nasogastric tube feeding is likely to be equally as effective as nasojejunal feeding in SAP. In terms of the timing of enteral nutritional support, relatively early administration within 48 or 72 h of hospital admission is suggested. However, current evidence does not support the application of immunoenhanced nutrients or probiotic supplements, and therefore they cannot be recommended for the management of acute pancreatitis at this time.

**References**

1 **Soares RL**, Chini G, Dutra SL. Enteral Nutrition in patients with Acute Pancreatitis. *Nutrition* 1988; **4**: 86-89

2 **McClave SA**, Greene LM, Snider HL, Makk LJ, Cheadle WG, Owens NA, Dukes LG, Goldsmith LJ. Comparison of the safety of early enteral vs parenteral nutrition in mild acute pancreatitis. *JPEN J Parenter Enteral Nutr* 1997; **21**: 14-20 [PMID: 9002079]

3 **Nakad A**, Piessevaux H, Marot JC, Hoang P, Geubel A, Van Steenbergen W, Reynaert M. Is early enteral nutrition in acute pancreatitis dangerous? About 20 patients fed by an endoscopically placed nasogastrojejunal tube. *Pancreas* 1998; **17**: 187-193 [PMID: 9700952]

4 **Kalfarentzos F**, Kehagias J, Mead N, Kokkinis K, Gogos CA. Enteral nutrition is superior to parenteral nutrition in severe acute pancreatitis: results of a randomized prospective trial. *Br J Surg* 1997; **84**: 1665-1669 [PMID: 9448611]

5 **Windsor AC**, Kanwar S, Li AG, Barnes E, Guthrie JA, Spark JI, Welsh F, Guillou PJ, Reynolds JV. Compared with parenteral nutrition, enteral feeding attenuates the acute phase response and improves disease severity in acute pancreatitis. *Gut* 1998; **42**: 431-435 [PMID: 9577354]

6 **Powell JJ**, Murchison JT, Fearon KC, Ross JA, Siriwardena AK. Randomized controlled trial of the effect of early enteral nutrition on markers of the inflammatory response in predicted severe acute pancreatitis. *Br J Surg* 2000; **87**: 1375-1381 [PMID: 11044164 DOI: 10.1046/j.1365-2168.2000.01558.x]

7 **Paraskeva C**, Smailis D, Priovolos A. Early enteral nutrition reduces the need for surgery in severe acute pancreatitis. *Pancreatology* 2001; **1**: 372

8 **Oláh A**, Pardavi G, Belágyi T, Nagy A, Issekutz A, Mohamed GE. Early nasojejunal feeding in acute pancreatitis is associated with a lower complication rate. *Nutrition* 2002; **18**: 259-262 [PMID: 11882400]

9 **Abou-Assi S**, Craig K, O'Keefe SJ. Hypocaloric jejunal feeding is better than total parenteral nutrition in acute pancreatitis: results of a randomized comparative study. *Am J Gastroenterol* 2002; **97**: 2255-2262 [PMID: 12358242 DOI: 10.1111/j.1572-0241.2002.05979.x]

10 **Gupta R**, Patel K, Calder PC, Yaqoob P, Primrose JN, Johnson CD. A randomised clinical trial to assess the effect of total enteral and total parenteral nutritional support on metabolic, inflammatory and oxidative markers in patients with predicted severe acute pancreatitis (APACHE II & gt; or =6). *Pancreatology* 2003; **3**: 406-413 [PMID: 14526151 DOI: 73657]

11 **Zhao G**, Wang CY, Wang F, Xiong JX. Clinical study on nutrition support in patients with severe acute pancreatitis. *World J Gastroenterol* 2003; **9**: 2105-2108 [PMID: 12970916]

12 **Louie BE**, Noseworthy T, Hailey D, Gramlich LM, Jacobs P, Warnock GL. 2004 MacLean-Mueller prize enteral or parenteral nutrition for severe pancreatitis: a randomized controlled trial and health technology assessment. *Can J Surg* 2005; **48**: 298-306 [PMID: 16149365]

13 **Petrov MS**, Kukosh MV, Emelyanov NV. A randomized controlled trial of enteral versus parenteral feeding in patients with predicted severe acute pancreatitis shows a significant reduction in mortality and in infected pancreatic complications with total enteral nutrition. *Dig Surg* 2006; **23**: 336-44; discussion 344-5 [PMID: 17164546 DOI: 10.1159/000097949]

14 **Targarona Modena J**, Barreda Cevasco L, Arroyo Basto C, Orellana Vicuña A, Portanova Ramírez M. Total enteral nutrition as prophylactic therapy for pancreatic necrosis infection in severe acute pancreatitis. *Pancreatology* 2006; **6**: 58-64 [PMID: 16327282 DOI: 10.1159/000090024]

15 **Casas M**, Mora J, Fort E, Aracil C, Busquets D, Galter S, Jáuregui CE, Ayala E, Cardona D, Gich I, Farré A. [Total enteral nutrition vs. total parenteral nutrition in patients with severe acute pancreatitis]. *Rev Esp Enferm Dig* 2007; **99**: 264-269 [PMID: 17650935]

16 **Doley RP**, Yadav TD, Wig JD, Kochhar R, Singh G, Bharathy KG, Kudari A, Gupta R, Gupta V, Poornachandra KS, Dutta U, Vaishnavi C. Enteral nutrition in severe acute pancreatitis. *JOP* 2009; **10**: 157-162 [PMID: 19287109]

17 **Qin HL**, Zheng JJ, Tong DN, Chen WX, Fan XB, Hang XM, Jiang YQ. Effect of Lactobacillus plantarum enteral feeding on the gut permeability and septic complications in the patients with acute pancreatitis. *Eur J Clin Nutr* 2008; **62**: 923-930 [PMID: 17579653 DOI: 10.1038/sj.ejcn.1602792]

18 **Wu XM**, Ji KQ, Wang HY, Li GF, Zang B, Chen WM. Total enteral nutrition in prevention of pancreatic necrotic infection in severe acute pancreatitis. *Pancreas* 2010; **39**: 248-251 [PMID: 19910834 DOI: 10.1097/MPA.0b013e3181bd6370]

19 **Cao Y**, Xu Y, Lu T, Gao F, Mo Z. Meta-analysis of enteral nutrition versus total parenteral nutrition in patients with severe acute pancreatitis. *Ann Nutr Metab* 2008; **53**: 268-275 [PMID: 19136822 DOI: 10.1159/000189382]

20 **Petrov MS**, van Santvoort HC, Besselink MG, van der Heijden GJ, Windsor JA, Gooszen HG. Enteral nutrition and the risk of mortality and infectious complications in patients with severe acute pancreatitis: a meta-analysis of randomized trials. *Arch Surg* 2008; **143**: 1111-1117 [PMID: 19015471 DOI: 10.1001/archsurg.143.11.1111]

21 **Marik PE**, Zaloga GP. Meta-analysis of parenteral nutrition versus enteral nutrition in patients with acute pancreatitis. *BMJ* 2004; **328**: 1407 [PMID: 15175229 DOI: 10.1136/bmj.38118.593900.55]

22 **Banks PA**, Freeman ML. Practice guidelines in acute pancreatitis. *Am J Gastroenterol* 2006; **101**: 2379-2400 [PMID: 17032204 DOI: 10.1111/j.1572-0241.2006.00856.x]

23 **McClave SA**, Chang WK, Dhaliwal R, Heyland DK. Nutrition support in acute pancreatitis: a systematic review of the literature. *JPEN J Parenter Enteral Nutr* 2006; **30**: 143-156 [PMID: 16517959]

24 **Yi F**, Ge L, Zhao J, Lei Y, Zhou F, Chen Z, Zhu Y, Xia B. Meta-analysis: total parenteral nutrition versus total enteral nutrition in predicted severe acute pancreatitis. *Intern Med* 2012; **51**: 523-530 [PMID: 22449657]

25 **Oláh A**, Romics L. Evidence-based use of enteral nutrition in acute pancreatitis. *Langenbecks Arch Surg* 2010; **395**: 309-316 [PMID: 20309576 DOI: 10.1007/s00423-010-0631-4]

26 **Besselink MG**, van Santvoort HC, Boermeester MA, Nieuwenhuijs VB, van Goor H, Dejong CH, Schaapherder AF, Gooszen HG. Timing and impact of infections in acute pancreatitis. *Br J Surg* 2009; **96**: 267-273 [PMID: 19125434 DOI: 10.1002/bjs.6447]

27 **Petrov MS**, Pylypchuk RD, Uchugina AF. A systematic review on the timing of artificial nutrition in acute pancreatitis. *Br J Nutr* 2009; **101**: 787-793 [PMID: 19017421 DOI: 10.1017/s0007114508123443]

28 **Marik PE**. What is the best way to feed patients with pancreatitis? *Curr Opin Crit Care* 2009; **15**: 131-138 [PMID: 19300086 DOI: 10.1097/MCC.0b013e328319910a]

29 **Sun JK**, Mu XW, Li WQ, Tong ZH, Li J, Zheng SY. Effects of early enteral nutrition on immune function of severe acute pancreatitis patients. *World J Gastroenterol* 2013; **19**: 917-922 [PMID: 23431120 DOI: 10.3748/wjg.v19.i6.917]

30 **Wereszczynska-Siemiatkowska U**, Swidnicka-Siergiejko A, Siemiatkowski A, Dabrowski A. Early enteral nutrition is superior to delayed enteral nutrition for the prevention of infected necrosis and mortality in acute pancreatitis. *Pancreas* 2013; **42**: 640-646 [PMID: 23508012 DOI: 10.1097/MPA.0b013e318271bb61]

31 **Sun JK**, Li WQ, Ke L, Tong ZH, Ni HB, Li G, Zhang LY, Nie Y, Wang XY, Ye XH, Li N, Li JS. Early enteral nutrition prevents intra-abdominal hypertension and reduces the severity of severe acute pancreatitis compared with delayed enteral nutrition: a prospective pilot study. *World J Surg* 2013; **37**: 2053-2060 [PMID: 23674254 DOI: 10.1007/s00268-013-2087-5]

32 **Li JY**, Yu T, Chen GC, Yuan YH, Zhong W, Zhao LN, Chen QK. Enteral nutrition within 48 hours of admission improves clinical outcomes of acute pancreatitis by reducing complications: a meta-analysis. *PLoS One* 2013; **8**: e64926 [PMID: 23762266 DOI: 10.1371/journal.pone.0064926]

33 **Bakker OJ**, van Santvoort HC, van Brunschot S, Ahmed Ali U, Besselink MG, Boermeester MA, Bollen TL, Bosscha K, Brink MA, Dejong CH, van Geenen EJ, van Goor H, Heisterkamp J, Houdijk AP, Jansen JM, Karsten TM, Manusama ER, Nieuwenhuijs VB, van Ramshorst B, Schaapherder AF, van der Schelling GP, Spanier MB, Tan A, Vecht J, Weusten BL, Witteman BJ, Akkermans LM, Gooszen HG. Pancreatitis, very early compared with normal start of enteral feeding (PYTHON trial): design and rationale of a randomised controlled multicenter trial. *Trials* 2011; **12**: 73 [PMID: 21392395 DOI: 10.1186/1745-6215-12-73]

34 **Eatock FC**, Brombacher GD, Steven A, Imrie CW, McKay CJ, Carter R. Nasogastric feeding in severe acute pancreatitis may be practical and safe. *Int J Pancreatol* 2000; **28**: 23-29 [PMID: 11185707 DOI: 10.1385/ijgc: 28: 1: 23]

35 **Eatock FC**, Chong P, Menezes N, Murray L, McKay CJ, Carter CR, Imrie CW. A randomized study of early nasogastric versus nasojejunal feeding in severe acute pancreatitis. *Am J Gastroenterol* 2005; **100**: 432-439 [PMID: 15667504 DOI: 10.1111/j.1572-0241.2005.40587.x]

36 **Kumar A**, Singh N, Prakash S, Saraya A, Joshi YK. Early enteral nutrition in severe acute pancreatitis: a prospective randomized controlled trial comparing nasojejunal and nasogastric routes. *J Clin Gastroenterol* 2006; **40**: 431-434 [PMID: 16721226]

37 **Eckerwall GE**, Axelsson JB, Andersson RG. Early nasogastric feeding in predicted severe acute pancreatitis: A clinical, randomized study. *Ann Surg* 2006; **244**: 959-65; discussion 965-7 [PMID: 17122621 DOI: 10.1097/01.sla.0000246866.01930.58]

38 **Jiang K**, Chen XZ, Xia Q, Tang WF, Wang L. Early nasogastric enteral nutrition for severe acute pancreatitis: a systematic review. *World J Gastroenterol* 2007; **13**: 5253-5260 [PMID: 17876897]

39 **Petrov MS**, Correia MI, Windsor JA. Nasogastric tube feeding in predicted severe acute pancreatitis. A systematic review of the literature to determine safety and tolerance. *JOP* 2008; **9**: 440-448 [PMID: 18648135]

40 **Chang YS**, Fu HQ, Xiao YM, Liu JC. Nasogastric or nasojejunal feeding in predicted severe acute pancreatitis: a meta-analysis. *Crit Care* 2013; **17**: R118 [PMID: 23786708 DOI: 10.1186/cc12790]

41 **Pupelis G**, Snippe K, Plaudis H, Rudakovska M. Early oral feeding in acute pancreatitis: an alternative approach to tube feeding. Preliminary report. *Acta Chir Belg* 2006; **106**: 181-186 [PMID: 16761474]

42 **Eckerwall GE**, Tingstedt BB, Bergenzaun PE, Andersson RG. Immediate oral feeding in patients with mild acute pancreatitis is safe and may accelerate recovery--a randomized clinical study. *Clin Nutr* 2007; **26**: 758-763 [PMID: 17719703 DOI: 10.1016/j.clnu.2007.04.007]

43 **Jacobson BC**, Vander Vliet MB, Hughes MD, Maurer R, McManus K, Banks PA. A prospective, randomized trial of clear liquids versus low-fat solid diet as the initial meal in mild acute pancreatitis. *Clin Gastroenterol Hepatol* 2007; **5**: 946-51; quiz 886 [PMID: 17613280 DOI: 10.1016/j.cgh.2007.04.012]

44 **Sathiaraj E**, Murthy S, Mansard MJ, Rao GV, Mahukar S, Reddy DN. Clinical trial: oral feeding with a soft diet compared with clear liquid diet as initial meal in mild acute pancreatitis. *Aliment Pharmacol Ther* 2008; **28**: 777-781 [PMID: 19145732]

45 **Foitzik T**, Kruschewski M, Kroesen AJ, Hotz HG, Eibl G, Buhr HJ. Does glutamine reduce bacterial translocation? A study in two animal models with impaired gut barrier. *Int J Colorectal Dis* 1999; **14**: 143-149 [PMID: 10460904]

46 **Hallay J**, Kovács G, Szatmári K, Bakó A, Szentkereszty Z, Lakos G, Sipka S, Sápy P. Early jejunal nutrition and changes in the immunological parameters of patients with acute pancreatitis. *Hepatogastroenterology* 2001; **48**: 1488-1492 [PMID: 11677993]

47 **Huang XX**, Wang XP, Ma JJ, Jing DD, Wang PW, Wu K. [Effects of enteral nutrition supplemented with glutamine and arginine on gut barrier in patients with severe acute pancreatitis: a prospective randomized controlled trial]. *Zhonghua Yi Xue Za Zhi* 2008; **88**: 2407-2409 [PMID: 19087716]

48 **Lasztity N**, Hamvas J, Biró L, Németh E, Marosvölgyi T, Decsi T, Pap A, Antal M. Effect of enterally administered n-3 polyunsaturated fatty acids in acute pancreatitis--a prospective randomized clinical trial. *Clin Nutr* 2005; **24**: 198-205 [PMID: 15784478 DOI: 10.1016/j.clnu.2004.12.008]

49 **Pearce CB**, Sadek SA, Walters AM, Goggin PM, Somers SS, Toh SK, Johns T, Duncan HD. A double-blind, randomised, controlled trial to study the effects of an enteral feed supplemented with glutamine, arginine, and omega-3 fatty acid in predicted acute severe pancreatitis. *JOP* 2006; **7**: 361-371 [PMID: 16832133]

50 **Petrov MS**, Atduev VA, Zagainov VE. Advanced enteral therapy in acute pancreatitis: is there a room for immunonutrition? A meta-analysis. *Int J Surg* 2008; **6**: 119-124 [PMID: 18325863 DOI: 10.1016/j.ijsu.2008.01.003]

51 **Asrani V**, Chang WK, Dong Z, Hardy G, Windsor JA, Petrov MS. Glutamine supplementation in acute pancreatitis: a meta-analysis of randomized controlled trials. *Pancreatology* 2013; **13**: 468-474 [PMID: 24075510 DOI: 10.1016/j.pan.2013.07.282]

52 **Hajdú N**, Belágyi T, Issekutz A, Bartek P, Gartner B, Oláh A. [Intravenous glutamine and early nasojejunal nutrition in severe acute pancreatitis -- a prospective randomized clinical study]. *Magy Seb* 2012; **65**: 44-51 [PMID: 22512878 DOI: 10.1556/MaSeb.65.2012.2.2]

53 **Oláh A**, Romics L. Early enteral nutrition in acute pancreatitis--benefits and limitations. *Langenbecks Arch Surg* 2008; **393**: 261-269 [PMID: 18266002 DOI: 10.1007/s00423-008-0291-9]

54 **Mangiante G**, Colucci G, Canepari P, Bassi C, Nicoli N, Casaril A, Marinello P, Signoretto C, Bengmark S. Lactobacillus plantarum reduces infection of pancreatic necrosis in experimental acute pancreatitis. *Dig Surg* 2001; **18**: 47-50 [PMID: 11244259 DOI: 50096]

55 **Akyol S**, Mas MR, Comert B, Ateskan U, Yasar M, Aydogan H, Deveci S, Akay C, Mas N, Yener N, Kocar IH. The effect of antibiotic and probiotic combination therapy on secondary pancreatic infections and oxidative stress parameters in experimental acute necrotizing pancreatitis. *Pancreas* 2003; **26**: 363-367 [PMID: 12717269]

56 **Muftuoglu MA**, Isikgor S, Tosun S, Saglam A. Effects of probiotics on the severity of experimental acute pancreatitis. *Eur J Clin Nutr* 2006; **60**: 464-468 [PMID: 16340953 DOI: 10.1038/sj.ejcn.1602338]

57 **van Minnen LP**, Timmerman HM, Lutgendorff F, Verheem A, Harmsen W, Konstantinov SR, Smidt H, Visser MR, Rijkers GT, Gooszen HG, Akkermans LM. Modification of intestinal flora with multispecies probiotics reduces bacterial translocation and improves clinical course in a rat model of acute pancreatitis. *Surgery* 2007; **141**: 470-480 [PMID: 17383524 DOI: 10.1016/j.surg.2006.10.007]

58 **Karakan T**, Ergun M, Dogan I, Cindoruk M, Unal S. Comparison of early enteral nutrition in severe acute pancreatitis with prebiotic fiber supplementation versus standard enteral solution: a prospective randomized double-blind study. *World J Gastroenterol* 2007; **13**: 2733-2737 [PMID: 17569144]

59 **Oláh A**, Belágyi T, Issekutz A, Gamal ME, Bengmark S. Randomized clinical trial of specific lactobacillus and fibre supplement to early enteral nutrition in patients with acute pancreatitis. *Br J Surg* 2002; **89**: 1103-1107 [PMID: 12190674]

60 **Oláh A**, Belágyi T, Pótó L, Romics L, Bengmark S. Synbiotic control of inflammation and infection in severe acute pancreatitis: a prospective, randomized, double blind study. *Hepatogastroenterology* 2007; **54**: 590-594 [PMID: 17523328]

61 **Besselink MG**, van Santvoort HC, Buskens E, Boermeester MA, van Goor H, Timmerman HM, Nieuwenhuijs VB, Bollen TL, van Ramshorst B, Witteman BJ, Rosman C, Ploeg RJ, Brink MA, Schaapherder AF, Dejong CH, Wahab PJ, van Laarhoven CJ, van der Harst E, van Eijck CH, Cuesta MA, Akkermans LM, Gooszen HG. Probiotic prophylaxis in predicted severe acute pancreatitis: a randomised, double-blind, placebo-controlled trial. *Lancet* 2008; **371**: 651-659 [PMID: 18279948 DOI: 10.1016/s0140-6736(08)60207-x]

62 **Rayes N**, Seehofer D, Neuhaus P. Prebiotics, probiotics, synbiotics in surgery--are they only trendy, truly effective or even dangerous? *Langenbecks Arch Surg* 2009; **394**: 547-555 [PMID: 19084991 DOI: 10.1007/s00423-008-0445-9]

63 **van Baal MC**, Kohout P, Besselink MG, van Santvoort HC, Benes Z, Zazula R, Rijkers GT, Gooszen HG. Probiotic treatment with Probioflora in patients with predicted severe acute pancreatitis without organ failure. *Pancreatology* 2012; **12**: 458-462 [PMID: 23127536 DOI: 10.1016/j.pan.2012.08.004]

64 **Cui LH**, Wang XH, Peng LH, Yu L, Yang YS. [The effects of early enteral nutrition with addition of probiotics on the prognosis of patients suffering from severe acute pancreatitis]. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue* 2013; **25**: 224-228 [PMID: 23660099 DOI: 10.3760/cma.j.issn.2095-4352.2013.04.011]

65 **Andersson RG**. Probiotics in acute pancreatitis. *Br J Surg* 2008; **95**: 941-942 [PMID: 18618863 DOI: 10.1002/bjs.6292]

66 **Soeters PB**. Probiotics: did we go wrong, and if so, where? *Clin Nutr* 2008; **27**: 173-178 [PMID: 18378362 DOI: 10.1016/j.clnu.2008.02.003]

67 **Mirtallo JM**, Forbes A, McClave SA, Jensen GL, Waitzberg DL, Davies AR. International consensus guidelines for nutrition therapy in pancreatitis. *JPEN J Parenter Enteral Nutr* 2012; **36**: 284-291 [PMID: 22457421 DOI: 10.1177/0148607112440823]

68 **Tenner S**, Baillie J, DeWitt J, Vege SS. American College of Gastroenterology guideline: management of acute pancreatitis. *Am J Gastroenterol* 2013; **108**: 1400-115; 1416 [PMID: 23896955 DOI: 10.1038/ajg.2013.218]

69 **Working Group IAP/APA Acute Pancreatitis Guidelines**. IAP/APA evidence-based guidelines for the management of acute pancreatitis. *Pancreatology* 2013; **13**: e1-15 [PMID: 24054878 DOI: 10.1016/j.pan.2013.07.063]

70 **Sun E**, Tharakan M, Kapoor S, Chakravarty R, Salhab A, Buscaglia JM, Nagula S. Poor compliance with ACG guidelines for nutrition and antibiotics in the management of acute pancreatitis: a North American survey of gastrointestinal specialists and primary care physicians. *JOP* 2013; **14**: 221-227 [PMID: 23669469 DOI: 10.6092/1590-8577/871]

71 **Duggan SN**, Smyth ND, O'Sullivan M, Feehan S, Ridgway PF, Conlon KC. A transatlantic survey of nutrition practice in acute pancreatitis. *J Hum Nutr Diet* 2012; **25**: 388-397 [PMID: 22591247 DOI: 10.1111/j.1365-277X.2012.01256.x]

72 **Andersson B**, Andrén-Sandberg A, Nilsson J, Andersson R. Survey of the management of acute pancreatitis in surgical departments in Sweden. *Scand J Gastroenterol* 2012; **47**: 1064-1070 [PMID: 22631566 DOI: 10.3109/00365521.2012.685752]

73 **Rebours V**, Lévy P, Bretagne JF, Bommelaer G, Hammel P, Ruszniewski P. Do guidelines influence medical practice? Changes in management of acute pancreatitis 7 years after the publication of the French guidelines. *Eur J Gastroenterol Hepatol* 2012; **24**: 143-148 [PMID: 22123707 DOI: 10.1097/MEG.0b013e32834d864f]

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**Table 1 Studies investigating the potential benefits of enteral *vs* parenteral feeding**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ref.** | **Year** | **Country/institution** | **No. of patients** | **Control arm** | **Benefits of** **Enteral *vs* parenterlal feeding** |
|
| Mc Clave *et al*[[2](#_ENREF_2)] | 1997 | United States/University of Louisville, KY | 30 | Parenteral feeding | Cheaper, better glucose control |
| Kalfarentzos *et al*[[4](#_ENREF_4)] | 1997 | Greece/University of Patras | 38 | Parenteral feeding | Lower complication rate, cheaper |
| Windsor *et al*[[5](#_ENREF_5)] | 1998 | United Kingdom/St James’s Univ Hospital London | 34 | Parenteral feeding | Decreased organ failure and complication rates |
| Paraskeva *et al*[[7](#_ENREF_7)] | 2001 | Greece/Pireus General Hospital | 23 | Parenteral feeding | Lower surgical intervention rate |
| Oláh *et al*[[59](#_ENREF_59)] | 2002 | Hungary/Petz A. Teaching Hospital, Gyor | 89 | Parenteral feeding | Less septic complications |
| Abou-Assi *et al*[[9](#_ENREF_9)] | 2002 | United States/Virginia Univ. Hosp., RA  | 53 | Parenteral feeding | Less septic complications, cheaper |
| Gupta *et al*[[10](#_ENREF_10)] | 2003 | United Kingdom/Southampton General Hospital | 17 | Parenteral feeding | Shorter hospital stay, cheaper |
| Louie *et al*[[12](#_ENREF_12)] | 2005 | Canada/University of Alberta | 28 | Parenteral feeding | Lower complication rate, better glucose control |
| Eckerwall *et al*[[37](#_ENREF_37)] | 2006 | Sweden/Lund University Hospital  | 69 | Parenteral feeding | Lower complication, MOF and mortality rates |
| Petrov *et al*[[13](#_ENREF_13)] | 2006 | Russia/Nizhny Novgorod Hosp.  | 22 | Parenteral feeding | No significant difference |

MOF: multi-organ failure.

**Table 2 Studies investigating the potential benefits of early *vs* late enteral feeding**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ref.** | **Year** | **Country/Institution** | **No. of patients** | **Control arm** | **Benefits of early *vs* late enteral feeding** |
|
| Sun *et al*[[29](#_ENREF_29)] | 2013 | China/Nainjing Medical University  | 60 | Late enteral feeding | Lower infective complication, MOF and SIRS rates |
| [Wereszczynska-Siemiatkowska](http://www.ncbi.nlm.nih.gov/pubmed?term=Wereszczynska-Siemiatkowska%20U%5BAuthor%5D&cauthor=true&cauthor_uid=23508012)*et al*[[30](#_ENREF_30)] | 2013 | Poland/Medical University Bialystok | 197 | Late enteral feeding | Lower complication and mortality rates |
| Sun *et al*[[31](#_ENREF_31)]  | 2013 | China/Nainjing Medical University | 60 | Late enteral feeding | Lower intra-abdominal hypertension rate  |

MOF: multi-organ failure; SIRS: systemic inflammatory response syndrome.

**Table 3 Anti-infective and immunomodulatory properties of immunonutrients**

|  |
| --- |
| **Anti-infective and immunomodulatory properties of immunonutrients** |
| Reduced bacterial overgrowthMaintenance of natural balance of intestinal flora Reduced intestinal permeabilityReduced serum endotoxin levelsAntagonist effect against pathogenic bacteriaPrevent pathogenic bacterial adherence to intestinal mucosaBacterocidal and bacterostatic effect (lactic acid production)Increased proportions of NK cells, T-lmphocytes, Ig-A producing plasma cellsIncreased phagocytosis |