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Gastric versus Postpyloric Feeding

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In this article, the pros and cons of delivering nutritional support to critically ill patients at a site distal to the stomach are discussed. Most of the studies that have evaluated this using randomized controlled trials have been in critically ill patients; hence the focus will be on this patient population. Generalization to other populations of patients should be done with caution. Regularly updated, peer-reviewed data with evidence-based recommendations for the nutrition support in critically ill patients are available at the Web site www.criticalcarenutrition.com [1].

Critically ill patients are at greater risk of complications and death than others, and consume a relatively large proportion of the cost of hospital budgets. Nutrition support has become accepted as an important cornerstone in the supportive management of patients cared for in intensive care units (ICU) around the world. Malnutrition and hypercatabolism have wide ranging effects on the human viscera, and are felt to play a role in the impairment of the immune system and organ dysfunction of critically ill patients. There is evidence that parenteral nutrition (PN) may have a negative impact on clinical outcomes of critically ill patients [2]. On the contrary, there is evidence that early enteral nutrition (EN) does improve clinical outcomes in this population [3].

Most enteral feeding in the ICU is delivered into the stomach, which is commonly associated with the problem of high gastric residual volumes (GRV). This can result in inadequate delivery of protein and energy, and is associated with increased length of stay and increased mortality [4,5], as well as a higher incidence of nosocomial pneumonia [5]. Therefore, giving the appropriate nutrients distal to the stomach may facilitate early adequate enteral feeding and improve outcomes of critically ill patients. Postpyloric enteral feeding at first appears to be the solution to the problem of delivering adequate nutritional support to the critically ill patient. This is discussed

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under the four themes that the author believes complicate this seemingly simple solution. These are: (1) pneumonia, (2) gastric dysfunction, (3) nutritional adequacy, and (4) the placement of postpyloric feeding tubes.

Pneumonia

Pneumonia is the most prominent complication associated with the administration of enteral feeding. The pathogenesis of nosocomial pneumonia, and specifically ventilator associated pneumonia (VAP), involves a complex interaction of pathophysiologies that are affected by different patient and system risk factors. A thorough discussion of this area is outside the scope of this article, and readers are referred to a publication of practice guidelines for the prevention of VAP [6] for further information. It is clear that the administration of enteral nutrition has been associated with the development of VAP [5]. The mechanism by which this may occur is presumably through gastroesophageal reflux in the setting of colonization of the gastric contents with pathogenic organisms. Even for patients fed distal to the pylorus, it has been demonstrated that there can be reflux of enteric feeds back into the stomach and into the oropharynx [7]. Factors that predispose to reflux of contaminated gastric secretions into the oropharynx and subsequent aspiration include but are not limited to gastric stasis, laxity of the lower esophageal sphincter, and alkalization of gastric contents.

It is noteworthy that a significant mechanism that may predispose to VAP is colonization of the oral pharyngeal secretions with pathogenic organisms in the absence of significant gastroesophageal reflux. Microaspiration of these contaminated oropharyngeal secretions may be a significant determinant of VAP [8]. Oral hygiene using chlorhexidine wash is associated with a reduction in the incidence of VAP [9] in some studies, but is not supported by a recent meta-analysis [10].

The diagnosis of VAP can be a challenging clinical problem. Suspicion of VAP is based on clinical criteria and confirmation relies on sampling of sputum in a noninvasive or invasive manner. With all of these techniques there is uncertainty and no specific gold standard. Although this may be the most important adverse outcome related to enteral nutrition, it is one of the more difficult ones to define. The studies that have been done in the area of enteral nutrition have used variable and nonstandard definitions of VAP, which lends a degree of uncertainty to the data that are generated, and thus weakens inferences that may be drawn.

Some studies have specifically examined the relationship between regurgitation and pneumonia in the ICU. Two randomized trials using radioisotopes that evaluated the route of feeding on rates of regurgitation and aspiration have been reported. Heyland and colleagues [7] randomized 33 critically ill patients to receive small bowel versus gastric feeds. ^{99}Tc-sulfur colloid was added to the EN for 6 hours of each of the first 3 days of the study, and the oropharnyx and trachea were sampled hourly during the

study period. As defined by an increase in radioactivity greater than 100 cpm/gram, patients fed into the stomach had more episodes of gastroesophageal regurgitation (39.8% versus 24.9% of samples, $P = .04$) and tended toward more pulmonary aspiration (7.5% versus 3.9% of samples, $P = .22$) compared with patients fed beyond the pylorus. Patients who had gastroesophageal regurgitation were much more likely to aspirate than patients who did not have regurgitation (OR 3.2, 95% CI, 1.36, 7.77). Finally, in a post-hoc analysis, the investigators demonstrated that the further down the small bowel the tip of the tube is located, the greater the reduction in regurgitation and pulmonary aspiration.

In another randomized trial of small bowel versus gastric feeding in 54 critically ill patients, Esparza and colleagues [11] added ^{99}Tc-sulfur colloid to continuously infusing feeds twice a week. On study days, patients and their pulmonary secretions were scanned with a gamma camera. In this study, aspiration was defined by detection of ^{99}Tc-sulfur colloid tracer in the lungs or greater than 1000 counts/mL per minute in pulmonary secretions. The investigators documented a low rate of aspiration and no statistical difference between the two groups (gastric 2/27 [7%] versus small bowel 2/24 [13%]).

Gastric dysfunction

Delayed gastric emptying or gastric dysfunction is the primary limiting factor around use of prepyloric feeding. This can contribute to inadequate nutrition support being delivered, and is a risk factor for gastric esophageal reflux and aspiration. There is no standardized diagnostic test to define this condition, however. On one extreme, the condition can be identified if the patient vomits a volume that is equal to or exceeds the volume of feeds having been instilled. On the other end of the spectrum is the patient who is not fed because the physician is concerned that the "gut may not work." The most commonly used bedside technique to monitor gastric emptying is the measurement of gastric residual volumes [12]. This is used as a surrogate marker of the motility of the stomach. There appears to be risk associated with aggressive prepyloric feeding if attention is not given to this issue. Although not randomized trials, three recent papers have identified the risk associated with early enteral feeding in mechanically ventilated patients [5,13,14]. This needs to be taken into consideration as we try to optimize the benefits and minimize the risks of enteral nutrition delivery.

Although measurement of gastric residual volumes is used commonly in ICUs, there is not a common technique that is agreed upon, and it has poor correlation to the risk of aspiration in critically ill patients [15]. Use of this technique has been discussed in the literature extensively, and there have been recent efforts to better standardize and quantify the measurement methodology [16]. A wide range of different gastric residual volume thresholds have been used to alert clinicians to a possible safety concern, but

a standard threshold has not been established. It is reasonable to consider a threshold for gastric residual volumes in mechanically ventilated patients to be somewhere between 250 and 500 mL.

There are several other strategies that can be used to minimize the risks associated with prepyloric enteral feeding. The use of continuous enteral nutrition delivery rather than bolus feeding can reduce the residual volume that is in the stomach, and perhaps limit the amount of regurgitation [17]. Another strategy for which there are limited evaluative data is the use of intermittent feeding [8], which involves continuous infusion of feeds over 16 hours of the day, and allowing the patient to fast for 8 hours. This allows the stomach to empty and acidification of the gastric contents to occur, thus reducing bacterial colonization.

In critically ill patients who experience feed intolerance (high gastric residuals, emesis), a motility agent may be used to improve gastric emptying. A recent systematic review of the literature analyzed randomized trials (RCTs) of cisapride, metoclopramide, and erythromycin [18], and since then two other RCTs [19,20] have studied this question. These data demonstrate that this class of drugs seem to have a physiologic benefit on gastrointestinal (GI) motility, and may improve tolerance to EN in critically ill patients. There is no demonstrated benefit on clinically important outcomes, but given the low probability of harm, favorable feasibility, and cost considerations, it is reasonable to consider motility agents as a strategy to optimize nutritional intake. Cisapride is no longer available, and given concerns of emerging bacterial resistance with the use of erythromycin, metoclopramide is the preferred agent.

A novel strategy to overcome the delayed gastric emptying associated with opioid use is the use of intragastric naloxone. Enteral administration of naloxone was associated with reduced gastric residual volumes and pneumonia [21]. The approach to the management of patients receiving opiates requires further study.

There is only one RCT that has compared the use of a feeding protocol with higher gastric residual volume threshold (250 mL) and the routine use of metoclopramide with a feeding protocol that used a lower gastric residual volume threshold (150 mL) [22]. There was a trend toward less time taken to reach target goal rate of feeding in the group that received the protocol with the higher residual volume threshold and prokinetics, and no harm was noted with the higher gastric residual volume threshold. There are insufficient data to make a recommendation about this issue, but if a feeding protocol is used, this study supports the use of a higher gastric residual volume threshold and metoclopramide.

Critically ill patients receiving EN should have the head of the bed elevated to 45°. Where this is not possible, attempts to raise the head of the bed as much as possible should be considered. Two RCTs have been done addressing the question of whether semirecumbency in critically ill patients receiving EN reduces the risk of pneumonia. One study demonstrated

a significant reduction in pneumonia with head of the bed elevation to 45° [23], whereas the other study failed to show any significant difference [24]. Patients in the latter study failed to achieve the target elevation of the head of the bed, however. Other observational data support the association between pneumonia and the supine position [25].

Nutritional adequacy

The topic of nutritional adequacy implies the appropriate timing of the initiation of enteral feeding as well as delivery of the correct nutrients at the appropriate dose to optimize patient outcome. There is compelling evidence that the provision of early enteral nutrition as defined by initiation of feeds within 24 to 48 hours of ICU admission is associated with improved patient outcome [1]. There is concern in many centers that the pursuit of insertion of small bowel feeding tubes and their confirmation of placement may delay the initiation of enteral feeding beyond this optimal time. The placement of prepyloric feeding tubes is simple enough that it does not pose a barrier to achieving this in most patients.

Once initiated, perhaps the next goal that clinicians target is the delivery of adequate macronutrients. This is when the presence of delayed gastric emptying can limit the achievement of therapeutic goals. The data available from randomized controlled trials suggest that the presence of small bowel feeding tubes overcomes the limitation of prepyloric feeding in achieving these goals. Several observational studies have now demonstrated the association between mortality in the ICU and the delivery of inadequate nutritional support, defined as delivery of less than 33% of the prescribed calories [26,27].

Intentional hypocaloric feeding is now becoming a topic for discussion. Benefits of this strategy may be realized by targeting 60% of the usual predicted energy requirements. This may reduce the carbohydrate load that is delivered and the subsequent hyperglycemia that may be witnessed as a result. The use of the prepyloric route of feeding acts as a natural brake on the amount of nutrition delivered, and may be beneficial in some circumstances. This topic is beyond the scope of this article and requires further study.

A new area to be considered is the use of micronutrients to improve patient outcome. Recent work has highlighted the potential benefits of micronutrients such as selenium, as well as other antioxidants [28]. The use of specific nutrients such as glutamine may in the future provide therapeutic benefit [29]. If delivery of these nutrients into the gut is important, the use of small bowel feeding tubes will allow more reliable administration.

Placement of small bowel feeding tubes

Insertion of gastric tubes is a simple bedside procedure, whereas accessing the small bowel provides some specific challenges. Small bowel feeding tubes can be inserted blindly at the bedside, fluoroscopically, endoscopically, or

surgically in the operating theater. These techniques have been aided by the use of prokinetic agents [18], as well as other external devices to assist in placement [30] or confirmation of placement [31] of the tubes.

Surgical placement of enteral feeding tubes is unwarranted in the majority of critically ill patients. If the patient requires a coeliotomy as part of care, an orally or nasally placed tube may be directly manipulated into the bowel, or a jejunostomy surgically created. The author has generally used tubes that are manipulated through the upper aerodigestive tract to avoid the potential problems associated with surgically created stomas [32].

Placement of small bowel feeding tubes in critically ill patients and attempting to start enteral nutrition in the first 24 hours of their stay can be challenging and even frustrating. Bedside techniques are not always successful. All other techniques require special skills and equipment, and are associated with potential complications. Moving a patient to a location for fluoroscopy can cause problems with line displacement, an increased need for sedation, and other complications [33]. Transport out of the ICU is associated with an increased risk of VAP [34]. During the early phase of critical illness, often other more important clinical problems take precedence, such as hemodynamic instability, difficulty with oxygenation or ventilation, coagulopathy, and so on. The additional skills and equipment necessary to obtain small bowel access add to the cost of the patient's care. Even if the tube is successfully placed beyond the pylorus, it may not remain in that location for the duration of the patient's care [35].

To date, there are no trials that define the best way to access the small bowel, and often the method used is determined by the equipment and personnel that are available locally. In the author's center, we have most commonly used a technique of bedside placement as described by Zaloga [36]. We also routinely administer erythromycin 250 mg [18] intravenously before the procedure, and insufflate the stomach with air during insertion [37]. When this is unsuccessful, we have used bedside endoscopy to insert the feeding tube into the small bowel. On rare occasions when this has been unsuccessful, the patient was transported to the diagnostic imaging department for placement of enteral feeding tubes using fluoroscopic guidance.

Maintenance of feeding tubes once they are in position can be challenging. Problems of misplacement and occlusion, particularly with postpyloric tubes, have been well-documented. A regimented approach to the management of the tube itself can reduce the tube-related issues that may develop [38]. A concomitant gastric decompression tube may be an important consideration to optimize the potential benefits of the postpyloric feeding to ensure removal of residual gastric fluid and reduce regurgitation [39].

Postpyloric feeding

Several published randomized trials and meta-analyses have evaluated the influence of postpyloric feeding compared with gastric feeding on

clinically important outcomes in critically ill patients. There are three meta-analyses that have been published using similar groupings of data to come up with slightly varying conclusions [40–42]. The aggregated data the author reports are taken from the meta-analysis done and posted through the Canadian Clinical Practice Guidelines for Nutritional Support in the Critically Ill, which was last updated January 8, 2007 [1].

There have been 11 randomized controlled trials [11,43–52] that have evaluated clinically important outcomes in critically ill patients being fed into the small bowel versus the stomach. It is worth noting that there is considerable heterogeneity between these studies with respect to design, definition of outcomes, methods for placing enteral feeding tubes, and management of the feeding regimen. One study that has caused considerable discussion is that by Taylor and colleagues [51]. This trial randomized patients to small bowel feeding versus gastric feeding, but the patients in the small bowel access group had a large number of protocol violations. As a result of these protocol violations, only 34% of the patients in the small bowel feeding group actually had small bowel access achieved. To analyze this on an intention-to-treat basis, it is necessary to keep these patients in the small bowel access group. Sensitivity analysis was performed by removing the data from the Taylor study for analysis and comparison. Aggregation of data from 9 studies reporting mortality showed no significant differences between the groups (RR 0.93, 0.72–1.20, $P = .6$). When the Taylor and colleagues study was excluded, the relative risks did not change. The meta-analysis of 9 studies reporting infections showed that small bowel feeding was associated with a significant reduction in infections (pneumonia) compared with gastric feeding (RR 0.77, 0.60–1.00, $P = .05$). The study by Taylor and colleagues contributes greatly to the results of this meta-analysis. With the data from the Taylor study removed, the statistical significance of reduction in infectious outcomes of small bowel feeding disappears (RR 0.83, $P = .3$). For the studies reporting on length of stay and ventilator days, no significant difference between the groups was identified. It is not possible to do meta-analysis of the data reporting the achievement of nutritional targets, but it appears that small bowel feeding was associated with an improvement in calorie and protein intake, and with less time taken to reach these targets.

One study has been performed comparing postpyloric feeding to gastric feeding in a group of hospitalized patients [35]. No significant difference in clinical outcomes was demonstrated between the groups.

In the setting of acute pancreatitis, two studies have evaluated the role of gastric enteral feeding compared with small bowel enteral feeding. One study compared small bowel enteral feeding to volitional oral intake [53]. This small study did not show a significant difference in clinically important outcomes, although there was a trend toward the orally fed group having a more frequent relapse of their abdominal pain. The other study, which evaluated patients who had severe acute pancreatitis, randomized patients

to feeding by a nasogastric or nasojejunal feeding tube [54]. This study did not demonstrate any significant difference in clinically important outcomes, but is small and not powered to detect small differences.

Summary

EN has become the standard of care for hospitalized patients, and particularly for those who are critically ill. It is important that the delivery of this nutrition be managed to optimize outcome. There is biologic rationale why postpyloric feeding may be advantageous in reducing the risks associated with enteral nutrition. The meta-analysis of the available studies suggests a small but clinically important reduction in pneumonia rates associated with feeding in the postpyloric location. The converse is that gastric feeding, in some patients, may be associated with inadequate delivery of nutrition, increased regurgitation, pulmonary aspiration and pneumonia, particularly if patients are held in the supine position.

The enthusiasm for small bowel feeding must be tempered by the inherent difficulties in obtaining and maintaining small bowel access. In units where dedicated personnel are readily available and able to place tubes into the small bowel, postpyloric feeding may be routine. In other units, the lack of readily available skilled individuals or the necessary equipment to complete the task may limit the application of this technique.

Based on the available evidence, postpyloric feeding should be considered for critically ill patients. Given the small studies that have been done to date, with significant heterogeneity in study design, it is not possible to make strong inferences; however, it is likely that within the heterogeneous population of critically ill patients there are groups who will benefit from postpyloric feeding rather than gastric feeding. The clinician is left with making this decision on a case-by-case basis.

To optimize the benefits of enteral nutrition, the clinician should have in place processes of care that ensure implementation of evidence-based clinical practice guidelines. Strategies to optimize the benefits and minimize the risks of enteral nutrition should include the initiation of early enteral nutrition in patients with an intact GI tract, the use of feeding protocols, the appropriate use of motility agents, and patients managed in the semirecumbent position. A regimented approach to the use of postpyloric feeding will also help achieve these results. In ICUs where small bowel access is readily achieved, this should be done routinely. In other units, it should be used for patients who have risk factors for intolerance to gastric feeding, such as those on inotropes, paralytic agents, and high-dose opioids. For patients who show evidence of delayed gastric emptying and are not achieving their nutritional goals, there should be an early warning system in place to trigger the clinician to pursue strategies to gain small bowel access for enteral nutrition in a timely manner. The use of PN should be a last resort to be considered when these strategies have been exhausted.

The uncertainty inherent in the data presented has implications for future research. Future trials of small bowel versus intragastric feeding should be adequately powered, and should use standardized strategies to optimize the benefits of enteral nutrition in both groups. Measurement of clinically important outcomes should be well-defined, and steps should be taken to ensure that enteral access is maintained throughout the course of the studies. Such a trial is currently underway in Australia, and hopefully will yield further information that will help clinicians with their bedside decision-making.

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