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What is This?
Appropriate Use of Parenteral Nutrition Through the Perioperative Period

Stephen A. McClave, MD1; Robert Martindale, MD, PhD2; Beth Taylor, MS, RD, CNSC3; and Leah Gramlich, MD4

Abstract
Recent advances in nutrition therapy of the patient undergoing elective surgery have focused on greater utilization of the gut, feeding closer to the time of surgery, avoiding extensive bowel preparations or use of nasogastric tubes and drains, and measures to promote and maintain intestinal motility. Failure to have protocols in place for delivery of enteral nutrition (EN) through the perioperative period should not lead to inappropriate use of parenteral nutrition (PN) as a default therapy, because in many circumstances, standard therapy with no specialized nutrition support may be associated with better outcome. In cases where EN is not feasible and the patient shows evidence of malnutrition, surgery should be delayed 7–10 days to provide perioperative PN. For patients requiring urgent surgery where EN is not feasible, the initiation of PN postoperatively should be delayed 5–7 days. Whether alternative sources for lipid emulsion and availability of parenteral immune-modulating agents in the future can improve the risk/benefit ratio of PN and expand its use through the perioperative period awaits further study. (JPEN J Parenter Enteral Nutr. 2013;37:73S-82S)

Keywords
parenteral nutrition; enteral nutrition; preoperative; postoperative; perioperative

Introduction
Deriving guidelines for the use of parenteral nutrition (PN) through elective surgery is problematic. Most elective surgery patients do not need specialized nutrition therapy. The ones who do require nutrition therapy are usually the ones who develop complications, become critically ill, and require placement in the surgical intensive care unit (ICU). The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) has no specific published guidelines for nutrition therapy through elective surgery, aside from small sections in a National Institutes of Health (NIH) consensus guidelines1 and joint guidelines for critical care patients with the Society of Critical Care Medicine (SCCM).2 The basic principles that guide the use of PN through elective surgery are based on older studies. Recent advances in clinical practice relate to increasing use of enteral nutrition (EN) through surgery. Results from a recent EPaNIC study from Europe reinforce the potential adverse impact on patient outcome from early use of PN in elective surgery patients.3

Use of PN through elective surgery is more likely to occur through default management, meaning that surgeons assume that PN should automatically be the next or default therapy if EN is not feasible. They may not realize that a third and sometimes more preferable choice of therapy exists, that of standard (STD) therapy, in which no specialized nutrition therapy is provided and patients are on their own to return to an oral diet. Any efforts to provide EN through elective surgery are hampered by a lack of nurse-driven protocols, traditional preoperative management requiring long periods of nil per os (NPO), and surgical dogma regarding feeding the patient with a recent gut anastomosis or postoperative ileus. Poor attempts at initiation, inappropriate delays, and recurrent interruptions of EN delivery result in inadequate feeding, and switching to PN becomes the default therapy. Surprisingly, studies suggest that providing STD therapy may be more appropriate in many of these settings. The experts attending this Summit believed that unfortunately, PN may be used most often and most inappropriately at institutions where the least expertise in nutrition exists and whose practice reflects unchallenged surgical tradition.

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The impact of malnutrition on the patient undergoing elective surgery has been shown in numerous studies dating back to the early part of the past century. The presence of malnutrition in the preoperative patient has been shown to increase the incidence of postoperative complications, hospital length of stay, and mortality. Malnutrition developing postoperatively or circumstances that result in delayed initiation of nutrition therapy following surgery have been shown to increase complications and mortality. When comparing groups of critically ill patients, surgical ICU patients were less likely to get EN (77.8% vs 54.6%, \( P < .05 \)), were more likely to get PN (13.9% vs 4.4%, \( P < .05 \)), and were likely to get less percent goal calories delivered from either route (45.8% vs 56.1%, \( P < .05 \)) than medical ICU patients. Patients undergoing cardiovascular or gastrointestinal (GI) surgery were at higher risk for poor nutrition therapy than all other surgical groups. These former patients were more likely to be placed on PN and receive less total nutrition therapy. Protocols for delivery of EN and glycemic control have been shown to improve adequacy of nutrition therapy. The aim of this report is to review the evidence for use of PN through the perioperative period, identify appropriate candidates for PN therapy, and determine strategies by which to optimize outcome benefits from PN.

Does PN Preferentially Benefit Surgery Patients?

Use of PN for patients undergoing elective surgery may have been promoted in the past by evidence in the literature to suggest that PN preferentially benefited surgery patients. In a 1998 meta-analysis, Heyland et al evaluated 27 studies comparing PN with STD therapy. In this report, they elegantly showed that the impact of PN on outcome was different when they compared 22 studies on use of PN in surgery patients with 4 studies in which EN was used in critically ill patients. Surgery patients demonstrated a significant reduction in overall complications with use of PN compared with STD therapy, whereas critically ill patients showed a trend toward increased complications with PN. With respect to mortality, critically ill patients showed a statistically significant increase in mortality with use of PN compared with STD therapy, whereas no difference was seen between the routes of therapy of nutrition support in surgery patients. However, in the same report, Heyland et al showed that this effect, or benefit from PN, was seen in older, less well-designed studies. Whereas PN appeared to reduce complications in studies published before 1989 or those with poor methodologic quality scores <7, that benefit was lost in studies with higher methodologic scores published after 1989. In a separate meta-analysis of 7 randomized trials (of which 6 involved surgery patients), Braunischweig et al showed a similar benefit of PN in older, less well-designed studies. A trend toward improved mortality was seen in studies published earlier than 1992 with a poor methodologic score, an effect that was lost in more recent, better designed studies.

Studies published after 1992 with high methodologic scores showed that PN was associated with significantly greater infection than STD therapy. Review of these studies indicates that evidence for proposed benefits of PN in older, less rigorously designed studies could not be reproduced by more recent investigations with better methodology. These data question the role of PN in supporting patients through elective surgery. Those 3 options include provision of nutrition by EN, PN, or STD therapy. Clinicians often make the mistake in assuming PN to be the automatic default therapy when tube feeding is not available. Doing nothing in certain circumstances may result in better outcomes than providing PN.

A key issue involves the identification of those circumstances where EN is not feasible (Table 1). Absolute contraindications to enteral feeding include intestinal obstruction, ischemia, or acute peritonitis. Relative contraindications, however, would include multiple fistulas with high output, severe malabsorption, severe shock with impaired splanchnic perfusion, and fulminant sepsis. In each of these circumstances, use of the enteral route for tube feeding should be individualized on a case-by-case basis. Inadvertent reasons leading to use of PN, however, may result because of the delays in initiation of EN. In situations in which patients are anticipated to return to surgery soon or undergo possible extubation and return to an oral diet, have hemodynamic instability following cardiovascular surgery, or have distal gut anastomoses, doctors are reluctant to initiate enteral feeding, postoperative ileus is perpetuated, and initiation of PN results as a default therapy. It is this last category of patients in whom changing institutional strategies, implementing nurse-driven protocols, and challenging traditional practices will result in more successful delivery of EN (Table 1).

Who Needs PN Before Surgery?

In a summary report from a conference sponsored by the NIH, Klein et al reported a meta-analysis of 33 randomized controlled trials involving >2500 surgery patients. Thirteen studies involved patients with GI cancer, thought to be at least moderately malnourished on the basis of weight loss, plasma proteins, or prognostic indices. Nine of the 13 studies showed that patients who received preoperative PN had fewer postoperative complications than the control group receiving STD therapy with no specialized nutrition therapy (the differences reached statistical significance in 5 studies). The pooled results from the meta-analysis indicated that PN was associated with an overall 10% reduction in the risk of postoperative complications (absolute risk reduction from 40% to 30%) compared with patients placed on STD therapy. This was one of the first reports to formally recommend that PN be given to “malnourished” patients with GI cancer for 7–10 days before surgery to
reduce postoperative complications, thereby implying that surgery should be delayed to provide this valuable therapy affecting outcome. Unfortunately, malnutrition or malnourishment was defined loosely by weight loss, plasma proteins, and prognostic indices. Subsequent reports have done a better job of defining malnutrition indices that would indicate the need to delay surgery. In a report from the Academy of Nutrition and Dietetics, significant malnutrition was defined as 5% weight loss over 1 month, 10% over 3 months, or 15% over 6 months or a body mass index (BMI) of <18.5 kg/m². The European Society for Parenteral and Enteral Nutrition (ESPEN) defined malnutrition by a 10% weight loss over 3 months or, similarly, a BMI of <18.5 kg/m². The A.S.P.E.N./SCCM guidelines indicated that the signs of malnutrition that would necessitate delay in surgery would be a recent weight loss of 10%–15% of actual body weight or an ideal body weight <90%.

The optimal duration of delivery of PN preoperatively was defined by comparison of the meta-analysis by Klein et al with an earlier meta-analysis by Detsky et al. In a 1987 report of 14 randomized controlled trials comparing PN with STD therapy given preoperatively for patients undergoing elective surgery, only 1 study showed a positive treatment effect, and the overall meta-analysis was negative. On further inspection, it was shown that 7 of the 14 studies provided the preoperative PN for 7 days or less. Ten years later, the Klein et al meta-analysis of 14 prospective randomized trials showed a much more consistent benefit from preoperative PN. As mentioned previously, 6 of 14 studies showed a positive treatment effect, with the pooled meta-analysis showing a 10% reduction in overall postoperative complications. Although there was some overlap between the 2 reports (5 studies of preoperative PN were included in both reports), the Klein report on preoperative PN included 8 studies not included in the original Detsky analysis. A detailed review of the Klein report showed that 13 of 14 studies provided PN for at least 7 days or longer, with only 1 report providing it for only 5–7 days. This led Klein et al to recommend that use of PN should not be considered unless the duration of therapy was anticipated to be a minimum of 7–10 days.

**Who Needs PN After Surgery?**

A surprising finding of the meta-analysis by Klein et al from 1997 showed that the benefit of PN was lost if it was first initiated in the postoperative period. This meta-analysis of 9 studies evaluated postoperative PN, initiated the day after surgery, in comparison to STD therapy. The use of PN was associated with a 10% increase in overall complications (an absolute increase from 30% to 40%). These studies were done in patients with GI cancer, again considered by the authors to be at least moderately malnourished. No difference in mortality was found between the 2 groups. Braunischweig et al showed similar findings in their meta-analysis from 2001 comparing PN with STD therapy in 7 studies (6 of which were done in surgery), in which 4 reports evaluated PN given only in the postoperative period. STD therapy (no nutrition support) was associated with better outcome, showing a reduction in infection by 23% (relative risk [RR] = 0.77, P < .05) and a trend toward reduced overall complications by 13% (RR = 0.087, P < .10) compared with postoperative PN, respectively. Findings from these 2 reports were reinforced by the most recent EPaNIC study by Casaer et al in 2011. Most patients involved in this study were surgery patients (60% had elective cardiovascular surgery). All were started on enteral tube feeding, randomized to receive early initiation of supplemental PN at 2 days (preceded by 2 days of delivery of intravenous [IV] glucose) or late initiation of PN at 8 days (if goal feeds were not met by EN alone). The authors reported on a subset of 517

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**Table 1.** Indication for Use of Parenteral Nutrition (PN) Predicated by Feasibility of Enteral Nutrition (EN).

<table>
<thead>
<tr>
<th>Absolute contraindication to EN: Consider use of PN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal obstruction</td>
</tr>
<tr>
<td>Bowel ischemia</td>
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<tr>
<td>Acute peritonitis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Relative contraindication to EN: Use of EN should be individualized on a case-by-case basis (and use of PN considered if EN deemed not to be feasible).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple fistulas with high output</td>
</tr>
<tr>
<td>Severe malabsorption</td>
</tr>
<tr>
<td>Severe shock with impaired splanchnic perfusion</td>
</tr>
<tr>
<td>Fulminant sepsis</td>
</tr>
</tbody>
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<tr>
<th>Reluctance to use EN: Changing institutional strategies, implementing nurse-driven protocols, and challenging traditional practices will increase use of EN (use of PN may be avoided).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticipated return to surgery</td>
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<tr>
<td>Anticipated extubation and return to oral diet</td>
</tr>
<tr>
<td>Hemodynamic instability after cardiovascular surgery</td>
</tr>
<tr>
<td>Recent gut anastomoses</td>
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<td>Postoperative ileus</td>
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patients in whom EN was surgically contraindicated because of bowel discontinuity. Because EN was not feasible, reports of this subset of patients represent a more recent study of postoperative PN vs STD therapy. Outcome was better if the initiation of PN was delayed, since infection decreased from 40.2% to 29.9% (\(P = .01\)) when early was compared with late initiation of PN. Also, the likelihood of being discharged alive increased by 20% when PN was delayed to the eighth day (\(P = .05\)).

Unfortunately, the exact duration for the provision of STD therapy with no specialized nutrition therapy (some portion of which patients may be kept NPO) that is tolerated without seeing an increase in morbidity is unknown. The only objective data that help determine how long PN should be held after surgery come from an older study by Sandström et al. Only after 14 days was a difference in outcome seen between use of STD therapy in postoperative patients and provision of PN. Continuing STD therapy (ie, withholding any specialized nutrition therapy) was associated with an increased mortality (21% vs 2%, \(P < .05\)) and an increased hospital length of stay (36.3 vs 23.4 days, \(P < .05\)) compared with initiation of PN at that point. Although some investigators support the conclusions of the Sandström et al report, others have been relatively uncomfortable delaying initiation of PN for a total of 14 days. Klein et al recommended initiating PN 5–10 days after surgery. Braunschweig et al recommended 7–10 days. McClave et al recommended initiating PN after 7 days. The results of the Casaer et al report supported initiating PN after 7 days. Consensus of Summit experts recommended that if EN was not feasible following urgent surgery, PN should be initiated after 5–7 days postoperatively.

When Should Supplemental PN Be Added to Hypocaloric EN?

When a patient undergoing elective surgery is placed on enteral tube feeding, but problems with tolerance prevent delivery of required goal calories, when should supplemental PN be added? Older data, done primarily in the burn population, showed that adding supplemental PN to hypocaloric EN tended to worsen outcome. In a study by Herndon et al of 39 burn patients with total body surface >50%, the addition of PN to hypocaloric EN increased mortality from 26% to 63% (\(P < .05\)) compared with patients who were randomized to receive EN alone. There was evidence in this study of immune suppression from the PN, as the ratio of helper to suppressor T cells was reduced in the group randomized to supplemental PN. A meta-analysis by Heyland et al aggregated the results from 5 studies and showed that although there was significantly greater cost with the addition of supplemental PN, there was no significant improvement in infection, hospital length of stay, or duration on mechanical ventilation. A trend was seen toward increased mortality with supplemental PN, but the difference did not reach statistical significance.

The results from the Casaer et al EPaNIC study, done primarily in elective surgery patients, provided evidence supporting an adverse effect from supplemental PN added the first week of hospitalization to hypocaloric EN. In a study of more than 4600 heterogeneous patients, all of whom were started on EN, those randomized to early supplemental PN initiated after 2 days showed significant reductions in infection, ICU length of stay, hospital length of stay, duration of continuous renal replacement therapy, duration on mechanical ventilation, and healthcare costs compared with controls randomized to late initiation of PN after 8 days. Although there was no significant difference in mortality between groups, patients were significantly more likely to be discharged alive from the ICU if they were randomized to late initiation of PN compared with those in whom PN was initiated earlier. Details of the study indicate that results are pertinent to the discussion of the elective surgery patient. Ninety percent of the percent of the patients in the EPaNIC study were surgery patients, with 58% being placed in the ICU after elective surgery. Most of these surgery patients underwent cardiovascular procedures, but others included those patients undergoing cancer operations or GI surgery. Initially, the study was criticized for reduced applicability to patient care because of methodologic issues, related to the fact that all patients received a large parenteral glucose load over the first 48 hours leading up to initiation of PN and all patients were managed on tight, intensive glycemic control. Also, because ICU length of stay averaged only 3–4 days, few patients in either group were actually exposed to PN. In the early PN group, 58% received PN for only 1–2 days, whereas only 25% of patients in the late PN group ever actually received PN.

With reluctance to implement these study results, the nutrition community tended to focus instead on a Swiss study performed by Heidegger et al in high-risk medical ICU patients. Similar to the EPaNIC study, all patients were placed on EN. Study patients, however, had supplemental PN added after 3 days if they were receiving <60% of measured energy requirements by the enteral route alone. Controls continued to receive EN regardless of caloric delivery. Results showed that those patients randomized to PN initiated by this strategy experienced a modest reduction in newly acquired nosocomial infections compared with controls. The fact that these study subjects were medical patients in an ICU limits its applicability to the elective surgery patient in this discussion.

A much more serious criticism of the EPaNIC study was that patients experienced only moderate surgical stress and therefore were not really candidates for supplemental PN therapy. Investigators went back and reanalyzed the EPaNIC study to look at the effect of supplemental PN on patients with greater disease severity. Patients were divided into quartiles based on an increasing Acute Physiology and Chronic Health Evaluation II (APACHE II) score. This reanalysis showed a significant increasing adverse effect from early supplemental PN, going from the lowest to the third highest quartile with respect to
increasing hospital length of stay, multiple organ failure, and mortality, compared with controls receiving late supplemental PN. Only with the highest quartile (APACHE II scores >30) was the adverse effect of early PN lost, although numbers of patients in this group may have been small and a percentage of patients in this group may have been preterminal. The results of this reanalysis suggest a tremendous adverse effect from the use of PN outside the setting of intestinal failure, and its use in the patient undergoing elective surgery should be closely scrutinized.

**How Can PN Be Modified to Optimize Outcome Benefits?**

**Parenteral Glutamine**

Supplementing PN with parenteral glutamine has been used extensively in the critical care setting, based on the proposed benefits that glutamine induces heat shock proteins, maintains gut integrity from the serosal side, and serves as a systemic antioxidant. Individual studies in the past in burn patients and in critically ill patients showed that patients randomized to PN supplemented with glutamine showed reduced infectious complications (23% vs 75%, P < .05), reduced hospital length of stay (12 vs 23 days, P < .05), and reduced mortality (33% vs 60%, P < .05) compared with patients randomized to PN alone. A meta-analysis of four studies by Heyland et al showed a pooled treatment effect of reduced mortality by 29% (RR = 0.71, P = .04) and a trend toward reduced infection by 25% (RR = 0.75, P = .08) with the addition of parenteral glutamine. Unfortunately, many of these studies were done with the product glutamine dipeptide, which is not available in North America. L-glutamine, which is available in North America, is limited in its application to clinical practice by its instability and poor solubility. Furthermore, there now have been 4 recent large negative studies, 3 of which have been published as full manuscripts and 1 published in abstract form only. These studies show no benefit of supplemental glutamine added to PN compared with controls receiving PN alone. The study by Ziegler et al in particular was done solely in the perioperative setting and involved patients undergoing cardiovascular, GI, and general surgery. Based on these recent negative studies, supplemental parenteral glutamine cannot be recommended.

**Permissive Underfeeding**

Permissive underfeeding or delivery of caloric provision, which has been intentionally restricted to 80% or less of caloric requirements, has been a strategy of some merit for use of exclusive PN in certain clinical situations. Three distinct scenarios are described in the literature in which permissive underfeeding has been used. In nonobese patients on enteral feeding, use of permissive underfeeding is a worrisome strategy. Studies would suggest that patients in a top tertile or quartile for delivery of nutrition therapy (both EN and PN) do have worse outcome than patients receiving less feeding, but these studies have significant design flaws. In the obese critically ill patient, permissive underfeeding is an important strategy, where patients receive 60%–70% of caloric requirements while receiving protein provision that meets or exceeds requirements. This strategy is supported by some evidence that lean body mass may be maintained while fat mass is decreased without an adverse effect on outcome. For purposes of this discussion of the elective surgery patient, however, the third scenario is most important. Permissive underfeeding in the nonobese patient receiving exclusive PN in the critical care setting (where approximately 80% of calories and protein is provided) may be an effective strategy and has been shown to improve insulin sensitivity and avoid the adverse effects of overfeeding. A meta-analysis of 5 studies by Jiang et al evaluated the impact of permissive underfeeding of PN in various surgical populations. Although 1 study involved exclusively trauma, the other 4 studies involved patients undergoing surgery for GI cancer, pancreatitis, intestinal obstruction, and various abdominal and chest procedures. Aggregating the data from the 5 studies involving 359 patients showed that intentional underfeeding with PN primarily in the postoperative setting reduced infection by 40% (RR = 0.60, P = .02) and hospital length of stay by 2.49 days (P = .0004) compared with patients randomized to full caloric provision at goal.

The application of these study results may be controversial. Benefits of this strategy might not be seen in the malnourished cancer patient for whom surgery has been delayed and is receiving preoperative PN. These patients have not yet undergone the physiologic stress of the surgical procedure, so there is little rationale for this strategy preoperatively. Immediately following surgery, however, for the same patient (now stressed) in whom EN is still not yet feasible, permissive underfeeding postoperatively might result in improved insulin sensitivity, and the outcome benefits of permissive underfeeding would be manifested.

**No Lipids for First Week of PN**

Theoretically, eliminating the immunosuppressive effects of the ω-6 soy-based lipid emulsion may better prepare the patient for the rigors of major surgery. In critically ill patients who are deemed appropriate candidates for PN, the strategy of providing PN without ω-6 soy-based lipids the first week of therapy has been shown to improve outcome. Although certain physiologic principles support this strategy because of the immunosuppressive effect of soy-based ω-6 lipid preparations, many of the supporting studies were done prior to the development of tight glycemic control. In 2 early studies by Battistella et al and McCowen et al, it is not clear whether the removal of lipids or the fact that the PN inadvertently was hypocaloric accounted for the significant reduction in infectious morbidity compared with controls receiving lipid-based PN. Heyland et
al5 similarly evaluated the effect of parenteral lipids on total complications in a meta-analysis of surgical studies. In 8 studies in which no lipids were provided, use of PN (half given preoperatively, half given postoperatively) significantly reduced total complications (RR = 0.59, P < .05) compared with STD therapy.5 No difference was seen between groups in 16 other studies comparing PN with STD therapy when a lipid emulsion was included in the parenteral regimen. The results of these studies again have to be applied with caution to the patient undergoing elective surgery. For the surgery studies that showed the outcome benefit from withholding fat from the parenteral solution, the PN was given preoperatively before a large GI surgical procedure.

Glycemic Control

The issue of glycemic control in surgery patients was first brought to light by the landmark study by Van den Berghe et al32 in 2001. In a population of surgical ICU patients, intensive insulin therapy keeping the glucose levels between 80 and 110 mg/dL reduced mortality significantly from 8.0% to 4.6% (P < .05) compared with similar patients randomized to conventional control (glucose levels 140–180 mg/dL).32 Initially, the argument was made that surgery patients undergoing cardiovascular procedures have been shown to benefit in the past from the strategy of providing glucose-insulin-potassium therapy for its cardioprotective effects. IV carbohydrate loading followed by intensive insulin therapy similarly might be cardioprotective with improvement in insulin resistance and protein metabolism.7 Such treatment benefits of tight glycemic control, however, could not be replicated when the study was repeated by the same investigators in medical ICU patients in 2006.33 A multicenter trial in 2009 failed to show a difference in mortality in a mixed ICU population between intensive and conventional insulin therapy.34 In the NICE-SUGAR Trial, however, intensive insulin therapy was associated with a higher mortality than conventional therapy (27.5% vs 24.9%, P < .05), and deaths were seen equally in surgery and medical patients.34 A greater frequency of hypoglycemia with its associated increases in mortality seen with intensive insulin therapy has resulted in widespread endorsement of moderate glycemic control in most centers in North America.

How Do You Manage PN Through Surgery?

Few data exist to direct therapy through the actual surgical procedure. Physiologic considerations, however, may provide guidance for the clinician. Early on, a potential contraindication to providing PN through surgery was voiced in a report involving diabetic patients by Goldberg et al,35 who showed that PN through surgery could significantly worsen glucose control and the likelihood for hyperglycemia. In light of the physiologic effects from surgical stress on insulin resistance, Summit experts suggested an appropriate strategy. In the patient receiving preoperative PN, infusion of the parenteral solution may be turned off 2–3 hours before surgery, with no taper required. If the PN infusion is inadvertently left running as the patient arrives in the operating suite, tapering to half the infusion rate for the first hour before turning it off completely would be an appropriate strategy. In the postoperative period, PN may be started the following morning if no enteral access was achieved in the operating room and PN is required to be delivered through the perioperative setting. Studies have shown that with abrupt cessation of glucose-containing PN, glucose levels return to preinfusion baseline within 60 minutes without symptoms of hypoglycemia. No difference in mean glucose values or key hormone levels (epinephrine, norepinephrine, insulin, glucagon, growth hormone, or cortisol) has been seen between abrupt and tapered discontinuation. Such strategy does not need to be modified for the patient with renal insufficiency. The short taper in the operating room is predicated by the evidence for immediate insulin resistance seen with the stress of the surgical procedure.36

Logistical considerations for providing PN in the perioperative setting include establishing goals for delivery of 25–30 kcal/kg/d. There should be no protein restriction, even for patients with renal or hepatic failure. Total fluid and electrolyte levels for patients should be monitored closely in those with evidence of organ failure.7 At this time in North America, no recommendation can be made for specialty proteins, such as parenteral glutamine, arginine, or branch-chain amino acids. Specialty lipid preparations, such as structured lipids, α-9 olive oil, or ω-3 fish oil, show good evidence in the literature for an outcome benefit and should be considered when available in the future in North America.

Conclusions

Provision of EN when feasible is always the first choice for nutrition therapy for the elective surgery patient undergoing a large operative procedure. Protocols should be in place to optimize the enteral delivery of nutrients and promote intestinal tolerance and gut contractility. Plans should be made for placement of enteral access during surgery.

Provision of PN is not the automatic default therapy in cases where enteral feeding is not feasible. Providing standard care with no specialized nutrition therapy is appropriate when EN is not feasible prior to surgery for a well-nourished patient or in the immediate postoperative period for any patient requiring urgent surgery.

If a patient is malnourished based on low BMI or weight loss prior to admission, surgery should be delayed to initiate PN 5–7 days preoperatively. Consideration should be given to withholding proinflammatory soy-based lipid emulsions to reduce the risk of postoperative complications. If no enteral access can be achieved at the time of surgery, the PN would be continued postoperatively 1 day after surgery. In the patient...
requiring urgent surgery when EN is not feasible, PN should not be initiated in the immediate postoperative period but should be delayed for 5–7 days. Initiate PN only if the duration of therapy is anticipated to be greater than 7 days, since any PN therapy less than 7 days would be expected to have no outcome benefit and may actually increase risk to the patient.

For the patient receiving appropriate perioperative PN, the surgeon may consider stopping the PN 2–3 hours before surgery and restarting the morning after surgery. Due to the physiologic stress of a major operation, PN may be modified in the postoperative period to promote permissive underfeeding (providing 80% of caloric requirements).

Discussion

Leah Gramlich: This is one place where we can learn from the ICU clinical practice guidelines, where it’s reasonable to make extrapolations to what we are doing now because the recommendations are pretty similar. Several considerations in the ICU guidelines talk about dose, timing, route, and composition. Think about the route. When people go into an ICU, they always have intravenous access. For the majority of patients on surgical units awaiting surgery, the use of peripheral parenteral nutrition (PPN) might be increased.

Stephen McClave: We prohibited PPN in our hospital because it led to so many abuses.

Leah Gramlich: PPN is widely used in the USA. Baxter is making their new 3-in-1 PN clinical aid in Canada, which may be valuable in our rural community hospitals for surgeons who want to use PPN. I think we need to think about PPN and the volume implications of it.

Stephen McClave: My biggest concern about PPN is that it promotes short-term therapy.

Beth Taylor: One of the questions I would ask you is if we think someone needs preop parenteral nutrition, we must first define how EN was not feasible and we should clearly state what should be tried before it’s determined to be not feasible. There should be use of antinausea medication, prokinetics, and such before we say it’s been a failure. Also, if you were going to give PN preoperatively, should there be any change in the composition? Should we make any recommendations on what the composition of the parenteral nutrition should be, not only preop, but periop and postop? Do we want to put anything in our recommendations on the percent of protein?

Stephen McClave: I would comment on 2 things. One is how we define a candidate for PN, where EN is truly not feasible. I think gastric outlet obstruction from gastric cancer or maybe a real tough esophageal cancer might be 2 examples. However, the issue of feasibility of EN depends on one’s ability to access the small bowel and get past the tumor. Institutional expertise might determine the issue of feasibility.

Beth Taylor: I would add patients coming in for a Whipple. Sometimes you see them preop and they’re just like, “I can’t eat anything, I have no appetite.” I don’t want physicians to think automatically these patients all need to go on parenteral nutrition. I’m just saying we need to be clear about those situations where EN is truly not feasible.

Stephen McClave: On a second point, as far as the makeup of the PN, if we decide that we don’t want to leave off the fat, then I think a fairly standard 20% of calories as protein, 30% as fat, and 50% as dextrose regimen would be fine. The big decision is whether to leave out the fat or not.

Beth Taylor: Who is going to be writing that PN prescription for that preop patient? It may not be the person who has the most knowledge about writing PN, so we need to give them some guidance.

Paul Wischmeyer: You mentioned the Caesar EPaNIC trial. In theory, performing that trial in the United States would be unethical. They delivered 0.8 grams per kilogram per day of protein to PN-receiving patients for 2 weeks, because that is the maximum they could give with the dilute solution they had. That is half the amount of protein recommended in our guidelines. I would never get that protocol through my investigational review board (IRB). My IRB would ask, “What’s the normal way you get nutrition, when you give PN?” The whole point of PN is that you’re giving complete nutrition; otherwise, why would we do it? The title of the EPaNIC paper should be “High Glucose and Fat in the First 3 Days of Critical Care Is Bad for You.” That’s the conclusion of that paper. In that trial, they fundamentally gave incomplete nutrition that we knew was going to fail. And that to me is the major criticism of that study. The A.S.P.E.N. guidelines say don’t feed for a week in well-nourished patients. But we know 50% of people in the hospital are not well nourished. So, my question is, how do we teach surgeons which patients are well nourished and which ones are not well nourished? Where’s that cutoff?

Stephen McClave: Are 50% of our patients malnourished? Where do you get that figure?

Paul Wischmeyer: A Clinical Nutrition publication from 2009 or 2011 went through a number of trials evaluating incidence of malnutrition in the hospital in every setting—general surgery, medical, etc. The average incidence was 41%, with a range from 30%–50%. In some settings, it may be 3%–5%, but in others it might go all the way up to 70% or 80%.

Stephen McClave: Based on nutritional parameters, not albumin?

Paul Wischmeyer: That information was based on Subjective Global Assessment (SGA) mostly. We know that we want to
feed enterally and all our guidelines say that. It’s really simple, but we’re failing. We know we deliver 50%–60% of the calories we prescribe. What do you do with patients whose BMI is below 25 and over 35, or who have a Nutrition Risk Score of 5 (Clin Nutr. 2003;22:321-336)? So in the patients that we’re enterally feeding, are we really protecting their gut by giving them 20 mL an hour of tube feed? Are we protecting their gut but providing only 0.4–0.6 grams per kilogram per day of protein? They’re getting half their caloric requirements. What do we do? What do we tell our surgeons to do?

**Beth Taylor:** For point of clarification, I don’t believe nor have I ever written that 20 mL of tube feedings is going to do anybody any good.

**Daren Heyland:** When you showed the meta-analysis that we published in 1998, we systematically concluded that studies in critically ill patients are different than studies in surgical patients. So I disagree with the assertion that we can make inferences about how to manage surgical patients based on anything related to critical illness from a mechanistic or from an outcome point of view.

**Stephen McClave:** You said in that paper that there were only 4 studies that represented critically ill patients who would end up in the medical ICU. The other 22 studies involved surgery patients, and the results therefore are pertinent to this discussion.

**Daren Heyland:** The McCowan study involved trauma ICU patient populations. Those are not relevant to elective surgery. Furthermore, you made the point that all the old studies prior to 1992 have a systematically different effect than the modern-day studies. In the modern-day studies, the products we use, the processes like glycemic control, are much different.

**Rosemary Kozar:** It looks to me like according to your recommendations, you’re saying all these people should be on PN postop.

**Stephen McClave:** No. For the first recommendation, it is very important to define when enteral feeding is not feasible. Sometimes EN is absolutely not feasible. Half of the time, though, EN is difficult but definitely feasible. The perception of poor feasibility often represents dogma, and EN provision can be accomplished through better, more appropriate institutional expertise. This distinction regarding true feasibility predicates everything.

**Rosemary Kozar:** Why wouldn’t you start PN immediately postop in a malnourished patient?

**Stephen McClave:** The recommendation to wait 5–7 days postop in those patients not previously on PN is taken directly from Sam Klein’s meta-analysis. But it’s reinforced by the results of the EPaNIC study. For those 517 patients in whom enteral feeding was not feasible because of bowel discontinuity, delaying PN until after 7 days resulted in better outcome. Preoperatively, if patients are malnourished and enteral feeding is not feasible, you delay surgery and start PN preop. But often you don’t have the choice to delay surgery; the surgery is urgent. For whatever reason, you have to go straight to surgery. For these patients, even though they may have been moderately or even severely malnourished, the data we have would suggest that we wait and we don’t start PN immediately postop.

**David Flum:** I suggest that this weekend’s activity focus on the prehospital management, which would include up to your first 2 recommendations. The first 2 seemed like a reasonable place to stop. I’m leaving other consensus activity to deal with what happens in the hospital. I think we can safely say early enteral is beneficial; that can still be right. I think there are still some recommendations you can make around postop. There are like 4 or 5 studies evaluating supplemental PN in the postoperative period that are under way. So if you tap that, those studies will be out in the next 1–2 years. Their results might reverse some of these recommendations. Beyond that, I would just make a quick comment that malnourished patients act completely differently than well-nourished patients. You alluded to it, but you have to be careful. I would throw out all the old meta-analyses, the primary reason being they ask a different question. In those studies where they used the term TPN, there often was no good attempt made at enteral feeding. TPN is not the way we manage patients today, but at that time that was the question. The Chiarelli study is a burn study. You have got to be careful mixing burn and trauma patients with elective surgery patients. Some of those patients got as much as 3800 calories; that was during the period of hypercaloric feeding. The best data for elective surgery come from GI studies. We did an analysis and subsequently wrote a paper called “Feeding People With Functional Guts.” For this report, we took some studies from Klein’s previous meta-analysis; I think 1985 was when it cut off the studies. We then looked at every study that used supplemental PN from 1985 on. We focused on those studies where there was severe gut dysfunction, where patients could be randomized to EN alone or EN supplemented with PN. What’s interesting about those patients is that they were all people who had a feeding tube placed. Attempts were made to try and feed them enterally. And for some reason after a number of days, and it varied, it didn’t work. At that point, patients were randomized, supplementing the one group with PN and not the other group. If you look at that elective surgery group...
(and almost all were GI surgeries, such as operations for colorectal cancer), there was a 34% decrease in complications with the addition of PN. There was no difference in mortality, just a difference in complication rates (like postop infection).

**Gary Zaloga:** Soybean oil is the most commonly used oil in the world for food products and it’s actually not bad. It’s not this big proinflammatory fat source. If Americans all went on soybean oil, there would be a decrease in cardiovascular disease, cancer, and everything else because the ω-6:ω-3 ratio of soybean oil is about 8:1. The average diet for the U.S. population is 15:1. So what would happen if you mobilize your fat? The average person actually mobilizes more ω-6s than if they receive soybean oil. The effect on cells from ω-6 oil is different than the total effect on people. If I take your white blood cells out and stick them in Intralipid, they would do a really bad thing. The studies of humans as a whole, and we just reviewed this for the FDA, you do not see proinflammatory responses. Usually you see very little differences in humans when you do this. It’s probably because arachidonic acid is preserved in the cell membrane. It is independent of the supply of linoleic acid, which is in the soybean oil. The other thing is that linoleic at high doses prevents elongation; it blocks off those elongase enzymes. So you don’t convert ω-6 oils to arachidonic acid. So we’ve got good data that show that if you put people on 20% versus 100% soybean oil, the difference in linoleic acid is huge, but the amount of arachidonic acid in the cell membranes, lymphocytes, platelets, in the phospholipid fraction of the white blood cells and red cells is unchanged. You do not manipulate arachidonic acid levels with these lipid emulsions. Whether you use fish oil or anything else, it just doesn’t change. Probably because the body is designed to preserve arachidonate in the membrane. What it does is move the other lipids around. If you put fish oil in the membrane, you kick out oleic. You kick out saturated fats, but you do not kick out arachidonic acid. So I think it’s wrong to say that soybean oil is this massive proinflammatory oil. Both ω-3 and ω-6 long-chain fat depresses white cell function regarding phagocytosis, oxygen burst, and release of cytokines. So for people like me who do lipid research, it is wrong to say that soybean oil is bad.

**Daren Heyland:** I have information that would directly contradict those statements. We have an abstract under review at Clinical Nutrition Week of 13 randomized trials of strategies that reduce ω-6 or soybean oil emulsions. These are PN studies that usually involve Intralipid versus some other ω-6 reducing strategy. Results of the meta-analysis show a trend towards reduced mortality with a P value of .08. So I’ll never be able to explain mechanistically, Gary, how that works, but there seems to be a different treatment effect with non-soybean emulsion lipid strategies. On a different point, there is a meta-analysis that I’m looking at here of 11 randomized trials of glutamine-supplemented PN in elective surgical patients. These are trials that are not ever part of the meta-analysis that we normally do because they are elective surgical cases. I think we’re moving in the wrong direction if we keep appealing to the literature in critical care. We need to bring in those studies that look at elective cases, getting PN, plus or minus glutamine, significant reduction in infection, significant reduction in length of stay. Why aren’t we talking about those?

**References**


