Endoscopist’s approach to nutrition in the patient with pancreatitis

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Abstract
Nutritional therapy has an important role in the management of patient with severe acute pancreatitis. This article reviews the endoscopist’s approach to manage nutrition in such cases. Enteral feeding has been clearly validated as the preferred route of feeding, and should be started early on admission. Parenteral nutrition should be reserved for patients with contraindications to enteral feeding such as small bowel obstruction. Moreover, nasogastric feeding is safe and as effective as nasojejunual feeding. If a prolonged course of enteral feeding (> 30 d) is required, endoscopic placement of feeding gastrostomy or jejunostomy tubes should be considered.

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Key words: Acute pancreatitis; Nutrition; Enteral nutrition; Total parenteral nutrition; Nasoenteric tube feedings; Percutaneous endoscopic gastrostomy; Percutaneous endoscopic gastro-jejunostomy; Direct percutaneous endoscopic jejunostomy

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INTRODUCTION
One of the earliest references to the pancreas as a distinct organ occurs in the Talmud in which the organ is referred to as the finger of the liver. Acute pancreatitis (AP) is an acute inflammatory disorder involving the pancreas, peripancreatic tissue, as well as adjacent organs. It has been estimated that in the United States there are more than 210,000 admissions yearly for AP with it being the third most common inpatient gastrointestinal diagnosis. In the majority of patient it is a self-limiting disease and will usually resolve with five days of supportive management. Unfortunately, AP is severe in 10%-20% of cases and results in a systemic inflammatory response syndrome which predisposes the patient to multiple organ dysfunction and/or pancreatic necrosis. The overall mortality is reported as 10%-15%, ranging from < 5% to those presenting with mild AP to 20% with severe AP.

Nutritional therapy has an important role in the management of AP patients. In this review article, we will discuss the endoscopist’s approach to manage nutrition in patients with AP. As mentioned before, AP resolves in majority of cases by supportive measures. Hence, it is important to know: When nutritional therapy is...
WHEN NUTRITIONAL THERAPY IS REQUIRED IN AP?

The majority of patients with mild AP respond to supportive care measures that form the hallmark of treatment in AP: bowel rest, intravenous hydration with crystalloid and analgesia. Oral intake is usually restored within 3-7 d of hospitalization once the patient is pain free in the absence of parenteral analgesia[6]. Supportive care with aggressive intravenous fluid replacement is of critical importance to counteract hypovolemia caused by third space losses, vomiting, diaphoresis, and greater vascular permeability caused by inflammatory mediators. There is abundant literature that has supported early aggressive fluid resuscitation in AP to improve the delivery of oxygen which in turn prevents or minimizes pancreatic necrosis and improves survival[4-6].

The nutritional support is needed in severe AP. Severe pancreatitis, defined by the Atlanta Symposium, is organ failure of at least one organ system (systolic blood pressure < 90 mm Hg, PaO2 < 60 mmHg, creatinine > 2.0 mg/dL after rehydration, and gastrointestinal bleeding > 500 mL/24 h) and the presence of local complications such as necrosis, pseudocyst, and abscess[7]. When it is clear that the patient will not be able to tolerate oral feeding, nutritional support should be initiated.

WHY NUTRITIONAL THERAPY IS IMPORTANT IN SEVERE AP?

Severe AP is a hypermetabolic state with negative energy balance due to the release of hydrolytic enzymes, toxins, and cytokines[8,9]. Protein catabolism can increase by 80%, with negative nitrogen balance up to 20-40 g/day[10-11]. The mortality increases tenfold in patients unable to achieve a positive nitrogen balance[12]. Glucose intolerance develops in 40%-90% of cases due to insulin resistance and islet cell damage[13]. Hypocalcemia is noted in 40%-60% of patients, and is related to the severity of the disease. Micronutrient deficiencies can complicate the picture, especially in alcoholic pancreatitis[14-15]. Consequently, nutritional therapy has emerged from adjunctive therapy to proactive primary therapy in severe AP[16].

HOW NUTRITIONAL THERAPY SHOULD BE GIVEN IN SEVERE AP?

Approaches adopted for nutritional support in severe AP include; total parenteral nutrition, nasojejunal feeding, nasogastric feeding, or direct enteral feeding.

Total parenteral vs enteral nutrition

It is important to rest the pancreas in order to avoid further inflammation. All common routes of enteral nutrition stimulate the pancreas to some extent. Studies have shown that pancreatic stimulation can only be avoided by parenteral route only[17-18]. Parenteral nutrition used to be the standard route of nutrition support in severe AP[19]. However, several studies have shown that total parenteral nutrition (TPN) impair humoral and cell mediated immunity, increases the vigour of the proinflammatory response, increases bacterial translocation, and increases infection rate in various critically ill patients[20-23]. Enteral nutrition (EN) prevents bacterial translocation, is less expensive, and is associated with fewer complications than parenteral nutrition. The concept of EN in AP originated from a study by Voitk et al[24] in 1970s. The beneficial effects were noted in six patients with complicated AP in resolution of sepsis and achievement of positive nitrogen balance by jejunal feeding of an elemental diet. Since then, multiple controlled studies have reported the beneficial effects of EN over TPN in patient with severe AP.

McClave et al[25] performed one of the earliest prospective studies which compared the safety, efficacy, cost, and impact on patient outcome of early EN vs TPN in AP. Patients who were admitted with AP were randomized to receive EN via endoscopically placed nasojejunal feeding tube vs TPN within 48 h of admission. Thirty patients were studied over 32 admissions, 16 were given TPN and 16 EN. The mean cost of TPN per patient was over four times greater than that for EN. Compared with TPN, EN may promote more rapid resolution of the toxicity and stress response to pancreatitis.

In a smaller prospective study by Windsor et al[26], 34 patients with severe pancreatitis were randomized to receive either TPN or nasojejunal tube feeds. Despite unchanged pancreatic injury on computed tomography, clinical benefits were noted with enteral feeding in the form of faster reduction in C reactive protein (CRP) and APACHE II scores. Kalfarentzos et al[27] randomized 38 patients with severe pancreatitis to receive either TPN or nasoenteric tube feeding. The authors noted less morbidity, septic complications, and lower hospital costs with EN. In a study by Hernández-Aranda et al[28], 22 patient who had undergone emergent surgery for severe pancreatitis were randomized to TPN or surgically placed jejunostomy tube feedings. EN was associated with fewer septic complications and lower costs.

Abou-Assi et al[29] studied 156 patients with AP in a prospective randomized comparative trial between tube feeding and bowel rest with TPN. 75% of the patients improved with bowel rest, of the 53 remaining 26 were randomized to enteral nasojejunal tube feeds and the 27 to TPN. Duration of feeding was shorter with EN; metabolic and septic complications were higher in TPN-fed patients as were hospital costs. In another larger
study, Petrov et al\textsuperscript{[30]} randomized 70 patients with severe pancreatitis to receive either EN or TPN within 72 h of symptoms onset. Decreased incidence of infected pancreatic complications, multiple organ failure, and overall mortality was noted with EN.

A meta-analysis of randomized controlled trials comparing EN to TPN in AP was performed by Mark et al\textsuperscript{[31]}. They concluded that EN should be the preferred route of nutritional support in patients with AP because it was associated with a significantly lower incidence of infection and a reduced length of hospital stay\textsuperscript{[31]} (Table 1).

### Methods of EN

The methods of delivering EN have evolved over the past millennium. There are reports that go as far back as the 15th century with the use of feeding tubes. In the 18th century, John Hunter, a pioneering British surgeon, used eel skin tubes for the purpose of EN\textsuperscript{[32]}. These EN devices are usually delivered either \textit{via} nasoenteric or direct enteral routes.

### Nasoenteric feeding tubes

These are made of silicone or polyurethane, and they may be placed unassisted at the bedside or with endoscopic or fluoroscopic guidance. They range from 3.5F to 16F in diameter and 15 to 170 cm in length. Nasogastric feedings \textit{vs} nasojejunal feedings has long been debated among experts as to which are the ideal approaches. A major concern relates to stimulation of pancreatic secretion when feeding is introduced into the stomach or duodenum. There is evidence that intraduodenal feedings increase pancreatic enzymes synthesis and secretion, which may lead to an exacerbation of abdominal pain associated with a greater amylase level\textsuperscript{[33,34]}. Nasojejunal placement overcomes the problem of gastroparesis, and any mechanical duodenal or gastric encroachment from pancreatic swelling or pseudocyst can be bypassed. Small bowel feeding increases energy delivery compared with gastric feeding. However nasojejunal feeding tube placement requires endoscopic placement, at times under fluoroscopic guidance and may require a suture or mechanical clip to anchor itself deep into the small intestine.

### Nasogastric vs nasojejunal feeding

Nasogastric feeding can be advantageous as they are easier to place without a need for endoscopic assistance, and can even be placed by non-physician personnel. Multiple studies have been performed comparing nasogastric and nasojejunal feeding tubes.

Eatock \textit{et al}\textsuperscript{[35]} compared nasogastric with nasojejunal feeding that was introduced at 72 h from onset of pain in patients with AP. The study questioned whether or not early nasojejunal feedings was as effective and safe as nasojejunal feeding in patients with severe AP. 49 consecutive patients with objectively graded severe AP were randomized to receive either nasogastric (27 patients) or nasojejunal (23 patients) feeding. The results demonstrated that nasogastric feeding was safe, with no differences in pain score, analgesic requirements, serum CRP or clinical outcome\textsuperscript{[35]}.

Kumar \textit{et al}\textsuperscript{[36]} compared early nasojejunal feeding to nasogastric feeding. A total of 31 patients with severe AP were randomized to receive feeding by either nasogastric (15 patients) or nasojejunal (16 patients) routes. The authors reported no difference in outcome measures (discharge, surgery, death) and satisfactory toleration of EN by both nasojejunal and nasogastric routes\textsuperscript{[36]}.

In a meta-analysis by Jiang \textit{et al}\textsuperscript{[37]} (articles 2-46), three randomized controlled trials including 131 patients with severe pancreatitis were reviewed. The authors concluded that early nasojejunal enteral feed was as effective and safe as early nasojejunal enteral feed or TPN in acute severe pancreatitis, without increase in mortality. In another meta-analysis by Petrov \textit{et al}\textsuperscript{[38]}, four studies on nasogastric tube feeding involving 92 patients with severe AP were analyzed. The enteral feeding was initiated within 24–72 h of admissions. The nasogastric enteral feeding was found to be safe and well tolerated in most of the patients with severe AP.

### Direct enteral feeding

Sinusitis, tube malposition, aspiration, nasal trauma, and significant patient intolerance are amongst the difficulties with nasoenteric tubes\textsuperscript{[39]}. Nasoenteric feeding is preferred for patients expected to resume oral feeding within 30 d (reference asge-enteral tubes articles)\textsuperscript{[40]}. If a prolonged course of enteral feeding is required, endoscopic placement of feeding gastrostomy or jejunostomy tubes is indicated.

Percutaneous endoscopic gastrostomy (PEG) tubes is indicated for patients that cannot consume adequate nutrition but have a working gastrointestinal tract. The
most common indications for PEG placements are dysphagia due to neurological causes, oropharyngeal or esophageal cancer, and severe facial trauma[44]. In patients with sequelae of severe pancreatitis, such as pancreatic pseudocyst, necrosis, abscess that can be managed as an outpatient the endoscopic approach is ideal.

Percutaneous endoscopic gastro-jejunoscopy (PEG-J) is an option for patients who cannot tolerate gastric nutritional infusions, are at considerable risk for aspiration, and/or require gastric decompression and jejunal feeds. The PEG-J procedure as initially described involved passing a jejunal tube through a PEG, grasping the J-tube with an endoscopic forceps or snare, and advancing the scope and J-tube into the duodenum[42,43] (Figure 1).

Direct percutaneous endoscopic jejunostomy (DPEJ) is a modification of PEG placement. The indications are the same as those of PEG-J, but also include post-surgical patients with anatomy precluding PEG[44,45]. A colonoscope is advanced through the mouth, into the jejunum and transillumination is performed. The procedure is complete as described for pull-type PEG placement. DPEJ is more difficult and time consuming to perform than PEG, and fluoroscopic guidance may be beneficial. Enteral formula infusion may begin immediately and adjusted to goal[46].

**Timings for initiation of EN**

Enteral feeding should be initiated shortly after admission with severe AP. Hegazi et al[47] studied early jejunal feeding and clinical outcomes in patients with severe AP. 31 patients were enrolled and underwent bedside placement of a nasojejunal feeding tube using transnasal endoscopy with jejunal guidewire deployment followed by introduction of a semi-elemental formula. This study demonstrated that early initiation of deep jejunal feeding in the intensive care unit was associated with reduced mortality in a cohort of patients with severe AP. Multiple randomized controlled trials of enteral vs parenteral nutrition in AP showed that initiation of EN within 48 h of admission was associated with better clinical outcomes[47,48,49]. However, a delay in initiation of enteral feeds may lead to prolonged ileums and reduced tolerance[50]. Low volume enteral feed via continuous low rate infusion can still be given in patients with significant ileums[19].

**Initiation of oral feeding after severe AP**

There is a paucity of data on the optimal timings or type of oral diet. Oral diet is usually initiated when abdominal pain or tenderness has subsided, there are no complications, and serum amylase and/or lipase levels are near normal[51]. A clear liquid diet is given first, followed by gradual advancement as tolerated to a diet rich in carbohydrates and protein but low in fat. The abdominal pain may recur, usually on day 2 or 3 of oral reseeding[51]. The risk factors are longer duration of initial pain (> 6 d), higher severity index on computed tomography scan, and higher serum lipase (> 3 times normal) the day before oral reseeding.

In conclusion, nutritional support is required in severe AP. It has emerged as a proactive primary therapy in such patients. Enteral feedings have been clearly validated as the preferred route for feeding patients with acute severe pancreatitis who require nutritional support. Parenteral nutrition is reserved only for patients who are intolerant of enteral feedings or have a contraindication to enteral feedings such as small bowel obstruction. EN should be initiated early (preferably within 48 h) of admission. Nasogastric feeding is safe and as effective as nasojejunal feeding. If a prolonged course of enteral feeding (usually over 30 d) is required, endoscopic placement of feeding gastrostomy or jejunostomy tubes should be considered.

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