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NUTRITION IN THE PERIOPERATIVE PATIENT

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Abstract The association of malnutrition with surgical morbidity and mortality is well recognized. The question of whether this relationship is causal or simply an association in sick patients has been hotly debated. The field of nutrition support has grown out of the belief that correcting malnutrition will modify associated risks for poor outcome. It has been easier to substantiate this belief in some clinical situations than in others. The evidence for nutrition support during the perioperative period is reviewed and recommendations are made about where nutrition support is most useful and where it may be counterproductive. Some of the important unanswered questions about perioperative nutrition support are raised.

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Introduction

Why is nutrition in the surgical patient such an important issue? The reason is simple: All surgeons know that a nutritionally depleted patient implies a much higher likelihood of postoperative morbidity and mortality. This association was first pointed out by Studley in 1936 (141). Chronic peptic ulcer patients undergoing gastrectomy had a 3.5% mortality rate if they had less than 20% preoperative weight loss, but a 33% mortality rate if they had lost more than 20%. This relationship between preoperative malnutrition and poor outcome has subsequently been confirmed in many other studies (26, 43, 39, 40) and received special emphasis by the Health and Public Policy Committee of the American College of Physicians (64). While the adequately nourished patient usually tolerates major surgery well with rapid recovery of gastrointestinal function, the severely malnourished patient may develop anastomotic breakdown, infection, and may even deteriorate into multiorgan failure.

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The impact of malnutrition on wound healing depends in part on the type of healing required. A wound that heals by primary intention, such as a bowel anastomosis, will often heal even in an emaciated patient so long as the healing process is not complicated by infection. Such wounds appear to have metabolic priority for one to two weeks post surgery. In contrast, a wound that heals by secondary intention, such as a decubitus ulcer or grafted burn, strongly reflects the patient's nutritional status. Even from the outset the malnourished patient's wound exhibits reduced or absent granulation.

If weight loss and hypoalbuminemia increase surgical morbidity and mortality, it would seem logical that providing perioperative specialized nutrition support (SNS) would reduce these complications. However, SNS carries its own risk of complications, for example sepsis if the SNS is parenteral and aspiration pneumonia if the SNS is tube enteral. These risks and the cost of SNS make it imperative that risk-benefit and cost-benefit is determined for parenteral and enteral SNS in different perioperative settings.

Parenteral SNS has been more extensively studied than tube enteral SNS. The reasons for this may be the early surgical enthusiasm for parenteral therapy, the fact that delivering enteral SNS can be more challenging, and the recognition that septic complications and the higher cost of parenteral SNS make randomized outcome studies more urgent. It should also be noted that the majority of surgical patients included in SNS trials had some form of cancer.

In theory the goals of perioperative SNS are first to restore the nutritional status of a depleted patient preoperatively, so operative risks are reduced, then to support the depleted patient through the catabolic phase induced by surgery, and finally to speed the healing process and the return of gastrointestinal function so normal oral food intake can be restored as soon as possible. What is the evidence that SNS does this and who are the patients that benefit from SNS intervention?

Preoperative Nutrition Support

Clearly preoperative SNS can only be considered in patients who do not require urgent surgical intervention.

PREOPERATIVE PARENTERAL NUTRITION This intervention is usually continued postoperatively, and in many studies, the control group also receives postoperative parenteral nutrition.

In the past four years there have been four meta-analyses examining prospective randomized controlled trials (PRCTs) of parenteral nutrition in perioperative patients (90, 146, 68, 93). As expected, there was considerable overlap in the trials evaluated in these meta-analyses, but because inclusion criteria and publication dates differed, there was some variation in the pooled data analyzed, as shown in Table 1. Two of the analyses treated pre- and postoperative studies separately (90, 146), while the other two treated them together and also included postoperative studies using hypocaloric parenteral nutrition, so-called protein sparing therapy (68, 93).

TABLE 1 Meta-analyses of perioperative parenteral nutrition, number of constituent studies (#), and pooled sample size (n)

	Data analysis			
	Preoperative		Postoperative	
	#	(n)	#	(n)
STUDY				
Klein et al. 1997 (90)	13[a]	(1358)	9[b]	(754)
Torosian 1999 (146)	13[c]	(1245)	8[d]	(710)
Heyland et al. 2001b (68)	11[e]	(1165)	16[f]	(1742) [6[g](899) ProtSpar]
Koretz et al. 2001 (93)	25[h]	(2164)	18[i]	(482) [13 (1033) ProtSpar]

The PRCTs included in these meta-analyses were:

[a]11, 12, 49, 50, 65, 106, 108, 112, 113, 138, 145, 149, 150

[b]2, 23, 33, 73, 86, 121, 123, 131, 155

[c]11, 12, 49, 50, 65, 106, 108, 112, 113, 138, 145, 149, 150

[d]23, 33, 73, 86, 121, 123, 131, 155

[e]11, 49, 50, 73, 106, 112, 113, 138, 145, 149, 150

[f]2, 6, 23, 46, 51, 54, 57, 60, 72, 78, 79, 87, 123, 131, 155, 157

[g]46, 51, 54, 57, 79, 87

[h]11, 12, 13, 25, 27, 35, 47, 49, 50, 71, 73, 84, 85, 86, 88, 106, 112, 113, 114, 116, 138, 145, 149, 150, 152

[i]2, 14, 23, 28, 29, 60, 62, 78, 79, 98, 100, 104, 119, 123, 125, 137, 156, 157

*Stated pooled sample size based only on study samples which were primarily verified. True pooled sample sizes are at least this large.

Most of the patients studied had moderate (10 to 20% weight loss, serum albumin <3.2 to >2.5 g/dl) or severe (>20% weight loss, serum albumin <2.5 g/dl) malnutrition. The duration of the preoperative parenteral nutrition varied from 5 to 14 days; for the majority the intervention lasted at least one week. The end points used were postoperative mortality and complications such as sepsis, mechanical catheter problems, anastomotic leaks, pneumonia, and other major surgical problems. Some studies also measured length of hospital stay.

The pooled results from all four meta-analyses showed no overall effect of preoperative parenteral nutrition on reducing surgical mortality.

Three of the four meta-analyses found a reduction in postoperative complications (90, 146, 68). Serious complications were reduced by 10%, from 40% in the control population to 30% in the preoperative parenteral nutrition patients. The fourth more global meta-analysis, which included several studies not published in English, found only a trend toward reduced postoperative complications (93).

The largest single trial of preoperative parenteral nutrition was the cooperative Veterans Administration (VA) study of 395 patients (149). The patients all had some evidence of malnutrition and underwent major abdominal surgery or noncardio thoracic surgical procedures. In the group as a whole preoperative

parenteral nutrition did not reduce postoperative complications (25.5% parenteral nutrition group, 24.6% controls). There were more infectious complications in the parenteral nutrition group (14.1% parenteral nutrition group, 6.4% controls). This increased rate of infection occurred chiefly in patients with only mild malnutrition. In the severely malnourished parenteral nutrition patients, there were fewer noninfectious complications (5% parenteral nutrition group, 43% controls). The noninfectious complications were anastomotic leaks, broncho-pulmonary fistulas, and organ failure. These results led the authors to recommend preoperative parenteral nutrition only in severely malnourished patients, or about 5% of elective surgical patients. Parenteral nutrition clearly created more risk than benefit in mildly or moderately malnourished patients.

It should be noted that two preoperative parenteral nutrition studies, which provided parenteral nutrition therapy for only three days (73) and five days (145) before surgery, found no reduction in postoperative complications, even though the patients studied were severely malnourished. This suggests preoperative parenteral nutrition requires a longer period than three to five days to induce a clinical benefit. All of the studies in severely malnourished patients that did show benefit provided preoperative parenteral nutrition for seven days or more.

PREOPERATIVE ENTERAL NUTRITION Although there have been fewer preoperative enteral nutrition studies, the results to date have been fairly encouraging. In the earliest report, from India (136), 110 malnourished patients awaiting surgery were randomized to 10 days of nasogastric feeding or the routine hospital diet. The patients who received the tube feedings showed significant improvement in body weight and serum protein levels compared to controls. Postoperative mortality was reduced 50% in the treated group (6.0% enteral nutrition group, 11.7% controls) and wound infections were reduced 75% (10.4% enteral nutrition group, 37.2% controls). Foschi et al. (53) randomized preoperative patients with obstructive jaundice undergoing transhepatic biliary drainage to 20 days of SNS (86% by the enteral route) or the routine hospital diet. Postoperative mortality was reduced 75% in the treated group (3.5% enteral nutrition group, 12.5% controls). Flynn & Leightty (52) randomized outpatients with squamous cell carcinoma of the head and neck to routine diet with a nocturnal supplement for 10 to 20 days prior to surgery or the routine diet alone. Postoperative complications were reduced 50% in the supplemented group (32% enteral nutrition group, 59% controls). Von Meyenfeldt et al. (150) randomized 151 patients with gastric or colorectal cancer to 10 days of either preoperative parenteral nutrition ($n = 51$) or preoperative enteral nutrition ($n = 50$). Fifty controls went to surgery without delay. Stratification for weight loss allowed for subset analysis. In the severely depleted patients, there was a significant decrease of intra-abdominal abscesses in both intervention groups compared to the depleted controls.

Le Cornu et al. (95) randomized 82 malnourished patients awaiting liver transplant to a treatment group who received a high-calorie oral supplement in addition to their usual diet and a control group who just had their usual diet. In this study

supplementation did not affect operative outcome. However, these investigators had carefully recorded dietary intake, and they showed a higher caloric intake from the usual diet in the controls. As a result, despite the 750 kcal, 20g protein supplement taken by the treatment group, their daily intake was only 2419 ± 157 kcal/d and 79.8 ± 5.99 g protein/d compared to the control group of 2234 ± 194 kcal/day and 86.5 ± 6.22 g protein/d. This very modest difference in calories may well explain the lack of effect of the supplement on surgical outcome. Indeed, this study underlines two important issues in regard to specialized nutrition interventions. First, the parenteral or enteral supplement may have an effect on regular dietary intake, and this must be assessed, as it was in the Le Cornu study. Second, it demonstrates the difficulty of providing artificial enteral nutrition. These hepatic failure patients were at high risk for esophageal/gastric varices and ascites, and there would be strong clinical reluctance to insert a nasogastric or percutaneous feeding tube. Unfortunately, an oral supplement, especially in the outpatient setting, is subject to many compliance issues, such as poor appetite, taste barriers, or cost factors if there is no insurance coverage.

The phenomenon of bacterial translocation from the bowel lumen to regional lymph nodes and ultimately the bloodstream has been firmly established in experimental animal models such as the laboratory rat. The translocation was thought to occur because of an increase in mucosal permeability of the poorly nourished or unused bowel. It was postulated that translocated bacteria or their toxins induced a systemic cytokine response that, if severe, could initiate the multiorgan failure syndrome (31, 101). This mechanism has not been entirely confirmed in humans. First, intraoperative studies in patients with inflamed bowel have not consistently cultured lumenal bacteria in regional lymph nodes or the bloodstream (89, 144). Second, intestinal permeability, measured by the lactulose/mannitol test, is not altered by the route of feeding, parenteral or enteral (124). Despite this, the concept that dysfunction of the gastrointestinal barrier allows toxins to enter the body and induce a cytokine response and multiple organ failure remains active (99). This has led to a number of trials using enteral immune-enhancing diets.

Gianotti et al. studied the effect of an enteral immune-enhancing diet providing arginine, omega 3 fatty acid, and nucleotides on the nutritional status and inflammatory response of patients with gastric and colorectal cancer (58). Fifty-eight patients were randomized to receiving 1 L/d of the test diet or 1 L/d of a standard isocaloric, isonitrogenous formula. The diet was given orally for seven days preoperatively and continued eight days postoperatively, via a nasoenteric tube. The test diet was more effective than the control diet at sustaining normal nutritional parameters through surgery and damping the inflammatory response of interleukin-6 (IL-6) and IL-1R11 to surgery. In a later phase, this same group showed the immune-enhancing diet translated into better clinical outcome with fewer operative complications and a shorter length of hospital stay (18). These benefits were most pronounced when the enriched formula was given both pre- and postoperatively. A similar clinical benefit was described by Senkal

et al. in 154 patients with upper gastrointestinal malignancies using the same immune-enhancing enteral diet (133).

One problem with this immune-enhancing diet is that several immunonutrients are present in the formula, and hence it is not clear if a particular nutrient confers the biological benefit. A recent study from Amsterdam (148) used a standard pre- and postoperative diet with and without added arginine. The arginine did not significantly improve nutritional or clinical outcome, which suggests that arginine may not be the critical factor.

Overall it is reasonable to conclude from these studies that preoperative enteral nutrition is of benefit in malnourished patients and the benefit may be amplified by the use of immune-enhancing diets. Once again the stumbling block is how to effectively deliver the enteral support preoperatively. In many clinical situations there is reluctance to subject the patient to a nasoenteric or percutaneous tube in advance of surgery. Furthermore, the most cost-saving approach would be to initiate preoperative enteral support at home, prior to surgical admission. But insurance carriers may not be willing to cover such therapy at home. For example, this is not an allowable cost under Medicare's home parenteral and enteral nutrition prosthetic device benefit (74). As a consequence, prescribing an expensive immune-enhancing formula for preoperative home buildup is not yet a feasible approach. It will take more studies to prove this is truly cost effective before funding will be provided.

Postoperative Nutrition Support

Postoperative nutrition support, by convention, refers to nutrition support initiated after surgery rather than preoperative nutrition, which is continued postoperatively. Postoperative support is potentially a larger issue than preoperative support since many operations cannot be delayed pending nutritional intervention, and preoperative support, at least administered parenterally, appears indicated only in the 5% of elective surgical patients who are severely malnourished.

POSTOPERATIVE PARENTERAL NUTRITION Nine studies involving more than 700 patients have compared parenteral nutrition to simple intravenous fluids. In many more studies parenteral nutrition was compared to early enteral nutrition, or the parenteral nutrition provided was hypocaloric protein-sparing therapy. The meta-analyses of these nine studies showed parenteral nutrition had no effect on mortality, and unfortunately increased morbidity by 10%, mostly through septic complications.

In Sandstrom's study of 300 patients, 60% of the postoperative patients resumed oral nutrition within eight to nine days regardless of whether they received parenteral nutrition or glucose only (131). The remaining 40% had delayed return of gastrointestinal function; those receiving parenteral nutrition were at increased risk for sepsis, and those receiving hypocaloric glucose were at increased risk for wound breakdown and mortality. These results strongly suggest routine

postoperative parenteral nutrition is inappropriate. However, some patients did appear to need nutrition support. Unfortunately, patients with delayed return of gastrointestinal function could not be identified by preoperative criteria. The Sandstrom study was important also because it showed a high risk of mortality and morbidity if postoperative patients receive only hypocaloric feeding for more than 14 days. The safe interval for withholding nutrition support is not precisely known, but withholding for two weeks is evidently too long.

In the two meta-analyses where hypocaloric protein-sparing therapy was evaluated, there was no benefit seen in terms of operative mortality or complication rates (68, 93).

POSTOPERATIVE ENTERAL NUTRITION Two studies in elderly women with hip fractures (8, 41) have shown enteral supplementation shortens the time until weight bearing, speeds return of independent mobility, and reduces length of hospital stay. In the most underweight women, there was a trend—but not a statistical difference—toward lower mortality in the supplemented group, 8% versus 22% in the controls. A similar but more recent study (10) randomized 101 malnourished postoperative patients to a treatment group that drank 400 mg of a formula providing 1 kcal/ml and 0.06 g protein/ml. The patients were encouraged to sip this supplement between meals. They were compared to a control group receiving standard care. In the control group, weight declined for two months after discharge. In the treated group only half the amount of weight was lost; this reached a nadir at four weeks, and then the treatment group began regaining. The treated group had fewer infections and required fewer antibiotics. Quality of life was assessed by the short form-36 questionnaire, and the treatment group showed significantly better physical and mental health compared with the control group. This study suggests nutritional status and quality of life are linked, and postoperative impairment can be substantially redressed by a simple, fairly inexpensive oral supplement.

Barium studies (77, 115) have shown that small bowel motility continues in the postoperative period, even though gastroparesis may be present for 24 to 48 hours and colonic paresis for 3 to 5 days. This finding has encouraged surgeons to try early postoperative jejunal feeding of an elemental diet as an alternative to intravenous isotonic glucose or parenteral nutrition. The jejunum is accessed either by a nasojejunal tube or percutaneous needle catheter jejunostomy placed intraoperatively. There are four PRCTs involving 142 patients, most of whom had gastrointestinal or head and neck cancer (80, 128, 130, 139). Although one study of 14 patients had fewer complications in those treated with the jejunal elemental diet compared to those receiving intravenous isotonic glucose (128), pooled data did not confirm a significant clinical or nutritional advantage. Thus routine early jejunal feeding with standard formulas is feasible but not clearly beneficial.

Given the preserved perioperative motility of the small bowel, Moncure et al. have questioned if jejunostomy feeds really need to be stopped eight hours prior to elective surgery, as is the standard of care for all forms of enteral intake (109). They randomized 82 patients undergoing nonabdominal operations to either

TABLE 2 Meta-analyses of peri-operative enteral nutrition, number of constituent studies (#), and pooled sample size (n)

	Data analysis			
	Preoperative		Postoperative	
	#	(n)	#	(n)
STUDY				
Klein et al. 1997 (90)	2[a]	(211)	4[b]	(142)
Torosian 1999 (146)	2[c]	(211)	4[d]	(142)
Heys et al. 1999 (70)			11[e]	(1009)*
Heyland et al. 2001c (69)	22[f]	(2419)*	9[g]	(1130)**
Beale et al. 1999 (9)	12[h]	(1482)*		

*Included both surgical and critically ill patients.

**Included only surgical patients.

The PRCTs included in these meta-analyses were:

[a]136, 150

[b]80, 128, 130, 139

[c]136, 150

[d]80, 128, 130, 139

[e]15, 19, 20, 37, 38, 94, 107, 111, 129, 132, 133

[f]7, 15, 18, 21, 24, 32, 37, 38, 48, 56, 58, 59, 94, 107, 111, 127, 132, 133, 134, 140, 151, Ross Prod. Div. Abbott Labs 1996 (unpublished)

[g]18, 21, 37, 38, 58, 132, 133, 134, 140

[h]7, 15, 19, 32, 37, 38, 55, 94, 111, 132, 133, 151

discontinuing their jejunostomy feedings when transported to the operating room or eight hours before surgery. The clinical outcome was the same in both groups of patients; there was no evidence of aspiration. The group fed until the last moment, as expected, received more calories and protein. While this study showed that continuing jejunal feeds until just before surgery is safe, any clinical benefit from the greater nutrient intake was not demonstrated.

A growing number of early postoperative tube enteral PRCTs have led to meta-analyses as summarized in Table 2.

Since the 1980s a number of PRCTs have compared early enteral nutrition to early parenteral nutrition in postoperative and other critically ill patients (trauma, burns, head injury, acute pancreatitis). These studies found enteral nutrition was superior to parenteral nutrition with fewer postoperative infections and shorter hospital stays (110, 111, 3, 94, 16). The better outcome with enteral nutrition was associated with a lower stress response and less endotoxin translocation (143, 142) and better peripheral protein synthesis (63). The initial interpretation of these studies was that enteral feeding was superior because it more effectively preserved the immunological barrier function of the intestinal mucosa. However, this interpretation has recently come under reappraisal (82, 83). It has been pointed out that most

of these comparative trials provided more calories to the parenteral patients, for while the trials were intended to be isocaloric and isonitrogenous, it was difficult to get the enteral patients up to the planned nutrient amounts. As a consequence the parenteral patients had higher glucose and insulin levels, and this metabolic perturbation may explain their greater stress response and higher infection rate. Recent obesity studies have shown that excessive caloric intake is associated with increased expression of tumor necrosis factor receptors and higher IL-6, leading to greater immunosuppression (34). Thus the enteral nutrition/parenteral nutrition comparisons may have to be repeated with greater attention to isocaloric-isonitrogenous feeding. In one recent study of nonsurgical patients, enteral nutrition was found to be more hazardous than parenteral nutrition. In 2001, Woodcock et al. (154) published what they described as a prospective "pragmatic" comparison of enteral and parenteral nutrition in 562 patients. This was not a strictly randomized study in that the patients' attending physician assessed gastrointestinal function and determined the route of nutrition support in 75% of the patients. The remaining 25% were randomized. The study showed enteral nutrition met with more technical difficulties, making it harder to achieve an adequate nutritional intake. More enteral nutrition patients died. There was no difference between the parenteral and enteral groups in terms of septic morbidity.

One more chapter in the story of postoperative enteral nutrition support has been the use of immune-enhancing diets compared to standard enteral formulas. Two meta-analyses have evaluated this issue in postoperative and in critically ill patients. In 11 PRCTs evaluated by Heys, 6 addressed postoperative patients, and in the 22 PRCTs evaluated by Heyland, 9 addressed postoperative patients. The pooled data found immuno-nutrition did not influence postoperative mortality, but it did reduce infectious complications shortening the length of the hospital stay (70, 69). In a recent subgroup analysis of the critically ill patients with ongoing infection and sepsis, Heyland has shown an increased mortality in those receiving immune-enhancing diets, especially diets high in arginine. Heyland has argued that while the immune-stimulating effect of these diets is likely to benefit the immune-suppressed postoperative patient; the critically ill patients with immune overresponsiveness may respond by fatal aggravation of their inflammatory process (69). Other forms of immune therapy are being tried in critically ill patients, notably antioxidants (134), probiotics (81), and thymopentine (17). All these interventions are aimed at damping, not augmenting, the patient's immune response.

Cost of Perioperative Nutrition

The cost of perioperative nutrition has chiefly been examined in patients receiving parenteral nutrition. Ten reports were published between 1982 and 1990 (5, 45, 44, 61, 120, 43, 103, 122, 126, 147), and they found parenteral nutrition cost an additional $75 to $530 per day. Some of these estimates may have included the fixed costs of hospitalization (47). In a detailed cost analysis of the Veterans Administration Cooperative Study of perioperative parenteral nutrition, Eisenberg et al. showed that incremental costs were highest ($3921) for patients who were

least likely to benefit from the therapy because they were only mildly or moderately malnourished. Such patients suffered increased infectious complications from parenteral nutrition and were housed in the expensive intensive care unit because of their parenteral therapy. The incremental costs were lowest ($3071) for the high-risk severely malnourished patients. In this cohort infectious complications were not increased and noninfectious complications were decreased. The cost savings from avoiding different noninfectious complications were not analyzed because of the small number of patients with any particular complication, but it seemed likely that a large fraction of these costs were already included by the altered length of stay. This study could not show a cost saving from parenteral nutrition for any subgroup of patients. The incremental cost of perioperative parenteral nutrition in the VA study was $196 per day in 1992. This in-depth analysis has potential for helping the VA system and other hospitals spend perioperative nutrition dollars more rationally.

Enteral nutrition has always been thought of as less expensive than parenteral nutrition, both in hospital and at home. Indeed, there is a tenfold difference in the Medicare reimbursement for these therapies in the home setting (76) (Table 3). In recent years, especially in perioperative patients, there has been a swing toward more post pyloric feeding. A PRCT using radioisotope-labeled enteral feeds has shown that feeding beyond the pylorus significantly reduces gastroesophageal regurgitation with a trend toward less microaspiration (67). Placement of post pyloric tubes can be achieved radiologically, endoscopically, or surgically (153). However, all these approaches require special expertise and usually special fluoroscopy units, which translate into significant cost. In addition, there is a tendency for jejunostomy tubes to flip back into the stomach or block because of their small caliber or simultaneous use for feeding and medications. This frequently requires

TABLE 3 Medicare allowable charges for HPEN therapy in 1992

	Parenteral (per day)	Tube enteral (per day)
NUTRIENT SOLUTION		
Glucose	$158–298	$10–35
Amino acids		
Lipids		$30–40
Additives	$7	
Dressing kit	$7	$0.5–2
Administration set	$22	$11
Pump loan (15mo only)	$12	$3.60
Mean* (range)	$280 ($238–390)	$33 ($25–50)

*The mean daily Medicare allowable charge was calculated from actual Medicare area reimbursement of 1000 days for Medicare patients receiving HPN and 1000 days for Medicare patients receiving HEN to five large nutrition support programs. This mean daily reimbursement was increased from 80% to 100% to derive the mean daily Medicare allowable charge (75).

jejunostomy tube replacement, which is a further expense. Thus, with modern enteral feeding obtaining and sustaining enteric access is a great deal more expensive than with the simple nasogastric tube (96, 22).

Unresolved Issues in Perioperative Nutrition

A number of important perioperative nutrition issues await clarification.

More studies are needed to test the feasibility of preoperative enteral nutrition, especially in the outpatient setting. This is a two-part issue. First, is tube access necessary to insure an increased intake? Second, how significant is the benefit in terms of reducing expensive postoperative complications? Since the few PRCTs available so far indicate a reduction in postoperative complications of 50 to 75%, more widespread use of preoperative enteral nutrition in the future may be highly appropriate.

Because postoperative enteral nutrition, especially with immune-enhancing formulas, appears to reduce postoperative complications and length of hospital stay, it is desirable that future studies include a control group receiving routine hospital care (isotonic glucose with gradual resumption of oral diet). This control arm has seldom been included, yet it would help to define when more complex enteral nutrition is justified.

Recent animal studies have demonstrated impaired tolerance of enteral nutrition in partial bowel ischemia (92). Currently there are no good clinical methods for assessing the degree of bowel ischemia in patients with poor splanchic perfusion. This is clearly another important issue in perioperative patients who have blood pressure instability.

As presented in this overview, preoperative parenteral nutrition reduces noninfectious complications in severely malnourished patients by 10%, but postoperative parenteral nutrition increases complications by 10%. Moreover, 60% of postoperative patients resume oral nutrition in eight to nine days, and in this cohort parenteral nutrition has no beneficial effect (131). It seems likely postoperative parenteral nutrition increases infectious rates, perhaps by inducing hyperglycemia. Under these circumstances, perhaps waiting to start or resume parenteral nutrition for a week could be an important step that deserves testing. Such an intervention might avoid the period of acute surgical stress and the risk of hyperglycemia and septic complications. It might also be possible to avoid postoperative parenteral nutrition altogether in patients who appear close to resuming oral nutrition. If postoperative patients who go for two weeks with only hypocaloric glucose have rising morbidity and mortality, the issue becomes a question of when it is not too early and not too late to intervene with parenteral nutrition. This is clearly an important and unresolved series of questions.

The final issue relates to the fact that the majority of perioperative patients studied had some form of malignancy. Cancer, like AIDS, is a wasting disorder that can lead to marked cachexia. Sometimes the weight loss reflects true starvation and is due to an inability to swallow or absorb nutrients. More often, however, the weight loss reflects altered metabolism due to abnormal hormonal

and cytokine factors. In this form of cachexia there is increased loss of lean body mass, and repletion with nutritional intervention is impaired. Shike et al. showed that parenteral nutrition in patients with small cell lung cancer led to weight gain, but this was due to increased body fat and total body water, not to increased lean body mass (135). In nonsurgical cancer patients, such as those undergoing radiation or chemotherapy, parenteral nutrition has been shown in over 40 PRCTs to provide no clinical benefit. Indeed in two meta-analyses (91, 105) the pooled data revealed evidence of net harm, since the parenteral nutrition-treated group showed a higher incidence of infection. In 1989 this finding led to a cautionary statement by the American College of Physicians advising against routine use of parenteral nutrition in cachectic cancer patients undergoing radiation or chemotherapy (4). Enteral studies in cancer patients undergoing radiation or chemotherapy also demonstrated no therapeutic benefit. Keeping these issues in mind the questions that arise are first, how many of the cancer patients included in the perioperative trials were suffering the metabolic syndrome of cancer cachexia and were therefore unlikely to improve with SNS? Second, might the response to perioperative nutrition be more positive if only noncancer patients were studied? These questions need to be answered so these expensive but potentially valuable SNS therapies can be used as safely and cost effectively as possible.

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