

The 115th Abbott Nutrition Research Conference

November 1-2, 2015

New York, New York, USA

*Nutritional Innovations to Improve Outcomes in
Gastrointestinal Surgery*



Welcome

Gastrointestinal (GI) surgery accounts for a substantial portion of hospital costs. At Abbott Nutrition, we are working to bridge the knowledge of evidence-based medicine and consensus among healthcare professionals on the value of nutritional innovations to improve outcomes in GI surgery. There is increasing consensus that nutrition support is a key factor in the management of perioperative physiologic and psychological stresses that slow recovery and increase the likelihood of costly complications.

The causes of malnutrition in GI surgical patients are multifactorial and involve altered nutrient processing, inadequate intake, malabsorption, and/or excess nutrient loss, depending on the surgery and the patient. Recognizing and treating malnutrition with early intervention can help wound healing, decrease incidence of pneumonia, lower infection rates, reduce comorbidities, shorten hospital length of stay, and reduce readmissions and mortality in the GI patient population. Ultimately, recognizing and treating malnutrition can help improve both clinical and economic outcomes.

This publication offers eight presentation summaries focusing on the cost of GI surgeries and what we can do to improve clinical and economic outcomes; procedures, complications, and nutritional implications of metabolic/ bariatric, upper GI, pancreatic, and colectomy surgeries; preoperative carbohydrate loading and oral nutritional supplements; nutritional management of emergency GI surgeries; and perioperative immunonutrition.

Barriers to change persist and better communication is needed – among scientists, researchers and clinicians, among interdisciplinary healthcare teams, and among clinicians and their patients. We offer the proceedings from this research conference to help guide your evidence-based care and best practices in GI perioperative nutrition.

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Nutritional Innovations to Improve Outcomes in Gastrointestinal Surgery

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115th Abbott Nutrition Research Conference Faculty and Speakers

Left to right, front: Dr Gary Fanjiang (Abbott), Dr Maria Isabel Correia, Dr Julie Marosky Thacker, Dr Sabrena Noria, Dr Jacqueline Boff (Abbott) Left to right, back: Dr Refaat Hegazi (Abbott), Dr Clifford Ko, Dr Alexander Sauper, Dr Hakim Bouzamondo (Abbott), Dr David Evans, Dr Kenneth Lee, Dr Krishnan Sriram.

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Nutritional Innovations to Improve Outcomes in Gastrointestinal Surgery

The 115th Abbott Nutrition Research Conference was held at the New York Academy of Sciences in New York, New York, USA on November 1-2, 2015. This Report contains summaries of presentations given by the following contributors.

Keynote Address

GI Surgeries: How Costly are They and What Can We Do to Improve Clinical and Economic Outcomes?

Julie K. Marosky Thacker, MD, FACS, FASCRS
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Perioperative medicine is a relatively new field with less scientific proof than one might think. Dr Thacker opened the 115th Abbott Nutrition Research Conference with her keynote address focusing on “understanding why we do what we do,” will improve outcomes, decrease costs, and benefit the science and the industry of perioperative nutrition for gastrointestinal (GI) surgeries. She argues that while there are many regulations and metrics in place to improve the delivery of services, we lack the ability to define and enforce evidence-based care. Worldwide, healthcare leaders are writing and adopting Enhanced Recovery protocols to improve surgical outcomes and the patient experience. Dr Thacker explains that the impact of decreasing complications has a much greater impact on the overall cost of operations. She concludes with the potential impact of combining our learnings from perioperative care and nutrition to optimize surgical outcomes and decrease cost of GI surgeries.

GI Surgery: Procedures, Complications, and Nutritional Implications

Metabolic/Bariatric Surgery: Nutritional Implications and Outcomes

Sabrena F. Noria, MD, PhD
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The obesity crisis is a worldwide problem, having doubled since 1980, such that there are 500 million obese adults globally. Obesity is a complex interplay between evolutionary, biological, psychological, sociological, economic and institutional factors. Dr Noria discusses obesity categories eligible for metabolic/bariatric surgery, and the surgical procedures most popular and effective for excess weight loss, resolution of obesity-related comorbidities, and mortality reduction. She explains the risks and complications of surgery, and identifies guidelines for biochemical monitoring of nutritional status and postoperative vitamin-mineral supplementation. Patients must undergo an extensive medical and dietary work-up prior to surgery, and close follow-up after surgery with both comprehensive education and nutritional supplementation.

Upper Gastrointestinal Surgery and Nutritional Implications

Krishnan Sriram, MD, FACS, FRCSC, FCCM
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The complexity of resections and reconstructions of the upper gastrointestinal (UGI) tract and the resulting nutritional implications before and after surgery place the patient at risk for malnutrition. Dr Sriram reviews UGI surgeries and associated risks for malnutrition both before and after surgery. There is clear evidence that providing oral nutritional supplements (ONS) for 7-10 days prior to any major UGI tract surgery is highly cost-effective and decreases wound complications, length of stay, duration on ventilator, and anastomotic leaks. He emphasizes that early resumption of enteral nutrition after surgery, avoiding routine nasogastric decompression, and encouraging early ambulation are vital for optimal wound healing and recovery. Enteral nutrition also has benefits for improving the patient's stress response and immune function, which are important for healing and recovery. Dr Sriram concludes that failure to prevent or treat malnutrition in the pre- and postoperative periods can result in serious postoperative complications. Adherence to evidence-based strategies for pre- and postoperative nutrition therapy is critical for enhanced recovery after UGI surgery.

Pancreatic Surgery: Procedures, Complications, and Nutritional Implications

Kenneth K.W. Lee, MD, FACS
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Pancreatic surgeries are most commonly performed upon the pancreas to remove problematic abnormalities or to treat consequences of acute or chronic inflammation of the pancreas. Dr Lee illustrates the anatomy and physiology of the pancreas and common pancreatic operations. He explains that complications associated with pancreatic surgery can arise not only from the resection itself, but also from the necessary reconstruction, as well as the physiologic and functional changes inherent to the surgical procedures. These various postoperative complications can result in macro- and micronutrient deficiencies. Moreover, preoperative malnutrition is common in pancreatic surgical patients. He cites studies that demonstrate preoperative malnutrition was a predictor of postoperative morbidity and mortality after pancreatic surgery. Dr Lee argues that nutrition strategies are critical, and should be employed to mitigate, diagnose, and treat the nutritional deficiencies in the perioperative care of patients having pancreatic surgery.

Colectomy: Procedures, Complications, and Nutritional Implications

Clifford Y. Ko, MD, MS, MSHS, FACS, FASCRS
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Colectomies involve a surgical resection of the colon. Dr Ko describes common colon surgical procedures, and issues with hydration, nutrition, weight loss, anastomotic leaks, and other complications that may exist after surgery. With the median length of stay at approximately 7 days for colectomy, Dr Ko shares concern that a patient will often remain without adequate nutrition support for 5-6 days, or even longer. In addition, most colectomy patients lose approximately 15 pounds of weight postoperative when healing is critical in this time period. He concludes that more information and evidence-based practice guidelines are needed to address the impact of preoperative and postoperative nutrition interventions on colorectal surgery outcomes. The American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) has developed a risk calculator to estimate a patient's risk for complications using information about the procedure and patient factors. This is a step in the process to improving outcomes for surgical patients.

Scientific Update on Perioperative Nutrition

Preoperative Carbohydrate Loading and Nutritional Supplementation: A Scientific Update

Maria Isabel Correia, MD, PhD
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One commonality among surgical patients is the organic response triggered by the stress of the operation. Dr Correia discusses this organic response and the insulin signaling defects that often occur with surgery. She further explains that insulin resistance is directly proportional to the magnitude of the surgical insult and is related to postoperative complications, and that the nutritional status of the patient plays a key role in the patient's organic response to stress and risk for insulin resistance. Preoperative carbohydrate loading is presented as a therapeutic approach to decrease preoperative discomfort (eg, thirst and hunger); and to reduce insulin resistance, hyperglycemia, nausea and vomiting, and preserve muscle mass following surgery. Dr Correia adds that providing early oral nutritional supplements (ONS) after surgery has shown an increase in energy and protein intake resulting in decreased number and severity of surgical complications.

Nutritional Management of Emergency GI Surgeries

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Emergency gastrointestinal (GI) surgeries are unplanned, often associated with a greater number of patient comorbidities, and trigger greater physiologic stress on the patient than elective GI surgeries. These surgeries create a catabolic insult where the patient's metabolic requirements increase, and because the fat mass is inefficiently utilized as an energy source under this physiologic stress, lean mass is primarily catabolized for energy. Dr Sauper explains that there is a window of opportunity within the first 24 to 72 hours following a hypermetabolic insult, such as surgery, in which starting enteral feedings are associated with preserving gut integrity as well as diminishing the activation of inflammatory and counterproductive cytokines. However, he cautions there is a limited amount of data regarding the use and benefits of early enteral nutrition in the emergency GI surgery population. With more data from evidence-based care, Dr Sauper foresees a change from traditional management to enhanced recovery protocols supporting early enteral feeding in suitable patients undergoing emergency GI surgery.

Perioperative Immunonutrition: Does One Size Fit All?

David C. Evans, MD, FACS
The Ohio State University, Wexner Medical Center
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Columbus, Ohio, USA

Stated goals of immunonutrition include attenuation of excessive inflammatory responses, supplementation of conditionally-essential nutrients that are rapidly depleted in certain stress states, and delivery of nutrients thought to aid recovery in specific disease and injury states. Dr Evans discusses the proposed mechanisms of action for various high-profile immunonutrients. In addition, he argues that it is challenging to draw valid conclusions from studies supporting the application of immunonutrition to surgical patients. Generally, it is thought that there is some synergism between the multiple immunonutrients that limits the efficacy of single immunonutrients and inhibits isolated clinical evaluation of any nutrient in isolation. Dr Evans identifies a meta-analysis that confirmed preoperative immunonutrition conferred no improved outcomes when compared to isonitrogenous standard high-protein oral nutritional supplements. However, when compared to an un-supplemented regular diet, oral immunonutrition supplements resulted in lower infectious complications and a reduction in hospital length of stay. He cautions that the precise immunonutrient profile, timing, dose and duration are issues that need to be resolved before immunonutrition can be optimally prescribed to diverse clinical populations.

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GI Surgeries: How Costly are They and What Can We Do to Improve Clinical and Economic Outcomes? 10
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GI Surgeries: How costly are they and what can we do to improve clinical and economic outcomes?

Julie K. Marosky Thacker, MD, FACS, FASCRS

Understanding why we do what we do might seem like an unusual question for surgeons to ask themselves. As a sub-specialty surgeon at a prestigious academic healthcare center, I could imagine several answers. I was trained by the best to provide patient care this way. I study all the literature and abide by it. My high-ranking health system has protocols in place for me.

In truth, however, how patients are managed from the time of the diagnosis of a surgically-managed problem through their operation and recovery is extremely variable. Additionally, most of the care received is based on tradition, meaning, the way surgeons have always delivered care or managed a particular problem. Perioperative medicine, in many ways, is a new field with less scientific proof than one might think.

When I was recruited to Duke Surgery (Duke University Medical Center, Durham, North Carolina), I had similar outcomes to the surgical team I joined. My anastomotic leak rates, infection rates, and hospital length of stay data were comparable to all of the surgeons in the two big private practice hospitals I was leaving, as well as, to the faculty I was joining. I had no external pressure to change my patient management. However, upon joining the Duke faculty, I chose to teach the medical students and residents about postoperative care of the colorectal surgery patient. I took this opportunity to create a literature library of the different care elements of the postoperative period. Immediately, I realized that most of how I practiced was dogma. Many care elements for the colorectal surgery patient, while proven scientifically, were not in my practice or in the practice of most of my peers. During this personal and professional search, I began seeing my patients' journey through diagnosis, preoperative preparation, their operations, and recovery as an integrated and important process of evaluation and optimization.

How costly are gastrointestinal (GI) surgeries? While I am a surgeon and not an economist or healthcare politician, my background is likely not important as there is no one who can tell you what an operation really costs in the United States (US). There are versions of this question that can be answered by certain people. How much does a certain operation cost the hospital to perform? How much will a surgeon bill a third party payor? How much does the patient portion of an operation cost? These fractions or partial costs are discernible, but for me to determine, from diagnosis to recovery, how much an operation costs is impossible.

So, while I cannot answer this specific question, I may be the best person to answer, "How can we make GI surgery as cost effective as possible?" Because this is the focus of my work, everyday. This is my "WHY." Working to change perioperative medicine, to make how I care for patients the evidence-based, best care I can provide is my WHY. To ask about the cost of GI surgery is to ask about my WHAT and my HOW. Which, in the Simon Sinek Golden Circle,¹ are the outer layers to the real purpose of our work. By focusing on providing the best patient experience through surgery, we provide the best patient outcomes.



The cost of GI surgery is essentially two components. One is nearly fixed, or at least comparatively fixed. Operations happen in hospitals and with similar techniques and equipment from hospital to hospital. The other component is the cost of what happens. If the patient does well and leaves the hospital and recovers as best as expected, the cost of the operation is the best guess cost of the first component, the cost of doing the operation. If the patient has any other outcome, be it no transportation on the day of discharge or a major complication requiring intensive evaluation and care, then the second component, the unpredictable cost of more care than anticipated, is added.

Any complication after an operation increases the cost of that operation by a factor of at least 2. If diagnostics are required to determine the management of a postoperative complication, the length of stay in the hospital can be 5-fold those of uncomplicated operations. Most importantly, complications have been shown to prolong recovery and shorten life.^{2,3} A patient who suffers a complication after surgery, even as simple as a wound infection, is at risk of a shortened life.

The top five most expensive conditions treated in US hospitals, according to a Centers for Medicare & Medicaid Services (CMS) review and an Agency for Healthcare Research and Quality (AHRQ) publication, were septicemia; osteoarthritis; complications of a device, implant, or graft; newborn services; and acute myocardial infarction.⁴ Three of these five can be a complication from surgery; two of these are known, reported complications from GI surgery.

Now, you can argue about robotics or expensive joints, but for the sake of this discussion, we will focus on a straightforward GI operation. Something done in every hospital with in-patient capacity. These are great examples of operations after which patient recovery impacts the cost of surgery.

While there are many regulations and metrics in place to improve the delivery of services, we lack the ability to define and enforce evidence-based care. Interestingly, it takes seventeen years on average to implement new evidence-based care into routine medical practice.⁵ One such example is the use of evidence-based perioperative care elements in a care paradigm from the time of diagnosis, through surgery, and recovery. A group in Europe has coined the phrase, Enhanced Recovery After Surgery (ERAS) to describe their perioperative care elements.⁶ The effort in the United Kingdom (UK) has included a rigorous aspect of fluid management, as well as, pain and nausea prevention. These components of care, typically managed by the anesthesia members of the surgery team, have been adopted by several US centers interested in perioperative medicine as well. This cooperative effort has resulted in care teams, including nurses, nurse anesthetists, anesthesiologists, and surgeons, to implement care elements.

The details of enhanced recovery programs are best understood with an explanation of what is now referred to as “traditional care,” or the common care plan of a GI surgery patient.

Traditional care of the GI surgery patient:

- 2 L bowel preparation and clear liquid diet for 2 days preoperatively
- 7 L crystalloid infusion during a 4-hour operation
- nasogastric tube to keep the stomach empty
- urinary tube to keep the bladder empty and measure urine made



- abdominal cavity drains
- postoperative starvation until resumption of bowel function
- bedrest for 24-48 hours after surgery
- no foods 2-day preop and 4-6 days postop = 6-8 days starvation during stress

When the physiologic stresses are considered, there are elements of care around the time of surgery that have been studied. Specifically, trying to minimize this physiologic stress response results in better outcomes from operations. In combination, these “Enhanced Recovery” elements have been studied to reduce insulin resistance, related infections, and perioperative complications (Fig 1).⁶

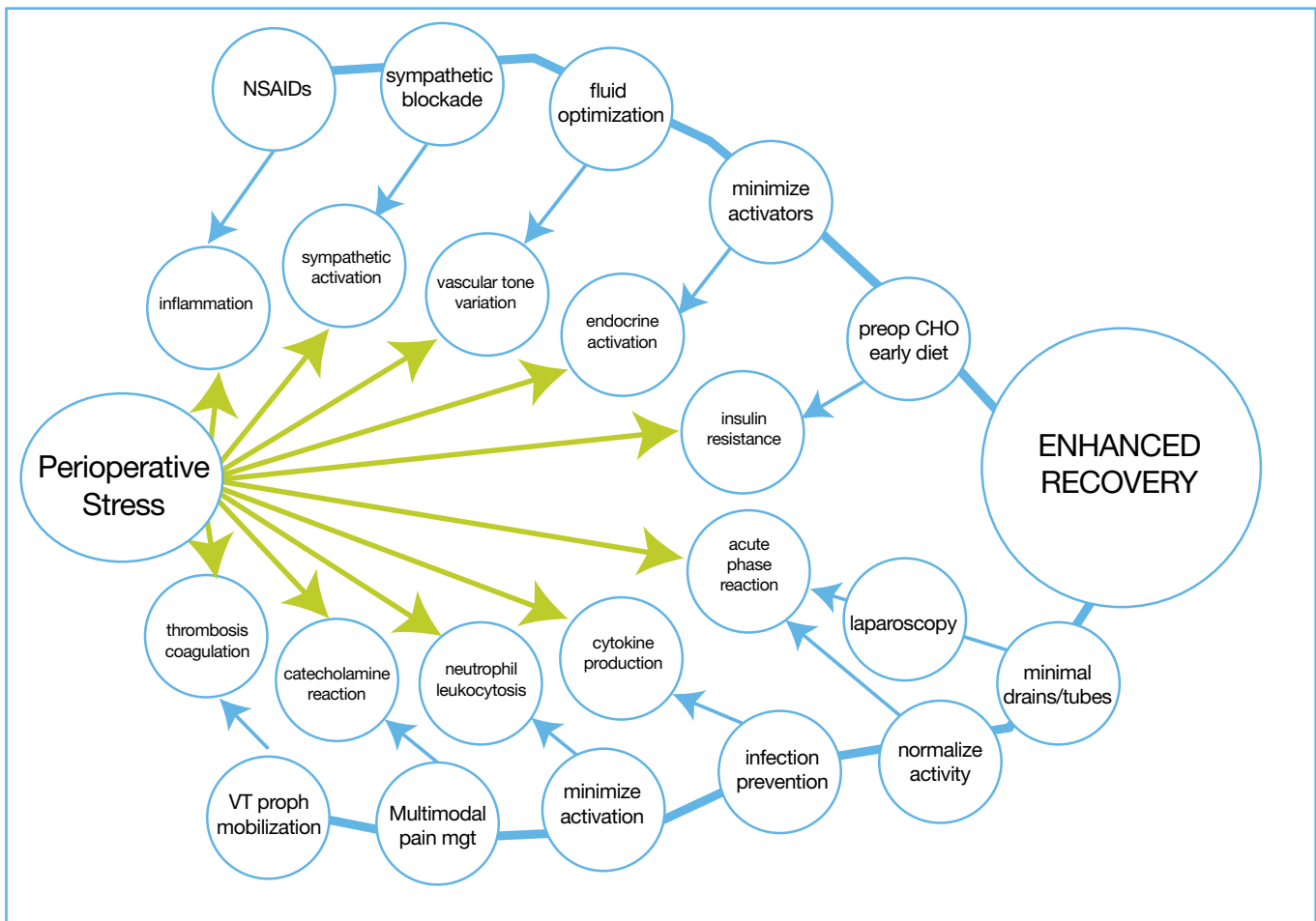


Fig 1. Enhanced recovery elements to minimize the perioperative physiologic stress response.⁶

NSAIDs=nonsteroidal anti-inflammatory drugs, CHO=carbohydrate, VT proph mobilization=venous thromboembolism prophylaxis mobilization, mgt=management



Evidence-based perioperative care (EBPOC) utilizing enhanced recovery protocols improves surgical outcomes and the patient experience. It involves the examination of current practices; implementation of every perioperative evidence-based medicine (EBM) care point; and a multimodal, multidisciplinary, patient-focused approach. Benefits of enhanced recovery include improved outcomes, improved efficiency, decreased variability, and increased value (ie, outcomes/cost). At Duke University Medical Center, our enhanced recovery elements focus on the patient’s journey through surgery (Fig 2).

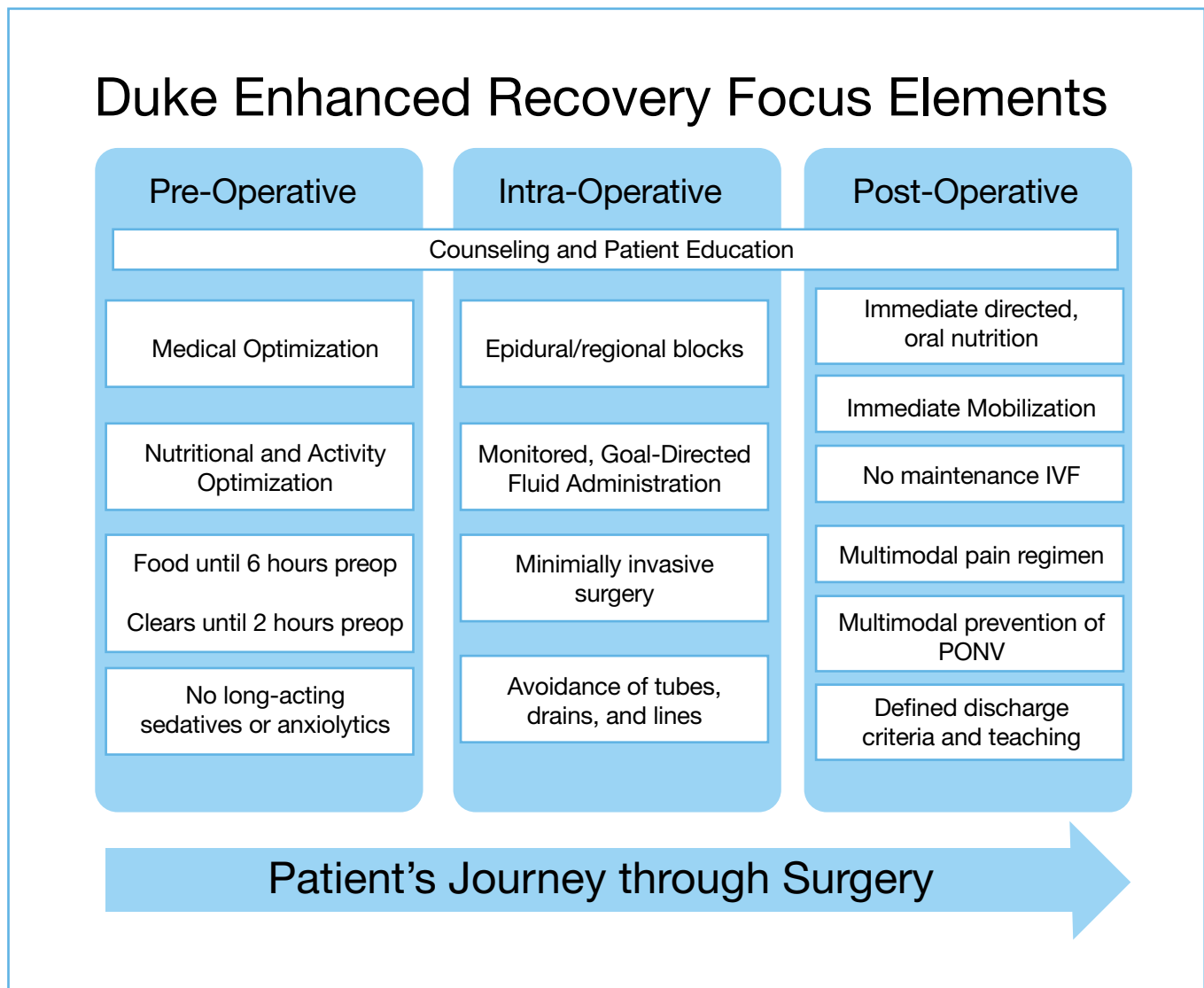


Fig 2. Duke Enhanced Recovery focus elements.
 IVF=intravenous fluids, PONV=postoperative nausea and vomiting



Why do I relate improving GI surgery outcomes to the cost of GI surgery? While surgery was only about 22% of 2012 CMS payments, this percentage of nearly 20% of the US gross national product (GNP) came to \$105 billion.⁷ So, operations do cost a lot. Metrics, comparisons, and restrictions may contain some variation of cost, but the impact of decreasing complications has a much greater impact on the overall cost of operations. We've seen this in our small study at Duke (Fig 3),⁸ and the same has been reported on a greater scale through studies at the US Department of Veterans Affairs (VA) and in Europe using ERAS protocols.

Significant Outcome Improvements 2010-2013					
	SSI	UTI	Sepsis	LOS	Readmission
Pre-ERAS	24.3%	24.2%	8.1%	8.2	20.2%
ERAS	6.7%	9.4%	0.5%	5.9	9.8%

Fig 3. Decreased GI surgery complications with ERAS protocols.⁸

ERAS=Enhanced Recovery After Surgery protocols, SSI=surgical site infection, UTI=urinary tract infection, LOS=length of hospital stay, average in days (median was 7 to 4). Readmission=all cause readmission within 30 days of index operation

By studying those patients who do best and by implementing the science we have already done, we can create a perioperative protocol to decrease complications from all types of surgeries. GI surgery, specifically colorectal surgery, was the first specialty of abdominal surgery in which these practices were created and implemented, but currently all types of operations are being impacted by this application.

The most important aspect of improving perioperative medicine, however, seems to be the application of principle, not details. Importantly, evidence-based perioperative medicine is not just protocolized or mandated. The tenet of enhanced recovery protocols is to provide best care for the patient at each step of his or her journey through surgery - not to just treat everyone the same. This begs the application of nutrition science toward the on-going work of enhanced recovery.

Merging the science of improved perioperative outcomes from perioperative nutrition evaluation and oral nutritional supplements (ONS) with the improved outcomes from perioperative care strategies (such as enhanced recovery) yield amazing results. These two paths have crossed during the discussion of preoperative nutrition, preoperative carbohydrate loading, and postoperative ONS, though the application of true nutrition science to the surgical patient in enhanced recovery is limited. This is interesting, given that the premise of the first few studies in Scandinavia around enhanced recovery were specifically interested in insulin resistance and the effect of such on infection rates and recovery.



Taking what we have learned about perioperative care from enhanced recovery efforts and team protocols and combining this with what we know about perioperative stress and nutrition is a perfect combination to optimize surgical outcomes. With such optimization, we will be decreasing complications and, thereby, costs of GI surgery, if not all types of operations. Focusing on WHY we are interested in the surgical patients, be it as a surgeon, an anesthesiologist, a nutritionist, or a nutrition scientist, we can apply a HOW to our desired outcomes and product (Fig 4).¹

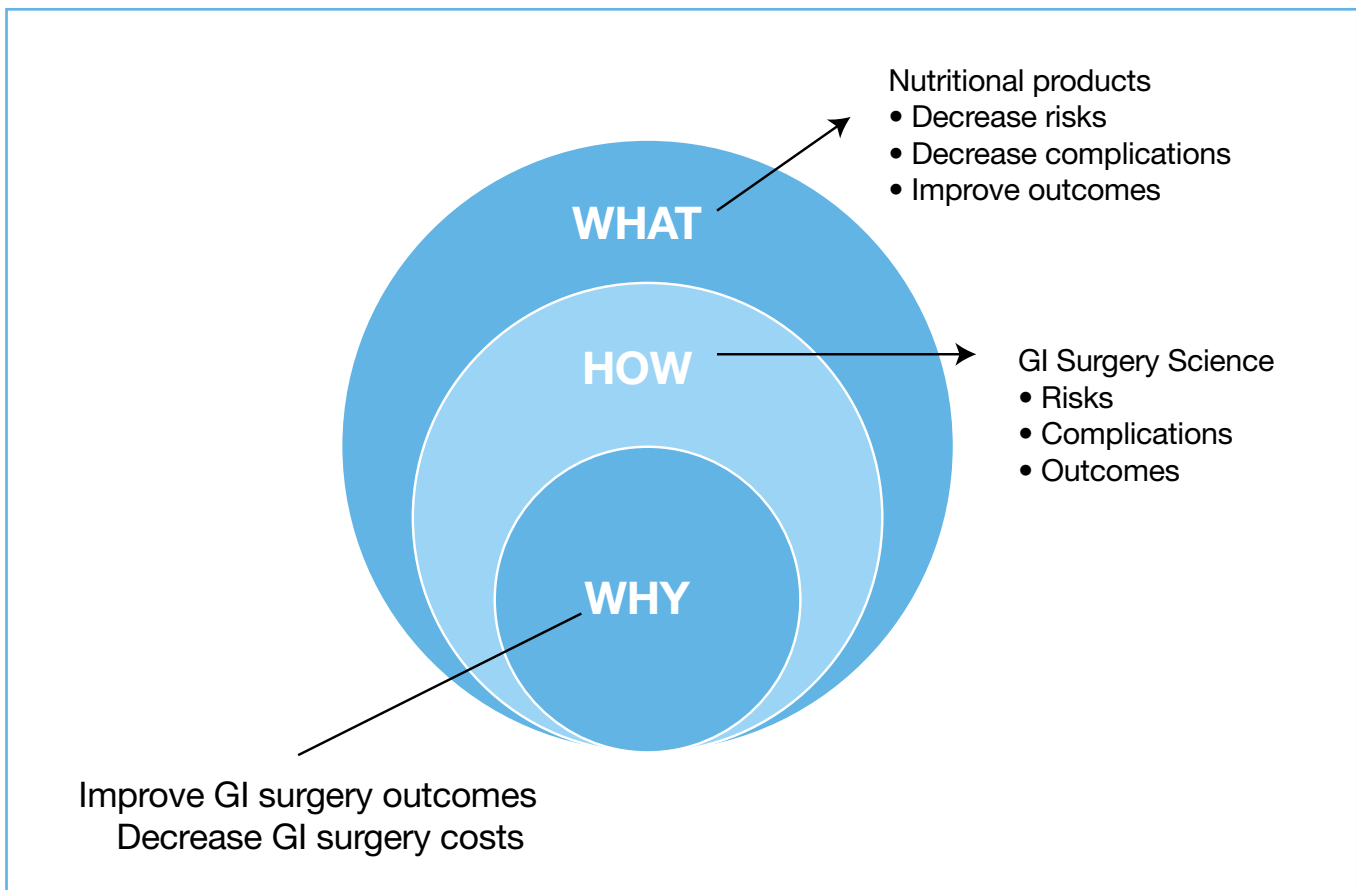


Fig 4. Applying the Golden Circle concept to improve outcomes in GI surgery.¹

Source: The Golden Circle. 2015 Simon Sinek, Inc. Available at <https://gumroad.com/d/8eaa76472308a1d96a944affc97e1898>. Accessed November 23, 2015.

The creation of alliances, a Venn diagram of each of our “WHYs” may then be the best focus of a forum such as this research conference. Understanding each other’s goals, in terms of the bigger picture, the reason why we do what we do, will improve outcomes, decrease costs, and benefit the science and the industry of perioperative nutrition. This is the perfect picture to open the 115th Abbott Nutrition Research Conference on “Nutritional Innovations to Improve Outcomes in Gastrointestinal Surgery.”



References

1. The Golden Circle. 2015 Simon Sinek, Inc. Available at <https://gumroad.com/d/8eaa76472308a1d96a944affc97e1898>. Accessed November 23, 2015.
2. Schilling PL, Dimick JB, Birkmeyer JD. Prioritizing quality improvement in general surgery. *J Am Coll Surg*. 2008;207:698-704.
3. Steele SR, Bleier J, Champagne B, et al. Improving outcomes and cost-effectiveness of colorectal surgery. *J Gastrointest Surg*. 2014;18:1944-1956.
4. Agency for Healthcare Research and Quality. The top five most expensive conditions treated in U.S. hospitals. HCUP Statistical Brief #160. Available at <http://www.ahrq.gov/sites/default/files/wysiwyg/research/data/data-infographics/images/most-expensive-conditions.html>. Accessed on January 5, 2016.
5. Urbach DR, Baxter NN. Reducing variation in surgical care requires innovative methods for getting evidence into surgical practice. *BMJ*. 2005;330:1401-1402.
6. Lassen K, Soop M, Nygren J, et al. Consensus review of optimal perioperative care in colorectal surgery: Enhanced Recovery After Surgery (ERAS) Group recommendations. *Arch Surg*. 2009;144(10):961-969.
7. Gonzalez JM. National Health Care Expenses in the U.S. Civilian Noninstitutionalized Population, 2011. Statistical Brief #425. November 2013. Agency for Healthcare Research and Quality, Rockville, MD. Available at http://meps.ahrq.gov/mepsweb/data_files/publications/st425/stat425.shtml. Accessed on January 5, 2016.
8. Miller TE, Thacker JK, White WD, et al. Reduced length of hospital stay in colorectal surgery after implementation of an enhanced recovery protocol. *Anesth Analg*. 2014;118:1052-1061.



GI Surgery: Procedures, Complications, and Nutritional Implications

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Metabolic/Bariatric Surgery: Nutritional Implications and Outcomes

Sabrena F. Noria MD, PhD

The Obesity Epidemic

Obesity has become a problem of epidemic proportion in the United States (US). According to the Centers for Disease Control and Prevention (CDC), from 1976–1980 approximately 15% of US adults were overweight or obese, and by 2010 that increased to 36%. On average, individuals are 24 pounds heavier than they were in 1960 and if this trend continues, by 2030 50% of Americans will be overweight or obese.¹ Unfortunately the obesity crisis is not isolated to the US, but is a worldwide problem, having doubled since 1980, such that there are 500 million obese adults globally.²

To assume obesity is an imbalance between energy consumption and expenditure is too simplistic. It is the product of a complex interplay between evolutionary, biological, psychological, sociological, economic and institutional factors. In fact, the United Kingdom (UK) government Foresight Research on obesity identified more than 100 variables that directly or indirectly affect obesity³ which, in turn, has serious social and economic implications. For example, the estimated annual global direct economic impact of obesity is 2 trillion US dollars, ranking it third behind smoking; and armed violence, war, and terrorism.⁴ This impact is related to both direct medical costs and non-medical costs.

Focusing on direct medical costs, it is estimated that in the US, every point of body mass index (BMI) above 30 kg/m² adds ~\$300 in per capita annual medical costs with a weighted average annual medical cost of \$5,500 for individuals with a BMI over 30 kg/m².⁴ These direct costs of obesity are related to the medical comorbidities associated with this disease. In particular, there has been extensive research on the relationship between obesity and type 2 diabetes, hypertension, hyperlipidemia, and obstructive sleep apnea.⁵ However, obesity affects every body system, and is also correlated with development of cancers including endometrial, esophageal, breast, and colorectal cancer. Finally, obesity has been shown to be an independent risk factor for death,⁶ such that as BMI increases above 35 kg/m² the estimated years of life lost for a 20-year-old white male in the US increases from 4 years up to 12 years when BMI climbs over 45 kg/m².⁷

There are multiple metrics for measuring obesity. However, the most commonly used is BMI, which is derived from weight (kg) divided by height (m²). While BMI is good for quantifying obesity on a population level, it is not as useful in the clinic as it is unigender and uniraical, fails to reflect the distribution of fat and muscle, and fails to indicate the severity of comorbidities.⁸ However, given its adoption by Medicare and US private carriers in 2004, it is the metric used to determine access to surgical care. Therefore, individuals are categorized as overweight (BMI = 25 kg/m² – 29.9 kg/m²); obese (BMI = 30 kg/m² – 34.9 kg/m² [Class I obesity]); and morbidly obese (BMI = 35 kg/m² – 39.9 kg/m² [Class II obesity]), 40 kg/m² – 49.9 kg/m² [Class III obesity]), and super-obese (BMI ≥ 50 kg/m²).⁹



In order to be eligible for surgery, an individual must be considered morbidly obese (also referred to as “clinically severe obesity”), which was defined by the 1991 National Institutes of Health (NIH) Consensus Conference Statement on Gastrointestinal Surgery for Severe Obesity as a BMI ≥ 40 kg/m² or a BMI ≥ 35 kg/m² in the presence of high-risk comorbid conditions.⁹ This degree of obesity is considered eligible for surgery because it is at this stage that it becomes “morbid”; significantly increasing the risk of one or more obesity-related health conditions or serious diseases that result either in significant physical disability or even death.

Preoperative Preparation for Metabolic/Bariatric Surgery

Methods of weight loss are broadly divided into medical and surgical. Medically-managed weight loss (ie, diet, exercise, meal replacements, pharmacotherapy) can be successful for individuals categorized as overweight; however, it has been proven ineffective for those with a BMI ≥ 30 kg/m².⁹ Only bariatric surgery has been proven effective over the long term for most patients with clinically severe obesity.⁹ Additionally, to qualify for surgery, patients cannot have a known endocrine or metabolic cause for their obesity; they cannot have a history of substance abuse, eating disorder, or major psychiatric problem that is untreated and/or unresolved; patients must have attempted medical weight loss treatments without success; they must be able to understand the risks of the operation and be able to give consent; and finally, patients must be prepared to commit to the lifestyle changes that are necessary for success after surgery. Given these requirements, successful and sustained weight loss requires more than just surgery. At a minimum, metabolic/bariatric surgery programs require a comprehensive team that includes nurses, dietitians, psychologists, exercise physiologists, endocrinologists, cardiologists, and pulmonologists.

In preparing patients for surgery, an initial intake evaluation requires a complete medical and dietary history. Focusing on the latter, although obesity is considered a state of “over-nutrition”, it is a risk factor for both macro- and micronutrient deficiencies (Table 1).¹⁰⁻¹³ Therefore, identifying and rectifying these deficiencies preoperatively, through education and supplementation, aids in preventing postoperative nutritional deficiencies.

Table 1: Obesity is a Risk Factor for Nutrient Deficiencies¹⁰⁻¹³

Nutrients	Prevalence of Deficiency in Obesity
Protein	16% ¹⁰
Iron	44% - 50% ^{11,12}
Vitamin C	36% ¹³
Vitamin D	25% - 80% ^{11,13}
Vitamin A	12.5% ¹³
Vitamin E	23% ¹³
Zinc	28% ¹³
Thiamin (B ₁)	15% - 29% ¹¹⁻¹³
Cobalamin (B ₁₂)	18% ¹³
Folate	6% ¹³



Surgical Procedures

Restrictive Procedures

Restrictive procedures limit the luminal diameter of the stomach, but do not re-route food through the gastrointestinal tract. Procedures may utilize some form of foreign material or “band” (ie, laparoscopic adjustable gastric band [LAGB]), and/or surgically resize the stomach with a stapler in order to create a small gastric pouch (ie, sleeve gastrectomy [SG]).

The LAGB was once the second most common bariatric procedure, but recently has been replaced by the SG.¹⁴ The procedure consists of placing an adjustable plastic and silicone ring around the proximal stomach just beneath the gastroesophageal junction. A subcutaneous access port allows the degree of band constriction to be adjusted by the injection or withdrawal of saline. Although the risk of mortality and major morbidity is low, the amount of excess weight loss (EWL) obtained is less than that seen with surgical malabsorptive procedures.^{15,16}

The laparoscopic sleeve gastrectomy (LSG) is emerging as one of the most popular surgical procedures for the management of obesity. It has gained popularity because it is considered less technically demanding, the entire stomach and duodenum are still accessible by endoscopy, and there is no risk of internal hernia formation. The procedure involves resection of the greater curvature of the stomach by stapling it over a sizing tube (bougie) ranging from 11 to 20 mm in diameter.¹⁷ Originally developed as part of the biliopancreatic diversion with duodenal switch,¹⁸ it was subsequently used as the initial procedure of staged surgery for the super-obese.^{19,20} Currently, LSG is most commonly applied as a stand-alone procedure,²¹ and is being used with increasing frequency, comprising 36.3% of primary bariatric operations in 2012.¹⁴ The effectiveness of LSG with respect to weight loss and resolution of comorbidities is positioned between that achieved after Roux-en-Y gastric bypass (RYGB) and LAGB.²² These results suggest that, at least in the short term, LSG is an efficacious method of weight loss.

Malabsorptive Procedures with Some Restriction

Malabsorptive procedures are designed to reduce the area of intestinal mucosa available for nutrient absorption. The jejunioileal bypass (JIB) involves bypassing most of the small intestine by anastomosing the proximal jejunum, past the ligament of Trietz, to the terminal ileum. While excellent weight loss is achieved, the blind jejunal-ileal limb leads to nutritional complications and hepatic cirrhosis secondary to bacterial overgrowth.²³⁻²⁵ As such, this procedure was abandoned, and the biliopancreatic diversion (BPD) was devised to improve upon the JIB.

The BPD consists of a partial gastrectomy, resulting in a 200–500 mL sized proximal gastric pouch, and creation of a distal roux and proximal biliary limb by division of the small bowel 250 cm proximal to the terminal ileum. The gastric pouch is then anastomosed to the end of the roux limb, and the biliary limb is attached 50 cm proximal to the ileocecal valve, thereby creating a very short common channel.²⁶ The procedure was later modified, creating the biliopancreatic diversion with a duodenal switch (BPD/DS). This entails fashioning a gastric sleeve with a maximum reservoir of 150–200 mL. The small bowel is then divided 4–5 cm distal to the pylorus, and 250 cm proximal to the terminal ileum. The proximal duodenal end is reconnected to the last 250 cm of small intestine, and the biliary limb is anastomosed 100 cm proximal to the terminal ileum.^{15,18,23} This procedure preserves



the antrum, pylorus, a short segment of duodenum, and vagal nerve integrity; thereby having a theoretical advantage of preserving a more physiologic digestive behavior, and diminishing the risk of dumping syndrome, ulcerogenicity, and hypocalcaemia.²³

Restrictive Procedure with Some Malabsorption

The Roux-en-Y gastric bypass (RYGB) is considered the “gold-standard” for bariatric surgery and is still the most commonly performed operation, although there has been a reduction in number of procedures commensurate with the increase in sleeve gastrectomies performed.^{14,23,26} Technically, the procedure involves creating a gastric pouch, roux-limb and biliary limb. Using surgical staplers, a small, vertically oriented gastric pouch with a volume < 30 cm³ is formed. Dividing the small bowel 30-40 cm from the ligament of Trietz creates the roux and biliary limbs. Restoration of continuity occurs by connecting the roux limb to the gastric pouch, creating a gastrojejunostomy, and anastomosing the biliary limb approximately 150 cm distal to the gastrojejunostomy. After a RYGB, the size of the pouch restricts the volume of ingested food, and creation of the Roux-en-Y effectively bypasses approximately 95% of the stomach, the entire duodenum, and a portion of the jejunum.²³

Risks and Complications of Surgery

As with all surgical procedures, metabolic/bariatric surgical procedures are associated with both early and late complications. Early complications (1–6 weeks postop) include staple/suture line leaks (RYGB [<1%], SG [<2%]), bleeding (<1.5%), infection (<1.5%), pulmonary embolism (<0.5%), pneumonia (<0.4%), cardiac arrest (<0.1%), sepsis (<0.5%) and death (RYGB [0.14%], SG [0.11%], LAGB [0.05%]).²²

Late complications (> 6 weeks postop) include staple/suture line leaks, gallstone disease, bowel obstruction, malnutrition and/or vitamin deficiencies, persistent nausea and vomiting, and failure to lose weight or weight regain. Late surgery-specific complications of RYGB include gastrojejunal ulceration leading to bleeding (0.6% – 4%) or stenosis (1.42%), internal hernias (0.1% – 5%), and gastrogastic fistulas (<1%).²² Late complications related to LAGB include port/tube malfunction (0.4%-7%), band slippage/migration (2%-10%), band erosion into the stomach (0%-3%), pouch dilatation (10%), and port infection (<1%).²²

Nutritional consequences of surgery are primarily related to micronutrients. Specifically, deficiencies in fat-soluble vitamins (A, D, K) and zinc are more common after BPD/DS. Additionally, vitamin B₁₂ and iron deficiencies are seen more commonly after RYGB due to exclusion of the majority of the stomach. Macronutrient deficiencies are rare, but can occur after any procedure (3% - 11%), and are related to poor oral intake (Table 2).^{12,13,27} In order to mitigate these complications, the American Society for Metabolic and Bariatric Surgery (ASMBS) provides guidelines for the type and timing of micronutrient supplementation (Table 3).¹²



**Table 2: ASMBS Guidelines: Biochemical Monitoring for Nutritional Status/
Nutritional Consequences of Metabolic/Bariatric Surgery^{12,13,27}**

Nutrient	Screening	Normal Range	Post-op Deficiency	Notes
B ₁ Thiamin	Serum thiamin	10–64 ng/mL	Rare unless high N/V	More common after RYGB (<18%) (↓ acid ↓ absorption)
B ₁₂	Serum B ₁₂	200–1000 pg/mL	12%–33%	More common after RYGB (↓ parietal cells ↓ IF)
Folate	RBC folate	280–791 ng/mL	Uncommon	More common after RYGB (< 45%) (due to bypass of proximal small bowel)
Iron	Ferritin	♂ 15–200 ng/mL ♀ 12–150 ng/mL	Avg: 20%–49% RYGB 15% BPD/DS 26%	More common after RYGB in menstruating women (51%), and patients with super obesity (49%–52%)
Vitamin A	Plasma retinol	20–80 µg/dL	Common with BPD/DS	Common (50%) with BPD/DS after 1 yr., up to 70% at 4 yr.; may occur with RYGB, AGB
Vitamin D	25(OH)D, Ca, PO ₄ , PTH	25–40 ng/mL	> 50%	Common with BPD/DS after 1 yr.; may occur with RYGB; prevalence unknown
Vitamin K	PT	10–13 seconds	51%	Common with BPD/DS after 1 yr.
Zinc	Plasma zinc	60–130 µg/dL	36% - 51%	Common with BPD/ DS after 1 yr.; may occur with RYGB
Protein	Albumin Total Protein	4–6 g/dL 6–8 g/dL	3% - 11%	Rare, but can occur with RYGB, AGB, and BPD/DS if protein intake is low

ASMBS=American Society for Metabolic and Bariatric Surgery, N/V=Nausea/Vomiting, RYGB=Roux-en-Y gastric bypass, IF=intrinsic factor, BPD/DS=biliopancreatic diversion with a duodenal switch, AGB=adjustable gastric band



Table 3: ASMBS Guidelines: Postoperative Vitamin-Mineral Supplementation¹²

Supplement	RYGB	BPD/DS	LAGB	Comment
Multivitamin-Mineral Supplement. <ul style="list-style-type: none"> • A high-potency vitamin containing 100% of daily value for at least 2/3 of nutrients • Choose a complete formula with at least 18 mg iron, 400 µg folic acid, and containing selenium and zinc in each serving 	200% of daily value	200% of daily value	100% of daily value	Begin on day 1 after hospital discharge
Additional Elemental Calcium <ul style="list-style-type: none"> • Choose a brand that contains calcium citrate and vitamin D₃ 	1500–2000 mg/d	1800–2400 mg/d	1500 mg/d	May begin on day 1 after hospital discharge or within 1 mo. after surgery
Additional Cobalamin (vitamin B ₁₂)	1000 µg/mo.			Begin 0–3 mo. after surgery
Fat-Soluble Vitamins		Vit A 10,000 IU Vit D 2,000 IU Vit K 300 µg		May begin 2–4 weeks after surgery

ASMBS=American Society for Metabolic and Bariatric Surgery, RYGB=Roux-en-Y gastric bypass, BPD/DS=biliopancreatic diversion with a duodenal switch, LAGB=laparoscopic adjustable gastric band

Outcomes of Surgery

Several studies have demonstrated that on average, both the RYGB and SG achieve 60% - 80% EWL within 2 years, and LAGB achieves 50% EWL within the same time frame.²⁸⁻³⁰ More importantly, bariatric surgery results in the improvement and/or resolution of diabetes, hypertension, hyperlipidemia and obstructive sleep apnea.^{28,30} Finally, in terms of mortality, a study by Arterburn et al³¹ demonstrated that bariatric surgery was associated with a lower mortality when compared to matched controls at 1–5 years postoperatively (adjusted hazard ratio (HR): 0.45 [0.36-0.56]; $P < 0.001$), and >5–14 years (HR: 0.47 [0.39-0.58]; $P < 0.001$).

Given the effect of bariatric surgery on resolution of diabetes, hypertension, sleep apnea, and hyperlipidemia, these procedures are now more appropriately considered metabolic surgery. Although the mechanisms through which these effects are realized have not been completely elucidated, three hypotheses exist to explain the effect of surgery on type 2 diabetes.³² The foregut hypothesis postulates that exclusion of nutrients from the proximal bowel blocks “anti”-incretins, which causes increased incretin levels (glucagon-like peptide-1/peptide YY [GLP-1/PYY]) and improved glucose control. The mid-gut hypothesis suggests that rapid delivery of nutrients to the distal small bowel enhances intestinal gluconeogenesis, leads to activation of the hepato-portal glucose signaling system, decreases hepatic glucose production, and decreases appetite. Finally, the hindgut hypothesis proposes that rapid delivery of nutrients to the distal small bowel leads to increased levels of GLP-1 and PYY. Certainly increases in both GLP-1 and PYY are seen after procedures that involve intestinal bypass (RYGB, BPD/DS) and



reduction of stomach size (SG), both of which cause rapid delivery of nutrients to the L-cells of the distal small bowel, and increased production of these incretins.^{32,33}

Summary

Metabolic/bariatric surgery is an effective tool for weight loss and resolution of obesity-related comorbidities. However, surgical manipulation of intestinal anatomy can result in malabsorption of key vitamins and minerals. In order to mitigate these problems, patients must undergo an extensive medical and dietary work-up prior to surgery, and close follow-up after surgery in order to identify and rectify nutrient deficiencies with both comprehensive education and nutritional supplementation.

References

1. Levi J, Segal LM, Thomas K, St Laurent R, Lang A, Rayburn J. F as in Fat: How Obesity Threatens America's Future. Project of the Trust for America's Health and the Robert Wood Johnson Foundation. 2013 Report. Available at <http://www.rwjf.org/content/dam/farm/reports/reports/2013/rwjf407528>. Accessed November 24, 2015.
2. Finucane MM, Stevens GA, Cowan M, et al. National, regional, and global trends in body mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. *Lancet*. 2011;377(9765):557-567.
3. Butland B, Jebb S, Kopelman P, et al. Foresight: Tracking Obesity: Future Choices – Project Report. UK Government Office for Science. 2nd Ed. October 2007.
4. Dobbs R, Sawers C, Thompson F, et al. Discussion Paper. Overcoming Obesity: An Initial Economic Analysis. McKinsey Global Institute. November 2014.
5. Willett WC, Dietz WH, Colditz GA. Guidelines for healthy weight. *N Engl J Med*. 1999;341(6):427-434.
6. Adams KF, Schatzkin A, Harris TB, et al. Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. *N Engl J Med*. 2006;355(8):763-778.
7. Fontaine KR, Redden DT, Wang C, Westfall AO, Allison DB. Years of life lost due to obesity. *JAMA*. 2003;289(2):187-193.
8. Chiu M, Austin PC, Manuel DG, Shah BR, Tu JV. Deriving ethnic-specific BMI cutoff points for assessing diabetes risk. *Diabetes Care*. 2011;34:1741-1748.
9. Buchwald H. Consensus Conference Statement: Bariatric surgery for morbid obesity: health implications for patients, health professionals, and third-party payers. *J Am Coll Surg*. 2005;200:593-604. Available at <https://asmbs.org/resources/consensus-statement>. Accessed on January 6, 2016.
10. Bavaresco M, Paganini S, Lima TP, et al. Nutritional course of patients submitted to bariatric surgery. *Obes Surg*. 2010; 20(6):716-721.
11. Flancbaum L, Belsley S, Drake V, Colarusso T, Tayler E. Pre-operative nutritional status of patients undergoing Roux-en-Y gastric bypass for morbid obesity. *J Gastrointest Surg*. 2006;10(7):1033-1037.
12. Aills L, Blankenship J, Buffington C, Furtado M, Parrott J. ASMBS Allied Health Nutritional Guidelines for the surgical weight loss patient. *Surg Obes Relat Dis*. 2008;4:S73-S108.
13. Xanthakos SA. Nutritional deficiencies in obesity and after bariatric surgery. *Pediatr Clin North Am*. 2009;56(5):1105-1121.



14. Nguyen NT, Nguyen B, Gebhart A, Hohmann S. Changes in the makeup of bariatric surgery: a national increase in use of laparoscopic sleeve gastrectomy. *J Am Coll Surg*. 2013;216(2):252–257.
15. Herron DM, Tong W. Role of surgery in management of type 2 diabetes mellitus. *Mt Sinai J Med*. 2009;76(3):281-293.
16. Parikh MS, Fielding GA, Ren CJ. U.S. experience with 749 laparoscopic adjustable gastric bands: intermediate outcomes. *Surg Endosc*. 2005;19(12):1631-1635.
17. Gagner M, Deitel M, Kalberer TL, Erickson AL, Crosby RD. The Second International Consensus Summit for Sleeve Gastrectomy, March 19-21, 2009. *Surg Obes Relat Dis*. 2009;5(4):476-485.
18. Hess DS, Hess DW. Biliopancreatic diversion with a duodenal switch. *Obes Surg*. 1998;8(3):267-282.
19. Regan JP, Inabnet WB, Gagner M, Pomp A. Early experience with two-stage laparoscopic Roux-en-Y gastric bypass as an alternative in the super-super obese patient. *Obes Surg*. 2003;13(6):861-864.
20. Almogly G, Crookes PF, Anthonie GJ. Longitudinal gastrectomy as a treatment for the high-risk super-obese patient. *Obes Surg*. 2004;14(4):492-497.
21. Lee CM, Cirangle PT, Jossart GH. Vertical gastrectomy for morbid obesity in 216 patients: report of 2-year results. *Surg Endosc*. 2007;21(10):1810-1816.
22. Hutter MM, Schirmer BD, Jones DB, et al. First Report from the American College of Surgeons Bariatric Surgery Center Network: Laparoscopic Sleeve Gastrectomy has Morbidity and Effectiveness Positioned Between the Band and the Bypass. *Ann Surg*. 2011;254(3):410–422.
23. Rubino F. Bariatric surgery: effects on glucose homeostasis. *Curr Opin Clin Nutr Metab Care*. 2006;9(4):497-507.
24. McFarland RJ, Gazet JC, Pilkington TR. A 13-year review of jejunoileal bypass. *Br J Surg*. 1985;72(2):81-87.
25. Baddeley RM. The management of gross refractory obesity by jejuno-ileal bypass. *Br J Surg*. 1979;66(8):525-532.
26. Colquitt JL, Picot J, Loveman E, Clegg AJ. Surgery for obesity. *Cochrane Database Syst Rev*. 2009;(2):CD003641.
27. Sawaya RA, Jaffe J, Friedenber L, Friedenber FK. Vitamin, mineral, and drug absorption following bariatric surgery. *Curr Drug Metab*. 2012;13(9):1345-1355.
28. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. *JAMA*. 2004;292(14):1724-1737.
29. Sjostrom L, Lindroos AK, Peltonen M, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *N Engl J Med*. 2004;351(26):2683–2693.
30. Chang SH, Stoll CRT, Song J, Varela E, Eagon CJ, Colditz GA. The effectiveness and risks of bariatric surgery: an updated systematic review and meta-analysis, 2003–2012. *JAMA Surg*. 2014;149(3):275-287.
31. Arterburn DE, Olsen MK, Smith VA, et al. Association between bariatric surgery and long-term survival. *JAMA*. 2015;313(1):62-70.
32. Quercia I, Dutia R, Kotler DP, Belsley S, Laferrere B. Gastrointestinal changes after bariatric surgery. *Diabetes Metab*. 2014;40(2):87-94.
33. Park CW, Torquati A. Physiology of weight loss surgery. *Surg Clin North Am*. 2011;91(6):1149-1161.



Upper Gastrointestinal Surgery and Nutritional Implications

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The surgical aspects of diseases of the upper gastrointestinal (UGI) tract and the nutritional consequences of disorders that may affect these structures are presented in this summary. The complexity of resections and reconstructions of these structures and the resulting nutritional implications before and after surgery place the patient at risk for malnutrition.

The upper gastrointestinal tract consists of the oropharynx, esophagus, and the stomach. The act of swallowing or deglutition is voluntary, but the coordination of the muscles is involuntary. Surgery for malignancies involving the pharynx usually also requires lymph node removal, which is a rather extensive procedure. During recovery, and while the patient's ability to consume a normal diet is likely to be impaired, other methods of providing nutrition are needed, such as via feeding tubes placed through the nose or directly into the stomach.

The esophagus is a tubular structure that connects the pharynx to the stomach. The upper and lower sphincters serve to regulate food passage in the intended direction. Dysfunction of the lower sphincter can cause the not uncommon condition of gastro-esophageal reflux. Most cancers of the esophagus are treated by resection, ie, removal of the diseased segment involving multiple incisions. Although, minimally invasive methods are becoming more common.¹ Continuity is re-established by using the stomach or a segment of the large bowel (colon). In many cases, the entire esophagus has to be removed and the stomach or colon is reconnected or anastomosed to the pharynx in the neck. Procedures for gastroesophageal reflux are less extensive, and consist of recreating a valve at the junction of the esophagus and the upper part of the stomach.

The stomach may be affected by benign diseases or malignant conditions. Acid-peptic disease is managed quite effectively in most cases by medications that decrease acid production by the gastric mucosa. Complications of duodenal ulcers include perforation or bleeding which may require operative intervention. Malignant lesions need operative resections as the lymph nodes, too, need to be removed. Resection of part of the stomach requires reconstruction and re-establishment of continuity using the duodenum or the jejunum.² The anatomy of the stomach is also altered in procedures done for weight reduction.

Abnormalities in function of the mouth, pharynx and esophagus can thus impair the ability to swallow a regular diet. Abnormalities in cell structure are more serious, especially malignancies, causing obstruction of varying degrees. A simple matter of swallowing food that most people take for granted becomes difficult and painful. Strictures or tumors of the esophagus cause progressive decrease in food intake. Tumors of the stomach likewise cause decreased intake due to early satiety and obstruction to the outlet of the stomach leading into the duodenum.

In addition to a decreased food intake due to mechanical obstruction and pain, tumors cause an ill-understood condition of cachexia: progressive anorexia and weight loss, which can be partly explained by metabolic changes induced by the cancer cells.³ Treatment modalities such as chemotherapy and radiation therapy also cause



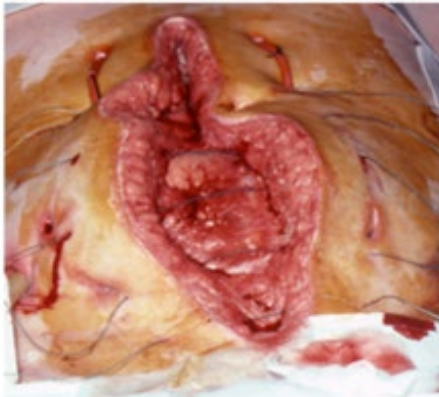
mucosal changes and ulcerations in the mouth, pharynx and esophagus further diminishing normal oral intake. The end result of advanced diseases of the upper gastrointestinal tract, whether benign or malignant, is weight loss, protein-energy malnutrition, and micronutrient deficiencies.

The nutrition care of patients with UGI tract problems begins in the preoperative period. There is clear evidence that providing balanced scientific enteral formulas as oral nutritional supplements (ONS) for 7 - 10 days prior to any major UGI tract surgery is highly cost-effective and decreases wound complications, length of stay, duration on ventilator, and anastomotic leaks.^{4,5} Preoperative nutritional supplementation is obviously not possible for emergency UGI surgical procedures. Under these circumstances, the clinician must maintain a high index of caution to establish a diagnosis of malnutrition risk based on a malnutrition screening tool.

Adjuvant therapeutic modalities are often needed for head and neck malignancies, and these include chemotherapy and radiation therapy. These often cause severe inflammation of the oropharyngeal mucosa, limiting normal intake and at times requiring termination of chemotherapy and radiation therapy. Paying close attention to the nutrition needs of the patient and providing optimal enteral feeding will often allow the physician to continue with the planned treatment.⁶

For optimal wound healing and recovery, enteral nutrition should be initiated as soon as possible after emergency surgical procedures, provided no major contraindications exist. The Enhanced Recovery After Surgery or ERAS protocols have been disseminated worldwide, although adherence to these recommendations is suboptimal. The protocols call for early resumption of oral feeding after surgery, avoiding routine nasogastric decompression, and encouraging early ambulation.⁷ The benefits of enteral nutrition on altering the stress response and immune function are important for healing and recovery.⁸ Parenteral nutrition may be necessary in specific conditions. Nutrition support should be maintained during and after treatment, irrespective of whether the treatment modalities include surgery, or non-surgical measures such as radiation therapy and chemotherapy. Enteral nutrition should be continued until the patient is able to consume an adequate regular diet by mouth. Failure to prevent or treat malnutrition in the pre- and postoperative periods can result in serious postoperative complications (Figure).

Case Study: Elective Stomach Surgery Postoperative Complication



Whose fault is this?

What went wrong?

- Advice of dietitian was ignored
- Obesity and sarcopenia not addressed
- Preop oral nutritional supplements not considered
- Enteral feeding was not started immediately postoperative
- Enteral nutrition was not advanced rapidly
- Lack of a system to address malnutrition

Figure. Elective stomach surgery postoperative complication.

Figure courtesy of Krishnan Sriram, MD,FACS,FRCSC,FCCM; Stroger Hospital of Cook County, Chicago, Illinois, USA.

Medications form an integral part of treating diseases of the esophagus or stomach, in addition to alterations in the diet. Medications often include acid-reducing agents; these can cause several nutrition-related side effects. Gastric acid enhances micronutrient availability, eg, zinc and iron from food, and deficiencies may occur after long term use of acid-reducing medications. Diarrhea due to overgrowth of *Clostridium difficile*, a “bad” bacteria in the colon, has been directly attributed to overuse of gastric acid-reducing agents.⁹ Drug-nutrient interactions must be kept in mind while caring for the nutrition needs of patients with UGI surgical problems.

Nutrition therapy of patients with UGI pathology forms an integral and crucial part of management. Preoperative nutrition assessment is important with nutrition interventions, including ONS, to attempt to decrease postoperative complications, such as leakage from anastomosis. Enteral feeding in the postoperative period is used preferentially, with parenteral nutrition reserved for the patient when gastrointestinal access is not possible, or enteral feeding is contraindicated. Adherence to evidence-based strategies for pre- and postoperative nutrition therapy is critical for enhanced recovery after UGI surgery.



References

1. Madden JL. *Atlas of Techniques in Surgery*, 2nd Ed. NY: Appleton—Century-Crofts, Meredith Publishing Co.; 1964:119,133.
2. Mann CV, Russell RCG, Williams NS. eds. *Bailey and Love's, Short Practice of Surgery*, 22nd Ed. London, UK: Chapman & Hall; 1995, Chapter 44, 682-683.
3. MacDonald N, Easson AM, Mazurak VC, Dunn GP, Baracos VE. Understanding and managing cancer cachexia. *J Am Coll Surg*. 2003;197(1):143-161.
4. Hegazi RA, Hustead DS, Evans DC. Preoperative standard oral nutrition supplements versus immunonutrition: results of a systematic review and meta-analysis. *J Am Coll Surg*. 2014;219(5):1078-1087.
5. Alshadwi A, Nadershah M, Carlson ER, Young LS, Burke PA, Daley BJ. Nutritional considerations for head and neck cancer patients: a review of the literature. *J Oral Maxillofac Surg*. 2013;71(11):1853-1860.
6. Bossola M. Nutritional interventions in head and neck cancer patients undergoing chemoradiotherapy. *Nutrients*. 2015;7(1):265-276.
7. Enhanced Recovery After Surgery (ERAS) Protocols. Available at <http://www.erassociety.org/>. Accessed September 18, 2015.
8. McClave SA, Martindale RG, Rice TW, Heyland DK. Feeding the critically ill patient. *Crit Care Med*. 2014;42(12):2600-2610.
9. Akamine D, Filho MK, Peres CM. Drug-nutrient interactions in elderly people. *Curr Opin Clin Nutr Metab Care*. 2007;10(3):304-310.



Pancreatic Surgery: Procedures, Complications, and Nutritional Implications

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The pancreas serves vital roles in the body's digestive and endocrine systems. Operations are most commonly performed upon the pancreas to remove abnormalities that are malignant, have malignant potential, or are causing symptoms, or to treat consequences of acute or chronic inflammation of the pancreas. This summary will provide an overview of the anatomy and physiology of the pancreas, describe common operations performed upon the pancreas, and discuss nutritional aspects of surgery performed upon the pancreas and complications of this surgery.

The pancreas lies deep in the upper abdomen behind the stomach, against the deep aspect of the abdominal cavity known as the retroperitoneum, and nestled in the curve of the duodenum. The pancreas is customarily described as having three regions: the head of the pancreas lies adjacent to the duodenum on the right side, the tail of the pancreas lies adjacent to the spleen toward the left side, and the body of the pancreas comprises the midportion between the head and tail. The bile duct passes through the head of the pancreas as it courses from the liver to the duodenum, and may be obstructed by processes affecting the head of the pancreas.

In its endocrine role, the pancreas produces chemicals (hormones) that enter directly into the circulation and exert their effects systemically. In contrast, in its digestive (exocrine) role, the pancreas produces a bicarbonate- and protein-rich fluid that enters into the duodenum where it mixes with and contributes to digestion of food. The exocrine pancreas comprises approximately 97% of the pancreatic mass. In contrast, the endocrine cells of the pancreas form clusters known as islets of Langerhans that are interspersed throughout the pancreas and comprise 2%-3% of the pancreatic mass.^{1,2} In contrast to the exocrine pancreas, the islets are not associated with or dependent upon ductal structures and therefore release their products directly into the bloodstream.

The acinar cells (the basic units of the exocrine pancreas) produce enzymes that are involved in the breakdown of food. Proteases breakdown polypeptides and proteins and comprise 80% of the proteins secreted by the pancreas.² These enzymes are stored and secreted in inactive forms in order to protect the pancreas from their actions. Trypsinogen is the most abundant protease. Lipases hydrolyze fats to fatty acids and triglycerides, amylase hydrolyzes starch into sugars, and nucleases cleave phosphodiesterase bonds in nucleic acids. Stimulated by secretin in the duodenum, the ductal cells secrete a bicarbonate-rich fluid that dilutes and alkalizes pancreatic juice, thereby neutralizing gastric acid and facilitating further digestion in the small intestine.

The most frequent indication for pancreatic surgery is for resection of neoplasms that are malignant or have malignant risk. This includes resection of pancreatic ductal adenocarcinoma and other less common malignancies, abnormalities with potential for development of pancreatic ductal adenocarcinoma such as intraductal papillary mucinous neoplasms or mucinous cystadenomas, pancreatic neuroendocrine tumors, and indeterminate masses. Surgery may also be performed for resection of benign but symptomatic masses, such as microcystic (serous) cystadenomas or pancreatic pseudocysts. Finally, surgery may be performed for treatment or prevention of complications of acute and chronic pancreatitis. This includes resection of



symptomatic enlargement of the pancreas (often referred to as “tumorous enlargement”) in chronic pancreatitis, ductal drainage procedures to drain obstructed and dilated pancreatic ducts, debridement and drainage of necrotic tissues or fluid collections including pseudocysts, and resection of the pancreas with recovery and autotransplantation of pancreatic islets in patients with or genetically predisposed to chronic and recurrent pancreatitis.

Operations performed upon the pancreas include resection procedures that remove portions of the pancreas (head, body, or tail), masses arising in the pancreas, or the entire pancreas. Operations may also be performed to drain the pancreatic duct when it is obstructed and dilated, as this may be the cause of chronic pain, or to drain fluid collections known as pseudocysts that result from leakage of pancreatic fluid caused by injury to the pancreas. Some procedures may also combine partial resection of the pancreas with drainage of the pancreatic duct. Debridement procedures are performed to remove portions of the pancreas and surrounding tissues that have died as a result of acute inflammation of the pancreas (pancreatitis).

Resection of the pancreatic head due to abnormalities is the most common operation performed upon the pancreas. Because the head of the pancreas, duodenum, and bile duct are intimately attached to one another and share their blood supplies, the duodenum and bile duct are removed together with the pancreatic head. This operation, known as a pancreaticoduodenectomy or Whipple procedure, requires reattachment of the stomach, bile duct, and remaining pancreas to the small intestine.

A left-sided, or distal pancreatectomy, is performed for resection of abnormalities arising in the body or tail of the pancreas. Commonly the spleen is also removed, as the blood supply to the spleen courses along the portion of pancreas being removed. To prevent leakage of pancreatic exocrine secretions, the divided end of the pancreas must be sealed, but in contrast to the Whipple procedure, no reconstruction is required after a left-sided pancreatectomy. Left-sided pancreatectomies are now commonly performed by minimally invasive (laparoscopic or robot-assisted) procedures. In a small number of specialized centers, pancreaticoduodenectomies (Whipple procedures) are performed as laparoscopic or robot-assisted minimally invasive procedures.

The range of complications associated with pancreatic surgery are best illustrated by the Whipple procedure, as complications can arise not only from the resection itself, but also from the necessary reconstruction, as well as the physiologic and functional changes inherent to this procedure. 30-day mortality has been estimated to be 1%-4%, 90-day mortality up to 8%, and 30-day morbidity to be 30%–60%.³⁻⁹

In addition to routine complications such as bleeding and infection, early complications may arise from the pancreatic, biliary, and gastrointestinal anastomosis. The pancreatic anastomosis is particularly prone to leak, potentially resulting in a pancreatic fistula, intra-abdominal abscess, or sepsis. Intra-abdominal leakage of activated enzymes in pancreatic secretions may cause pseudoaneurysms to form from ligated arteries, leading to major intra-abdominal bleeding.

Management of pancreatic fistulas includes drainage and control of infection. Nutrition support is critically important. Pancreatic rest is of uncertain benefit, but is frequently sought by means of distal enteral feeding or parenteral nutrition, use of somatostatin analogues, and pancreatic enzyme replacement therapy. For patients who have undergone distal pancreatectomies, pancreatic duct stenting may be helpful to promote normal antegrade flow of pancreatic secretions into the duodenum.



Fistulas may also arise from the anastomosis of the stomach or duodenum to the jejunum. This results in sepsis, fluid and electrolyte abnormalities, and diversion of the nutrient stream. Management consists of sepsis control, drainage, skin care, and correction of fluid and electrolyte abnormalities. Nutrition support is essential. When possible, enteral nutrition should be given. This may require feeding distal to the site of the fistula. Parenteral nutrition may at times be necessary.

The incidence of delayed gastric emptying after Whipple procedures is reported to be between 13% and 60%.¹⁰⁻¹² Consequences of delayed gastric emptying include nausea, vomiting, aspiration, malnutrition, prolonged hospitalization, and increased hospital cost. In patients who develop delayed gastric emptying, nutrition support should be initiated promptly. Nasojejunal feeding tubes placed through the gastro- (duodeno-) jejunal anastomosis allow for administration of enteral nutrition instead of parenteral nutrition.

Both Whipple procedures and distal pancreatectomies reduce the functional pancreatic mass. A Whipple procedure also results in altered pancreatic function. As a consequence, pancreatic exocrine insufficiency may result.

Preoperative malnutrition is common in patients undergoing pancreatic surgery. In patients with severe acute pancreatitis who require surgery, the systemic inflammatory process creates a highly catabolic state. Additionally, treatment of acute pancreatitis by means of limiting oral nutrition in order to achieve pancreatic rest may further contribute to malnutrition in patients with severe acute pancreatitis who require surgery.

The metabolic effects of cancer frequently lead to significant malnutrition in patients undergoing surgery for periampullary and pancreatic malignancies. Duodenal obstruction caused by such tumors in the pancreatic head may further contribute to preoperative malnutrition. La Torre et al¹³ reviewed 143 consecutive patients undergoing resection of such malignancies. Hypoalbuminemia was present in 36%, and was severe (≤ 2.5 g/dL) in 14%. In the 6 months prior to surgery, 72% lost more than 5% of their weight. Each of three clinical tools for assessment of malnutrition (Subjective Global Assessment, Nutritional Risk Index, and Malnutrition Universal Screening Tool) showed a high incidence of moderate and severe malnutrition. Most importantly, they found that preoperative malnutrition was a predictor of postoperative morbidity and mortality after pancreatic surgery (Figure).

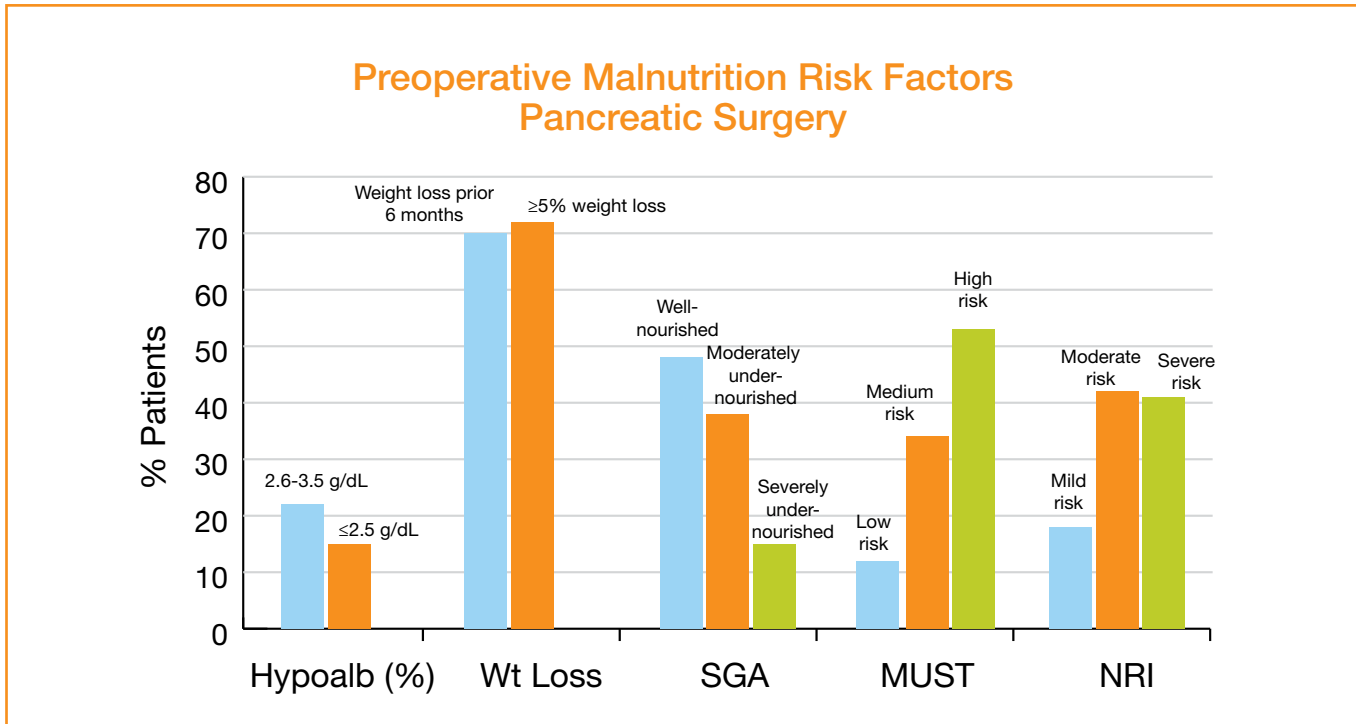


Figure. Preoperative malnutrition is common in patients undergoing pancreatic surgery.¹³

SGA=Subjective Global Assessment, MUST=Malnutrition Universal Screening Tool, NRI=Nutritional Risk Index, Hypoalb=hypoalbuminemia, Wt=weight

Source: La Torre M et al. Malnutrition and pancreatic surgery: prevalence and outcomes. *J Surg Onc.* 2013;107:702-708.

Nutritional deficits are common after pancreatic operations and compound pre-existing malnutrition. In a recent series of consecutive patients from our institution, 50% of patients lost 10% or more of their preoperative weight within 60 days of undergoing Whipple procedures (Lee, unpublished data). Some studies have shown return to preoperative weight within 4 to 6 months.^{14,15} However, in a series of 192 patients undergoing Whipple procedures with median follow up of 41 months and no evidence of recurrent malignancy, weight loss was persistent. The degree of weight loss averaged as much as 24 pounds in patients who had been treated for pancreatic adenocarcinoma.¹⁶

Decreased pancreatic exocrine function contributes to nutritional deficiencies occurring after pancreatic surgery. This may result from resection of pancreatic mass, and also from decreased pancreatic function. Stricture of the pancreaticojejunostomy may obstruct the flow of exocrine secretions into the intestine, and may also lead to atrophy of the obstructed pancreas with further loss of pancreatic function. Resection of the duodenum (the primary source of cholecystinin-releasing protein, cholecystinin, and secretin) may also alter stimulation of pancreatic secretion, and further contribute to decreased exocrine function.

Pancreatic exocrine insufficiency results in maldigestion of fat and protein. Although overt steatorrhea is not evident until 90% of pancreatic exocrine function has been lost, GI symptoms and nutritional deficiencies may result at lower levels of loss. Weight loss, bloating, cramping, increased flatulence, and diarrhea may occur. Fat-soluble vitamin (A, D, E, and K) deficiencies may also develop.¹⁷



Awareness of the potential for exocrine insufficiency is therefore important, and testing for nutritional and pancreatic exocrine insufficiency should be considered. In addition to nutrition and biochemical assessments including fat-soluble vitamin levels, tests of pancreatic function can be performed. Direct pancreatic function tests are specific and sensitive but cumbersome to perform. Consequently, indirect tests of pancreatic function are usually employed instead. However, these tests are less sensitive and frequently do not detect mild or moderate pancreatic insufficiency. When pancreatic insufficiency is diagnosed, pancreatic enzyme replacement therapy should be initiated. Ten percent of normal lipase secretion is usually sufficient to control steatorrhea.¹⁸ Enzymes should be timed to mix thoroughly with food, and degradation by gastric acid should be avoided through use of enteric-coated enzyme preparations and acid suppressive therapy.

In summary, a variety of operations are performed on the pancreas for treatment of mass lesions and complications of pancreatitis. Malnutrition is often present in patients undergoing these operations, and increased morbidity and mortality are associated with these operations. These operations may cause loss of pancreatic mass or alterations in pancreatic function which, together with normal postoperative recovery and surgical complications, place patients undergoing pancreatic surgery at significant risk for developing nutritional deficiencies. Strategies should be employed to mitigate, diagnose, and treat these nutritional deficiencies.

References

1. Lacy PE. The pancreatic beta cell. Structure and function. *N Engl J Med*. 1967;276(4):187-195.
2. Chang EB and Leung PS. Pancreatic physiology. In: Leung PS, ed. *The Gastrointestinal System: Gastrointestinal, Nutritional and Hepatobiliary Physiology*. Ed. Springer Science+Business Media, Dordrecht, Netherlands;2014.
3. Braga M, Capretti G, Pecorelli N, et al. A prognostic score to predict major complications after pancreaticoduodenectomy. *Ann Surg*. 2011;254(5):702-707.
4. Winter JM, Cameron JL, Campbell KA, et al. 1423 pancreaticoduodenectomies for pancreatic cancer: a single institution experience. *J Gastrointest Surg*. 2006;10(9):1199-1210.
5. Balzano G, Zerbi A, Capretti G, Rocchetti S, Capitanio V, Di Carlo V. Effect of hospital volume on outcome of pancreaticoduodenectomy in Italy. *Br J Surg*. 2008;95(3):357-362.
6. Asbun HJ, Stauffer JA. Laparoscopic vs open pancreaticoduodenectomy: overall outcomes and severity of complications using the Accordion Severity Grading System. *J Am Coll Surg*. 2012;215(6):810-819.
7. Pugalenth A, Protic M, Gonen M, et al. Postoperative complications and overall survival after pancreaticoduodenectomy for pancreatic ductal adenocarcinoma. *J Surg Oncol*. 2016;113(2):188-193.
8. Hata T, Motoi F, Ishida M, et al. Effect of hospital volume on surgical outcomes after pancreaticoduodenectomy: a systematic review and meta-analysis. *Ann Surg*. 2015 Nov 28. doi:10.1097/SLA.0000000000001437. Epub ahead of print.
9. Ceppa EP, Pitt HA, Nakeeb A, et al. Reducing readmissions after pancreatectomy: limiting complications and coordinating the care continuum. *J Am Coll Surg*. 2015;221(3):708-716.
10. Malleo G, Crippa S, Butturini G, et al. Delayed gastric emptying after pylorus-preserving pancreaticoduodenectomy: validation of International Study Group of Pancreatic Surgery classification and analysis of risk factors. *HPB (Oxford)*. 2010;12(9):610-618.



11. Wente MN, Bassi C, Dervenis C, et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery*. 2007;142(5):761-768.
12. Traverso LW, Hashimoto Y. Delayed gastric emptying: the state of the highest level of evidence. *J Hepatobiliary Pancreat Surg*. 2008;15(3):262-269.
13. La Torre M, Ziparo V, Nigri G, Cavallini M, Balducci G, Ramacciato G. Malnutrition and pancreatic surgery: prevalence and outcomes. *J Surg Onc*. 2013;107:702-708.
14. Niedergethmann M, Shang E, Soliman MF, et al. Early and enduring nutritional and functional results of pylorus preservation vs classic Whipple procedure for pancreatic cancer. *Langenbecks Arch Surg*. 2006;391(3):195-202.
15. Park JW, Jang JY, Kim EJ, et al. Effects of pancreatectomy on nutritional state, pancreatic function and quality of life. *Br J Surg*. 2013;100(8):1064-1070.
16. Huang JJ, Yeo CJ, Sohn TA, et al. Quality of life and outcomes after pancreaticoduodenectomy. *Ann Surg*. 2000;231(6):890-898.
17. DiMagno EP, Go VL, Summerskill WH. Relations between pancreatic enzyme outputs and malabsorption in severe pancreatic insufficiency. *N Engl J Med*. 1973;288(16):813-815.
18. Fieker A, Philpott J, Armand M. Enzyme replacement therapy for pancreatic insufficiency: present and future. *Clin Exp Gastroenterol*. 2011;4:55-73.



Colectomy: Procedures, Complications, and Nutritional Implications

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Colectomies involve a surgical resection of the colon. Three aims are presented in this summary. First, to describe the anatomy, common colon operations, and indications for surgery; second, to discuss complications associated with colon operations; and third, to discuss the direct and indirect nutritional implications associated with colon surgery.

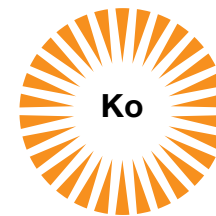
The intestine is sectioned into upper and lower tracts, with the lower tract identified as the lower gastrointestinal (GI) tract, or large intestine. The large intestine is divided into the colon, rectum, and anus. The border between the small and large intestine is the ileocecal valve, where the ileum (the most distal part of the small intestine) connects to the most proximal part of the large intestine, also known as the cecum. Parenthetically, the appendix is located as an appendage at the base of the cecum. After the cecum, the colon is commonly divided into the ascending colon, the hepatic flexure, the transverse colon, the splenic flexure, the descending colon, and sigmoid colon. The rectum and anus follow the sigmoid colon, with the endpoints of the large intestine serving as a conduit and reservoir, and area of defecation, respectively.

Many colon and rectal “resections” are performed in surgery, and often are described by the anatomic part of the large intestine that is being removed – eg, ileo-cecectomy involves resection of the distal portion of the ileum and the cecum with removal of the ileocecal valve. A sigmoid colectomy involves removal of the sigmoid colon. When a portion of the large intestine is removed, the most commonly performed “reconstruction” is to join the two pieces together to restore bowel continuity (ie, with an anastomosis). Depending on the location of the anastomosis and other factors (such as nutritional status), a proximal diversion may be performed, commonly known as an ostomy. Patients often refer to their ostomy as a “bag” or “stoma”. Depending on the site of the ostomy and if the ileocecal valve is removed, issues with hydration, nutrition, and other complications may exist.

The many reasons for resecting the large intestine are beyond the scope of this review. It should be recognized that the disease process, malignant or benign, influences the location and amount of resection. Within each of these distinctions, there are different stages usually aligning with the severity of the disease process. Finally, patient factors such as comorbidities (eg, diabetes) and nutritional status can also play a role in the location and amount of resection.

When we think of results or outcomes of a procedure, one primary focus is the outcome of the disease process. For example, the outcome of the disease process involves assessment for cancer cure, or relief of symptoms, eg, pain. Complications or occurrences are other outcomes of importance to the surgeon and healthcare organization. Occurrences can be categorized in numerous ways. Some of the more common occurrences include infection, dehydration, anatomic/mechanical complications, patient-reported outcomes/issues, increased resource use (eg, readmission, reoperation, length of stay), and nutritional issues.

Colectomy



The American College of Surgeons (ACS) has one of the best and most accurate clinical data registries in surgery known as the National Surgical Quality Improvement Program (ACS NSQIP). The ACS NSQIP Risk Calculator was developed from data in this registry. This tool estimates a patient's risk for complications using information about the procedure and patient factors. The ACS NSQIP Risk Calculator is available on the American College of Surgeons website (www.facs.org).¹

In the current healthcare environment, value is an increasingly important priority. In this regard for surgical operations, the outcome is one part of the value equation, with the other part being the economic impact. The economic part of the equation is measured in several ways, with "resource use" often measured. A common resource metric in surgical operations is length of stay – a longer length of stay increases resource use. A study published in 2009 found that hospitals performing colon operations have great variability in terms of length of stay, even when patient factors are accounted for.² Today the results from these analyses are unchanged – with variability in terms of length of stay for colectomy, and looking only at patients who have no complications.

What is interesting from these types of analyses for length of stay is that the median length of stay remains about 7 days for colectomy.² Of concern is that a patient will often remain without adequate nutrition support for 5-6 days or even longer. Food intake is often very limited following a colon operation, and through the early stages of recovery.

Several studies have examined nutritional issues in colon surgery. Montomoli et al³ addressed the impact of preoperative serum albumin on 30-day mortality following colorectal cancer surgery. This population-based cohort study (Denmark) found that 12% of patients undergoing colorectal operations are hypoalbuminemic. The risk of hypoalbuminemia is higher if the operation is non-elective, or the cancer stage is advanced. 30-day mortality increased from 4.9% among patients with albumin level 36-40 g/L to 26.9% among patients with albumin ≤ 25 g/L, compared to 2% among patients with albumin above 40 g/L (Figure).

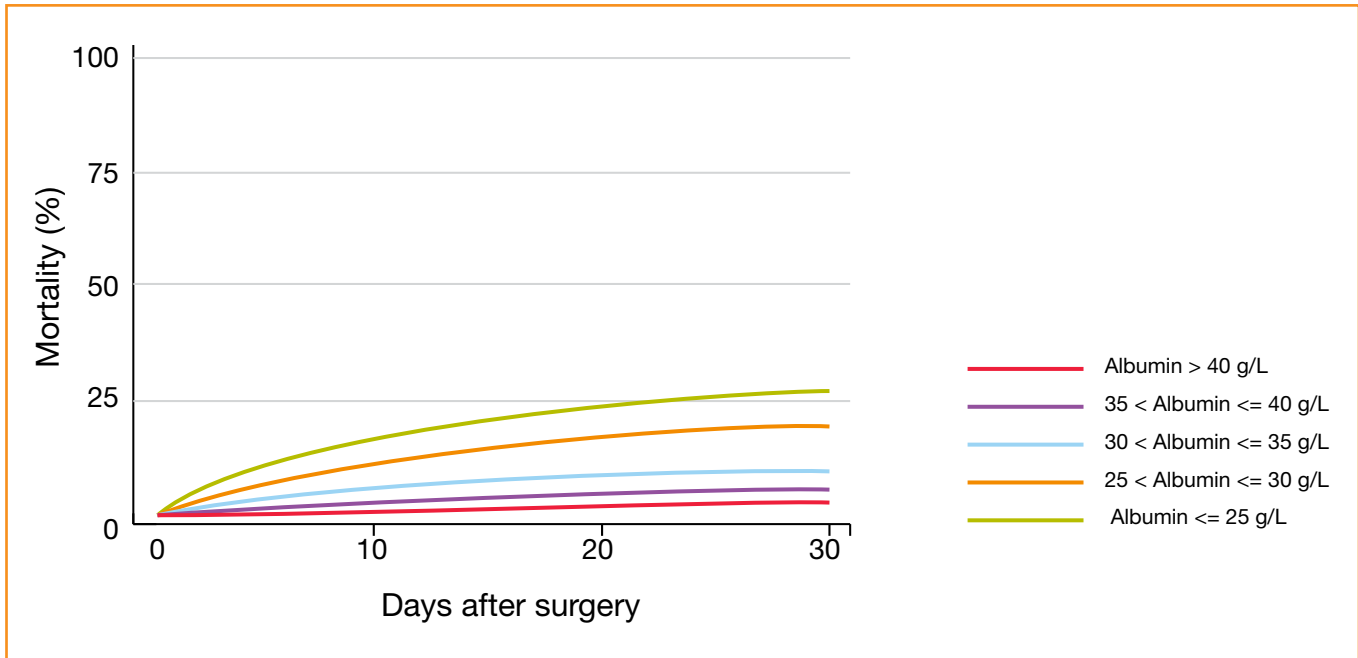


Figure. Crude 30-day mortality curves for patients undergoing surgery for colorectal cancer according to preoperative serum albumin concentration.³

Source: Montomoli J et al. Impact of preoperative serum albumin on 30-day mortality following surgery for colorectal cancer: a population-based cohort study. *BMJ Open Gastroenterol.* 2015; 2(1): e000047. doi: 10.1136/bmjgast-2015-000047.

Frasson et al⁴ and Telem et al⁵ identified the possible association of lower albumin levels and occurrences, including anastomotic leak and 30-day mortality. While these studies have some methodological limitations, there are trends and associations of low albumin and anastomotic leak and mortality. This is important because while disease processes may or may not be mutable, the issue of malnutrition can be addressed.

After a routine colorectal operation, most patients lose approximately 15 pounds of weight. This weight loss from nutritional and hydration deficits is often a potentially important issue given postoperative healing substantially occurs in this time period. This may be at least part of the reason why hypoalbuminemia has been found to be associated with unfavorable occurrences. Although imperfect, using albumin as a marker has shown trends and is still often used to assess risk.

There is little information in the peer-reviewed published literature on patient dietary intake and food-related symptoms following colorectal operations, especially in the period after hospital discharge. With social media and public patient blogs, it is enlightening to review the patient's perspective on food tolerances, dietary progression, and intestinal/ostomy issues in the care continuum following hospital discharge after a colorectal operation.

More information and evidence-based practice guidelines are needed to address the impact of preoperative and postoperative nutrition interventions on colorectal surgery outcomes.



References

1. American College of Surgeons. ACS NSQIP Surgical Risk Calculator. Available at <http://riskcalculator.facs.org/>. Accessed November 19, 2015.
2. Cohen ME, Bilimoria KY, Ko CY, Richards K, Hall BL. Variability in length of stay after colorectal surgery: assessment of 182 hospitals in the national surgical quality improvement program. *Ann Surg.* 2009; 250(6):901-907.
3. Montomoli J, Erichsen R, Antonsen S, Nilsson T, Sorensen HT. Impact of preoperative serum albumin on 30-day mortality following surgery for colorectal cancer: a population-based cohort study. *BMJ Open Gastroenterol.* 2015;2(1):e000047. doi: 10.1136/bmjgast-2015-000047.
4. Frasson M, Granero-Castro P, Rodriguez JL, et al. Risk factors for anastomotic leak and postoperative morbidity and mortality after elective right colectomy for cancer: results from a prospective, multicentric study of 1102 patients. *Int J Colorectal Dis.* 2016;31(1):105-114.
5. Telem DA, Chin EH, Nguyen SQ, Divino CM. Risk factors for anastomotic leak following colorectal surgery: a case-control study. *Arch Surg.* 2010;145(4):371-376.



Scientific Update on Perioperative Nutrition

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Preoperative Carbohydrate Loading and Nutritional Supplementation: A Scientific Update

Maria Isabel Correia, MD, PhD

The gastrointestinal surgical patient is one among many, but despite the different types of procedures these patients undergo, one commonality among surgical patients is the organic response triggered by the stress of the operation. In this regard, the body behaves according to its previous metabolic, immunologic, and nutritional status, which directly depends on previous and/or concomitant comorbidities. These web-like phenomena are the response to the different surgical stimuli that start before the operation, such as the psychological stress of the surgical challenge, the common preoperative fasting state, and a suboptimal nutritional status.¹

The organic response is marked by the release of stress hormones such as the corticotropin-releasing hormone (CRH), the antidiuretic hormone (ADH), aldosterone, glucagon, and several catecholamines (dopamine, norepinephrine and epinephrine). Once the stress event occurs, the activated sympathetic nervous system triggers the release of CRH in the hypothalamus, which goes on to stimulate the adrenal gland to produce catecholamines. Simultaneously, the alpha-pancreatic cells release glucagon, which together with the catecholamines, induce the liver production of the enzyme phosphorylase that converts stored glycogen to glucose. The enzyme phosphorylase is only available in the liver; the other organs depend on other mechanisms to produce glucose. Simultaneously to this event, the available plasma glucose depends on cell insulin carriers for transport inside muscle and fat cells. However, the phenomenon “insulin resistance” often occurs as a result of insulin signaling defects, mainly on the glucose transporter type 4 (GLUT4) carrier. According to the World Health Organization, insulin resistance is a state in which, under hyperinsulinemic-euglycemic conditions, glucose uptake is below the lowest quartile for the population under investigation.²

Insulin resistance, which happens together with decreased muscle glucose oxidation, and increased muscle catabolism leading to negative nitrogen balance, is further associated with decreased muscle mass, and thus reduced muscle strength. Insulin resistance is directly proportional to the magnitude of the surgical insult and is related to postoperative complications due to different events. For example, reduced muscle mass and strength impair respiratory function causing increased risk of pulmonary complications, such as pneumonia. It is still unclear as to whether all of these events have a common signaling pathway. Nonetheless, insulin resistance is a risk factor for hyperglycemia, which negatively impacts surgical outcomes.³

Ata et al⁴ assessed a 2,090 general and vascular surgery patient database. They reported that, among general surgical patients, those with serum glucose levels between 110 to 140 mg/dL had a risk of surgical site infection (SSI) of 3.61; for those with levels between 141 to 180 mg/dL, the risk was 6.26; in between 181 to 220 mg/dL, it was 5.62; and higher than 220 mg/dL, there was a very high risk of SSI (odds ratio of 12.13).

Metabolically speaking, under normal physiological conditions, insulin is the predominant hormone released throughout the day, leading to storage of substrates. When excess carbohydrates are present, fat is stored. On the contrary, nighttime fasting states normally result in a decrease in insulin production while the hormones



glucagon and cortisol increase. Thus, there is substrate breakdown of fat and carbohydrate release. Under the organic response to stress, the latter process is complicated by the release of all the other aforementioned hormones, essentially glucagon and cortisol, leading to increased substrate breakdown (release of glucose), which at the same time, due to insulin resistance, will lead to hyperglycemia. Concomitantly, the muscle lacks energy (ie, no glucose available from outside and no enzyme phosphorylase), therefore it undergoes protein breakdown to provide glucose through gluconeogenesis. It is noteworthy to mention that the nutritional status of the patient also plays a key role in this whole metabolic milieu.

It has long been acknowledged that a deficient nutritional status negatively impacts body composition and function. In a 1950 Minnesota study, healthy young men that underwent a 24-week semi-fasting period lost approximately 23% of their usual weight and developed mental and physical function impairments. The level of depression among these men increased by 30%, while muscle and respiratory function decreased by 30% and overall physical functional capacity decreased by 70%.⁵ In a historical study from 1936 assessing surgical patients, Studley reported the association between nutritional status and surgical outcomes among patients undergoing gastric procedures for ulcer treatment.⁶ Those that lost more than 20% of their usual body weight had a 33% mortality rate versus 3.1% in the group that lost less than 20% of their usual weight. In a later historical study from 1955, Rhoads and Alexander clearly showed the association between preoperative nutritional status and surgical outcomes.⁷ More recently, Kassin et al., used the standard National Surgical Quality Improvement Project protocol to assess postoperative outcomes on patients undergoing general surgery procedures at a single academic center between 2009 and 2011.⁸ They showed that “failure to thrive/malnutrition” was the third most common risk factor for hospital readmissions. It is evident from these studies that the association between poor nutritional status and negative surgical outcomes has been documented for many years.

It seems there would be a logical pathway between this apparent malnutrition associated with surgical patients and a call to action to reduce these aforementioned complications. However, metabolic and nutritional conditioning of surgical patients is still not widely recognized among surgeons. It seems there is a gap that exists between what is known and what is done. This is well expressed in Ana Cleveland’s article, “Miles to go before we sleep: education, technology, and the changing paradigms in health information”.⁹

Preoperative fasting is routine worldwide, although clear liquids can be safely offered up to two hours before surgery.¹⁰ Standard clear liquids, however, do not contain enough carbohydrates to provide sufficient energy. Providing a metabolic conditioning drink preoperatively, ie, a carbohydrate-rich drink, would model the fasting state in a postprandial status. The first studies on preoperative oral carbohydrate-rich drinks from the 1990’s and early 2000’s showed that this approach was not only clinically feasible, but also impacted insulin production and insulin resistance.^{11,12} In addition, preoperative carbohydrate drinks improved patient well-being mainly through improvement in thirst and hunger sensations.¹³

More recently, it was shown that preoperative carbohydrate loading (175-200 g CHO) attenuates protein breakdown and maintains whole-body protein balance following surgery.¹⁴ Overall, preoperative carbohydrate loading has been shown to improve clinical outcomes. However, carbohydrate loading is still not a reality in most surgical centers.



Carbohydrate Loading

In summary-CHO loading

- Reduces insulin resistance and hyperglycemia
- Reduces preoperative discomfort
- Decreases postoperative nausea and vomiting
- Preserves muscle mass

If malnutrition *per se* interferes with surgical outcomes, providing preoperative nutrition therapy to these patients should be a standard practice. Simple nutrition screening and assessment tools, such as those proposed by the feedM.E. (Malnutrition Awareness & Education) Global Study Group, can quickly and effectively address preoperative nutritional status and intervention (Figure).¹⁵ Providing early oral nutritional supplementation, for those with no contraindication to use the gastrointestinal tract, was shown to increase energy and protein intake resulting in a favorable impact on the number and severity of surgical complications.^{15,16}

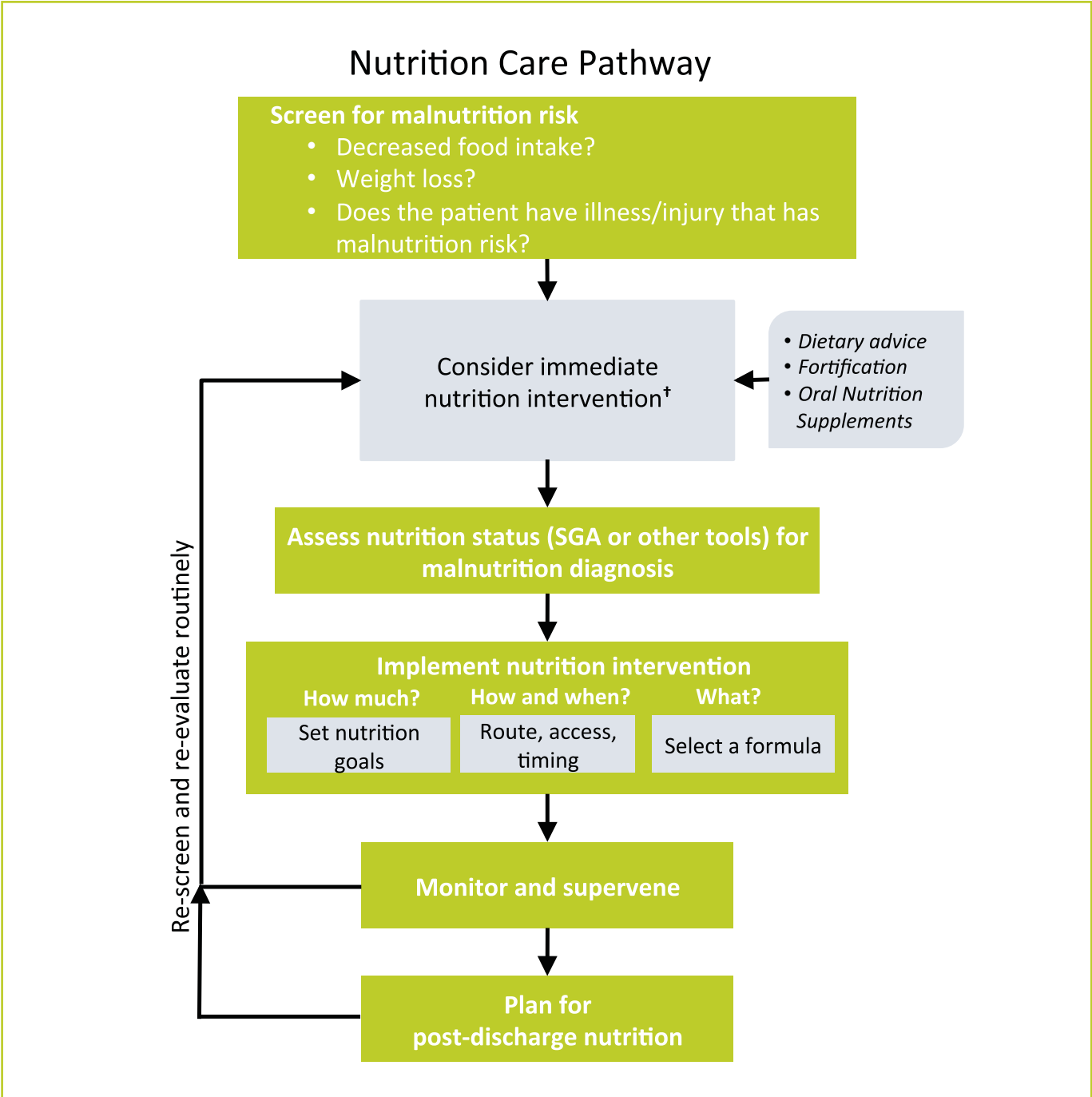


Figure. The Nutrition Care Pathway.¹⁵

†For individuals who can tolerate oral feeding
SGA=Subjective Global Assessment

Source: Correia MI et al. Evidence-based recommendations for addressing malnutrition in health care: an updated strategy from the feedM.E. Global Study Group. *J Am Med Dir Assoc.* 2014;15(8):544-550.



In conclusion, the metabolic and nutritional conditioning of surgical patients should be prioritized based on current scientific knowledge. However, communication strategies must be improved to more effectively implement science into practice.

References

1. Correia MI. Organic response to stress. In: Cresci GA, ed. *Nutrition support for the critically ill patient*. Second ed. Boca Raton, Florida, USA: Taylor and Francis; 2015.
2. Alberti KG, Gray DP. The care of diabetes. *Diabet Med*. 1998;15(Suppl 3):S3-S4.
3. Schrickler T, Lattermann R. Perioperative catabolism. *Can J Anesth*. 2015;62(2):182-193.
4. Ata A, Lee J, Bestle SL, Desemone J, Stain SC. Postoperative hyperglycemia and surgical site infection in general surgery patients. *Arch Surg*. 2010;145(9):858-864.
5. *The Biology of Human Starvation*. Keys A, Brozek A, Henschel O, Mickelson O, Taylor HL, ed. Minneapolis: University of Minnesota Press; 1950.
6. Studley HO. Percentage of weight loss: basic indicator of surgical risk in patients with chronic peptic ulcer. *JAMA*. 1936;106(6):458-460.
7. Rhoads JE, Alexander CE. Nutritional problems of surgical patients. *Ann N Y Acad Sci*. 1955;63(2):268-275.
8. Kassin MT, Owen RM, Perez SD, et al. Risk factors for 30-day hospital readmission among general surgery patients. *J Am Coll Surg*. 2012;215(3):322-330.
9. Cleveland AD. Miles to go before we sleep: education, technology, and the changing paradigms in health information. *J Med Libr Assoc*. 2011;99(1):61-69.
10. Pogatschnik C, Steiger E. Review of preoperative carbohydrate loading. *Nutr Clin Pract*. 2015;30(5):660-664.
11. Nygren J, Thorell A, Jacobsson H, et al. Preoperative gastric emptying: effects of anxiety and oral carbohydrate administration. *Ann Surg*. 1995;222(6):728-734.
12. Nygren J, Soop M, Thorell A, Sree Nair K, Ljungqvist O. Preoperative oral carbohydrates and postoperative insulin resistance. *Clin Nutr*. 1999;18(2):117-120.
13. Hausel J, Nygren J, Lagerkranser M, et al. A carbohydrate-rich drink reduces preoperative discomfort in elective surgery patients. *Anesth Analg*. 2001;93(5):1344-1350.
14. Svanfeldt M, Thorell A, Hausel J, et al. Randomized clinical trial of the effect of preoperative oral carbohydrate treatment on postoperative whole-body protein and glucose kinetics. *Br J Surg*. 2007;94(11):1342-1350.
15. Correia MI, Hegazi RA, Higashiguchi T, et al. Evidence-based recommendations for addressing malnutrition in health care: an updated strategy from the feedM.E. Global Study Group. *J Am Med Dir Assoc*. 2014;15(8):544-550.
16. Correia MI, Hegazi RA, Diaz-Pizarro Graf JI, et al. Addressing disease-related malnutrition in healthcare: a Latin American perspective. *JPEN J Parenter Enteral Nutr*. 2016;40(3):319-325.



Nutritional Management of Emergency Gastrointestinal (GI) Surgeries

Alexander Sauper, MD, FACS

Introduction

Emergency gastrointestinal (GI) surgery is different than elective GI surgery in many ways. Emergencies are unplanned, are often associated with a greater number of patient comorbidities, and impart greater physiologic stress on the patient than elective operations.¹⁻³ Although the overall goals of treatment are essentially the same regardless of the urgent/emergent nature of the surgical procedure, there are some important nutritional considerations to take into account that are unique to the emergency GI surgery population.

Metabolism

The human body is composed of fat and lean masses. Fat mass, the larger of the two energy compartments, is metabolically inactive and is primarily used for energy storage. Lean mass is much smaller, but is both highly metabolically active and regulated. This lean compartment is composed largely of skeletal and smooth muscles.

Under normal circumstances, energy is obtained from the metabolism of ingested food, whereas the fat compartment is used to either store excess calories, or provide calories in times of need assuming adequate oxygen is available for energy production. Protein intake is used for protein synthesis and maintaining lean mass.

In starvation conditions, the metabolic rate decreases to about 20-25 kcal/kg/day with the majority of energy (>90% of kcal) obtained from the fat mass. The lean mass protein store is protected with <10% of energy sourced from protein. Following a catabolic insult, however, no adaptive response is achieved and there are several consequences: the metabolic rate increases to as high as 40 kcal/kg/day, lean mass is catabolized for energy, and the fat mass is inefficiently utilized as an energy source.⁴

Malnutrition

The malnutrition syndrome is the modern classification of different metabolic states in undernutrition and obesity (Figure). Undernutrition refers to three different disease states: chronic starvation without inflammation, chronic disease with inflammation (eg, cancer cachexia), and acute disease/injury with inflammation (eg, perforated ulcer). Undernutrition contributes to macronutrient (protein and fat) and micronutrient (vitamin and mineral) deficiencies, and sarcopenia.⁵

Obesity is not protective from complications relating to malnutrition since the lean mass compartment is preferentially catabolized in the face of acute stress. Additionally, obesity is associated with sarcopenia and the metabolic syndrome. Complications of the metabolic syndrome, eg, high blood pressure, high cholesterol/triglycerides, and insulin resistance, are risk factors for cardiovascular disease, diabetes, and stroke.⁵

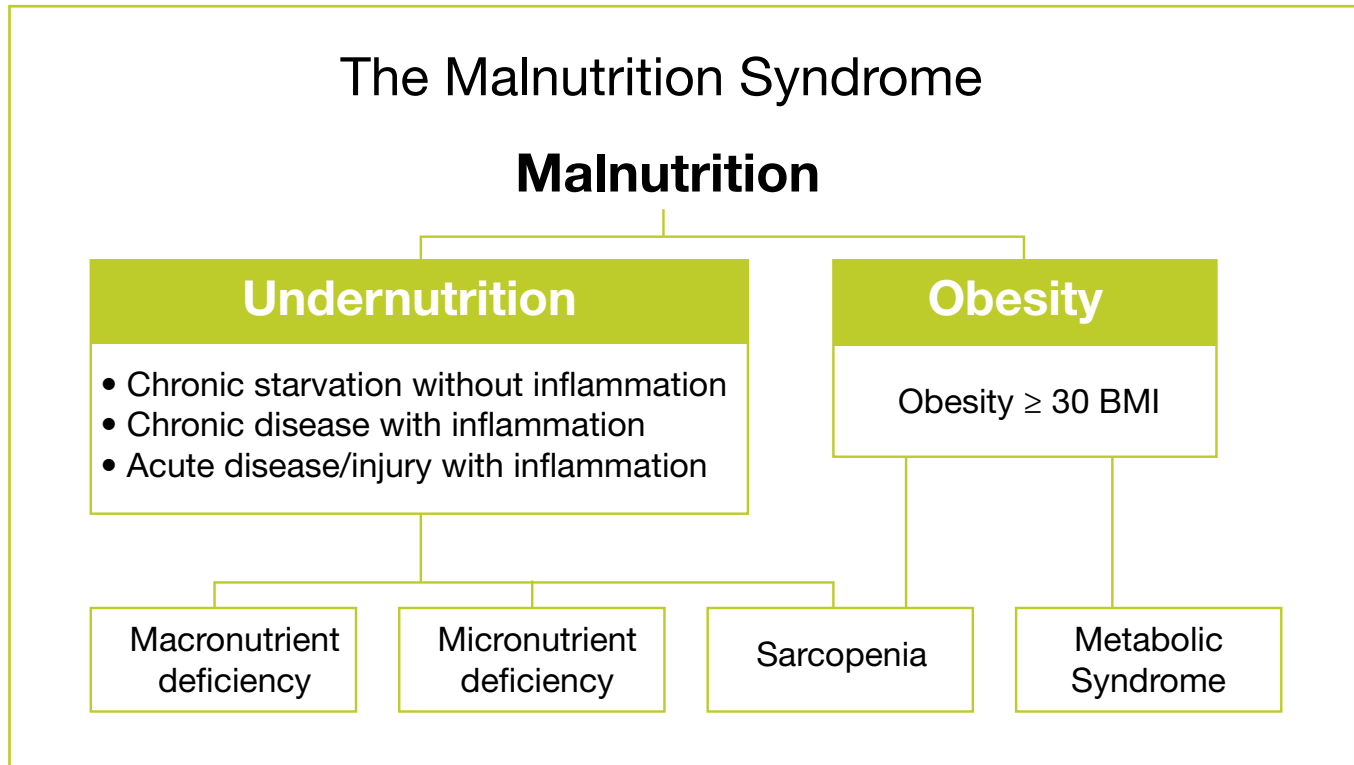


Figure. The malnutrition syndrome.⁵

BMI=Body Mass Index

Source: Advisory Faculty: Correia MI, Hegazi R, Llido L, Rugeles S, Sriram K. TNT 3.0. Total Nutrition Therapy. An Integrated Approach to Patient Care. Chicago: Abbott Nutrition Health Institute. 2011.

GI Surgeries

The indications for performing an emergency GI surgery are for organ perforation, ischemia (lack of blood flow) with or without organ death, bleeding, infection, obstruction, or loss of function. This might involve removing all or part of an organ, draining a deep infection, altering the flow of the various GI contents (eg, bile, pancreatic fluid, food transit), or restoring function to an organ (eg, relieving an obstruction). Some or all of these procedures may be combined depending on the complexity of the problem. In essence, the goals are to treat the condition, such as bleeding or perforation, and restore GI continuity so the body can continue to function.

The technical aspects of performing an operation are only part of the treatment plan, and consideration must be given to how the clinician manages the patient both pre- and postoperatively so the body can heal properly while avoiding, or at least minimizing, complications. There is a window of opportunity within the first 24 to 72 hours following a hypermetabolic insult, such as surgery, in which starting enteral feedings are associated with preserving gut integrity as well as diminishing the activation of inflammatory and counterproductive cytokines.⁶



Enteral versus Parenteral Nutrition

Because of the challenges involved in patient care, prescribing the proper nutrition support has been given much attention and has led to the creation of national guidelines by multiple collaborating national and international societies. In an intensive care unit (ICU) setting, there are many barriers to the successful implementation of enteral feeding due to the complexity of these patients. One example mnemonic, “CAN WE FEED,” is helpful to the clinician by simplifying the process of prescribing nutrition support. It involves assessing the patient, defining the timeframe in which to start feeding, determining formula selection, and monitoring for tolerance and complications.⁷ One might ask why not simply feed everyone intravenously with total parenteral nutrition until they are recovered and avoid having to go through this evaluation process? The answer is the medical literature has definitively established the benefit of enteral nutrition over parenteral nutrition in multiple studies across a wide variety of patients in terms of cost, complications, and benefit.⁶ In essence, if the gut works, use it.

In the event parenteral nutrition is required, the American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) guidelines recommend a “late” approach, ie, after seven days of inadequate nutrition support as opposed to their European counterpart (European Society for Clinical Nutrition and Metabolism, ESPEN), who suggests an “early” approach may be better, ie, within 48 hours.^{6,8} In one recent study of critically ill patients that were not malnourished at baseline, those who had parenteral nutrition and started “late” did better than those started “early” in terms of infections, ventilator days, and ICU stay. There was no difference in mortality. Furthermore, in the subgroup of sicker patients with complicated pulmonary or abdominal surgery, a lower infection rate was also noted with a relative increase in earlier ICU discharge alive. The authors concluded that earlier achievement of nutritional goals by utilizing parenteral nutrition did not improve outcomes for critically ill patients.⁹

Several studies utilizing the National Surgical Quality Improvement Project database (NSQIP) have examined the difference between elective and emergency GI surgeries. In general, elective GI surgery patients are undergoing planned operations with minimal to no stress response preoperative. In addition, they have less complications as well as a lower mortality than emergency GI surgery patients.³

In the elective GI surgery population, the safety and efficacy of early enteral nutrition have been very well established and is supported by numerous major international organizations. Furthermore, it has been incorporated into the Enhanced Recovery After Surgery (ERAS) concept and adopted by many medical centers and hospitals in the care of those patients.¹⁰ In the general critically ill population, it has also been established that early enteral feeding is beneficial.¹¹ The question that remains is what can be done about one of the sickest populations--emergency GI surgery patients--who have more complications and die more frequently than the elective patients? Can the data from elective surgery be extrapolated to emergency GI surgery populations to improve outcomes?

There is a limited amount of data regarding the use of early enteral nutrition in the emergency GI surgery population. Several smaller observational studies, a retrospective analysis, and a randomized controlled trial have examined this issue, and found that in both traumatic and non-traumatic conditions leading to emergency GI surgery, there is no increase in surgical complications, such as anastomotic leak, wound dehiscence, sepsis, and death with early enteral nutrition. Vomiting appears to be the only identified complication from initiating early enteral nutrition in these patients. Unfortunately, there are many different clinical permutations in these patients



that make it very difficult to establish a “one size fits all” approach to nutrition support in the emergency GI surgery patients.¹²⁻¹⁵

Several key points regarding the management of nutrition support are important to highlight. Nutrition support planning should start from admission in terms of the type of support needed (parenteral vs enteral), how it will be administered (eg, oral, enteric tubes, central line), and when it will start. Enteral nutrition should always be the default choice, being mindful of the difference between true contraindications and barriers to initiating enteral nutrition. Other patient-related and practical considerations also need to be taken into account such as the ability to recognize both complications of enteral nutrition as well as intolerance. In patients who are unable to communicate, this can be especially challenging.

Summary

Routine early initiation of parenteral nutrition does not appear to be beneficial to GI surgery patients, and early enteral nutrition in emergency GI surgery patients is not worse than “traditional” management, and may have benefit. Many of the traditional barriers to feeding the gut are based on dogma rather than data, and hopefully over time, practice will reflect a simpler evidence-based philosophy of ‘if the gut works, use it...but don’t abuse it!’

References

1. Sorenson LT, Malaki A, Wille-Jorgensen, et al. Risk factors for mortality and postoperative complications after gastrointestinal surgery. *J Gastrointest Surg*. 2007;11(7):903-910.
2. Ingraham AM, Cohen ME, Bilimoria KY, et al. Comparison of 30-day outcomes after emergency general surgery procedures: potential for targeted improvement. *Surgery*. 2010;148(2):217-238.
3. Havens JM, Peetz AB, Do WS, et al. The excess morbidity and mortality of emergency general surgery. *J Trauma Acute Care Surg*. 2015;78(2):306-311.
4. The Department of Surgery, Brigham and Women’s Hospital; Burn and Wound Program, Health South Braintree Rehabilitation Hospital. *Wounds*. 2000;12(1). Health Management Publications. Available at <http://www.medscape.com/viewarticle/407543>. Accessed November 8, 2015.
5. Advisory Faculty: Correia MI, Hegazi R, Llido L, Rugeles S, Sriram K. TNT 3.0. Total Nutrition Therapy. An Integrated Approach to Patient Care. Available from: Abbott Nutrition Health Institute. Chicago. 2011.
6. McClave SA, Martindale RG, Vanek VW, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: (SCCM and A.S.P.E.N.). *JPEN J Parenter Enteral Nutr*. 2009;33(3):277-316.
7. Miller KR, Kiraly LN, Lowen CC, Martindale RG, McClave SA. “CAN WE FEED?” A mnemonic to merge nutrition and intensive care assessment of the critically ill patient. *JPEN J Parenter Enteral Nutr*. 2011;35(5):643-659.
8. Singer P, Berger MM, Van den Berghe G, et al. ESPEN guidelines on parenteral nutrition: intensive care. *Clin Nutr*. 2009;28(4):387-400.
9. Casaer MP, Mesotten D, Hermans G, et al. Early versus late parenteral nutrition in critically ill adults. *N Engl J Med*. 2011;365(6):506-517.



10. Lewis SJ, Andersen HK, Thomas S. Early enteral nutrition within 24h of intestinal surgery versus later commencement of feeding: a systematic review and meta-analysis. *J Gastrointest Surg.* 2009;13(3):569–575.
11. Marik PE, Zaloga GP. Early enteral nutrition in acutely ill patients: a systematic review. *Crit Care Med.* 2001;29(12):2264-2270.
12. Singh S, Ram RP, Khanna SK. Early postoperative enteral feeding in patients with nontraumatic intestinal perforation and peritonitis. *J Am Coll Surg.* 1998;187(2):142-146.
13. Malhotra A, Mathur AK, Gupta S. Early enteral nutrition after surgical treatment of gut perforations: a prospective randomised study. *J Postgrad Med.* 2004;50(2):102-106.
14. Lee SH, Jang JY, Kim HW, Jung MJ, Lee JG. Effects of early enteral nutrition on patients after emergency gastrointestinal surgery: a propensity score matching analysis. *Medicine (Baltimore).* 2014;93(28):e323.
15. Klappenbach RF, Yazzi FJ, Alonso Quintas F, Horna ME, Alvarez Rodriguez J, Oria A. Early oral feeding versus traditional postoperative care after abdominal emergency surgery: a randomized controlled trial. *World J Surg.* 2013;37(10):2293 – 2299.



Perioperative Immunonutrition: Does One Size Fit All?

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Over the past twenty years, numerous articles have been published in the field of immune-modulating formulas, also called “immunonutrition.” Hailed for various beneficial effects, these formulas are typically high protein enteral formulations or oral supplements with high levels of “pharmakonutrients.” The most common of these immunonutrients are arginine, omega-3-fatty acids, glutamine, ribonucleic acids, selenium, and other antioxidants. These nutrients are often present in combination at levels many times higher than the levels found in standard nutritional products.

Stated goals of immunonutrition include attenuation of excessive inflammatory responses, supplementation of conditionally-essential nutrients that are rapidly depleted in certain stress states (eg, glutamine and arginine), and delivery of nutrients thought to aid recovery in specific disease and injury states. Examples of these strategies include the well-described supplementation of arginine and glutamine after abdominal operations for gastrointestinal disease, use of anti-inflammatory lipids (mixtures of omega-3 and borage oils) in Acute Respiratory Distress Syndrome (ARDS) patients, and the use of specialized supplements in patients after brain injury.

Arginine has been and continues to be the most highly touted of the immunonutrients. It has been shown to stimulate cell-mediated immunity with activation of T lymphocytes, upregulation of T-helper cell populations, improved phagocytosis, and respiratory burst generation.¹ Arginine specifically promotes healing by two additional mechanisms: increased nitric oxide production with subsequent tissue perfusion due to vasodilation, and augmented collagen production as a precursor to proline. Arginine depletion after surgery is well described due to upregulation of arginase, particularly more than 24 hours after surgery.² Previously unavailable in most supplements due to patent restrictions, the now more widely-available arginine precursor, citrulline, has the potential to replace arginine due to improved bioavailability, better tolerance, and the achievement of higher sustained arginine plasma levels.³

The omega-3 fatty acids docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) are the other premier ingredients in most immunonutrition products. However, how omega-3s result in improved surgical outcomes is less evident. They are known to reduce oxidative injury, modify endothelial expression of adhesion molecules such as E-selectin, inhibit inflammatory responses due to downregulation of arachidonic acid, and to generate resolvins and other novel anti-inflammatory modulators.⁴ High dose intravenous fish oil appears to modulate the inflammatory response in surgical patients, but oral fish oil supplementation at standard doses did not show benefit in a large cardiac surgery trial (Omega-3 Fatty Acids for Prevention of Postoperative Atrial Fibrillation [OPERA]).⁵

After arginine and fish oil, glutamine historically has been the most discussed immunonutrient. Recognized as the preferred fuel of the enterocyte and other rapidly dividing cells as well as the most abundant free amino acid with a significant antioxidant effect, glutamine supplementation has long been encouraged in surgical patients. Enthusiasm has waned since the large multinational REDUCING Deaths due to OXIDATIVE Stress (REDOXS) trial in critically ill patients (not all surgical) demonstrated a 5.2% increase in mortality due to high-dose parenteral



and enteral supplementation of glutamine.⁶ At a more practical dose, the European MetaPlus study failed to demonstrate any benefit from high glutamine enteral immunonutrition in critically ill patients (only some of which were surgical).⁷

In reviewing the literature regarding the application of immunonutrition to surgical patients, it is challenging to draw valid conclusions because of a lack of clarity in numerous aspects of study design, comparability of studies, and the role of combining multiple immunonutrients. Generally, it is thought that there is some synergism between the multiple immunonutrients that limits the efficacy of single immunonutrients and inhibits isolated clinical evaluation of any nutrient in isolation. Over time, nutrient compositions of commercial formulas have changed. Studies that evaluate various immunonutrition formulas in a variety of settings—before surgery (preoperative), after surgery (postoperative), and both before and after surgery (perioperative)—have been used to justify grandiose claims not always supported by study design or even by physiology. The literature is also unclear because many studies lack an isocaloric, isonitrogenous control. Without standard nutritional supplementation in the control group, these studies fail to distinguish the benefit of immunonutrients from the benefit of the supplemental protein, carbohydrate, and standard nutrients many traditional oral nutritional supplements provide.

A meta-analysis confirmed preoperative immunonutrition conferred no reduction in wound infections, infectious and non-infectious complications, or length of stay when compared to isonitrogenous standard high-protein oral nutritional supplements (Figure).⁸ However, when compared to an un-supplemented regular diet in the same meta-analysis, oral immunonutrition supplements resulted in lower infectious complications and over a two-day reduction in hospital length of stay ($P<0.01$).⁸

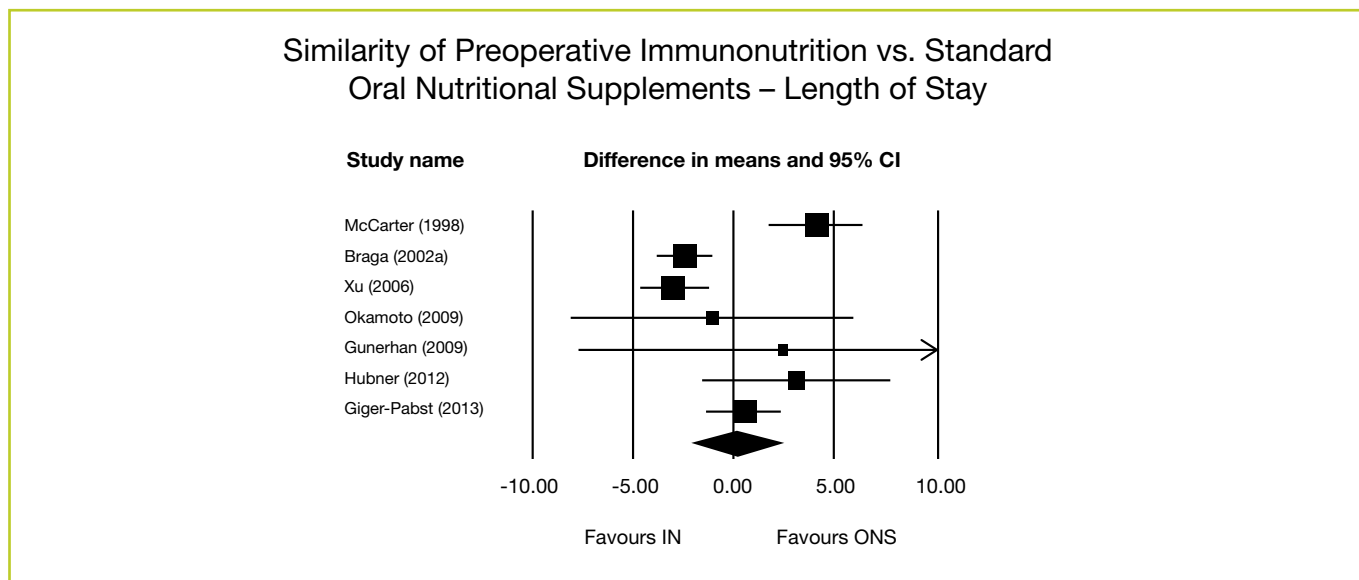


Figure. Comparison of preoperative immunonutrition vs standard oral nutritional supplements.⁸

Meta-analysis confirmed no reduction in length of stay between immunonutrition and standard high-protein oral nutritional supplements in the preoperative setting.

CI=Confidence Interval, IN=immunonutrition, ONS=oral nutritional supplement

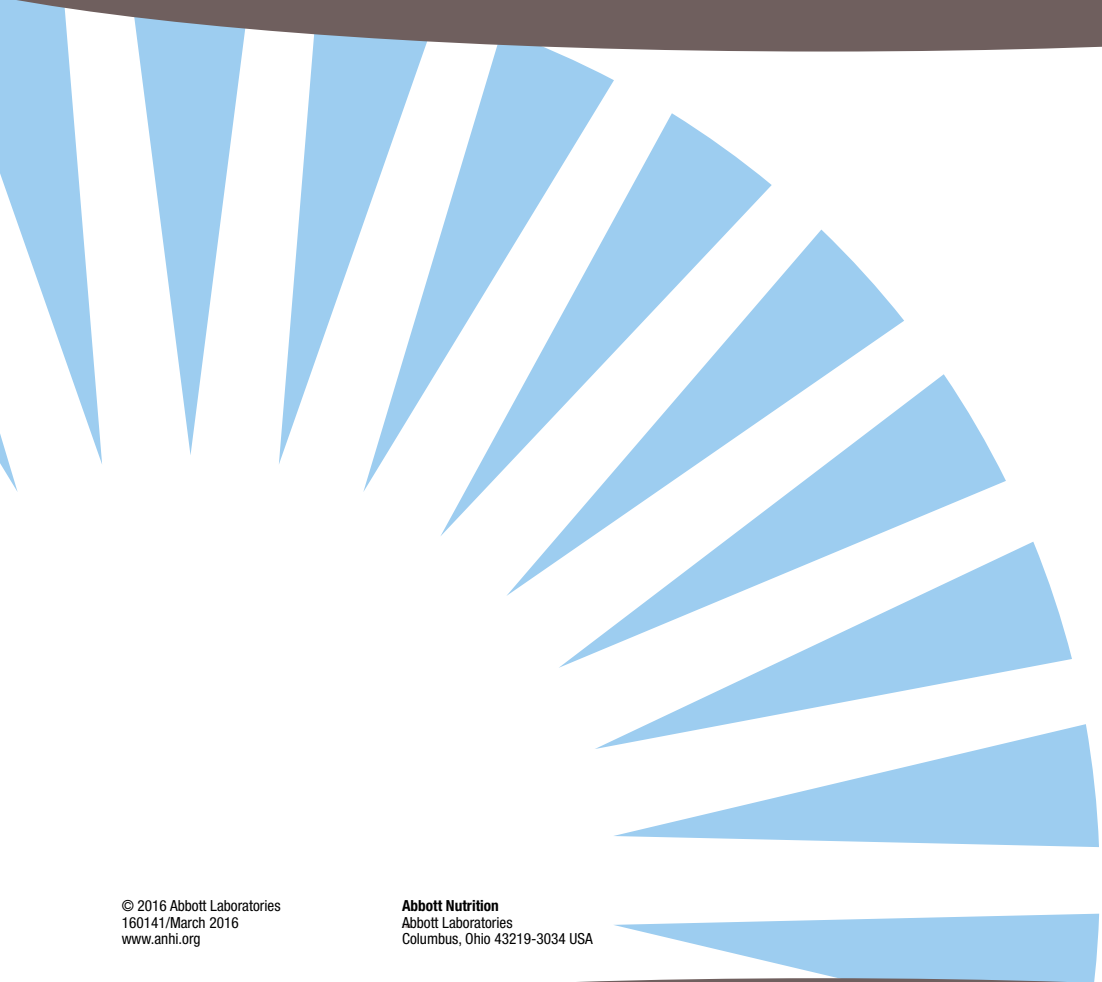
Source: Hegazi RA et al. Preoperative standard oral nutrition supplements vs immunonutrition: results of a systematic review and meta-analysis. *J Am Coll Surg.* 2014;219(5):1078-1087.



Both American and European guidelines published in the 2000's made major recommendations for immunonutrition, but recent and emerging guidelines make only weak recommendations for immunonutrition.⁹ Despite limited evidence, quality improvement efforts based on the use of preoperative immunonutrition oral supplements are slowly proliferating in the United States. The precise immunonutrient profile, timing, dose and duration are all issues that need to be resolved before immunonutrition can be optimally prescribed to diverse clinical populations. In the future, immunonutrition may be tailored to target specific mechanistic derangements observed in specific clinical populations. Modulation of immune dysfunction is tricky business, and no successful pharmaceutical therapies have emerged from over a hundred human drug trials in this arena. Therefore, we must be cautious and not look to immunonutrition as a panacea. It does not appear to be a "one size fits all" solution.¹⁰

References

1. Kemen M, Senkal M, Homann HH, et al. Early postoperative enteral nutrition with arginine-omega-3 fatty acids and ribonucleic acid-supplemented diet versus placebo in cancer patients: an immunologic evaluation of impact. *Crit Care Med*. 1995;23(4):652-659.
2. Makarenkova VP, Bansal V, Matta BM, Perez LA, Ochoa JB. CD11b+/Gr-1+ myeloid suppressor cells cause T cell dysfunction after traumatic stress. *J Immunol*. 2006;176(4):2085-2094.
3. Wijnands KA, Vink H, Briede JJ, et al. Citrulline a more suitable substrate than arginine to restore NO production and the microcirculation during endotoxemia. *PLoS One*. 2012;7(5):e37439.
4. Evans DC, Martindale RG, Kiraly LN, Jones CM. Nutrition optimization prior to surgery. *Nutr Clin Pract*. 2014;29(1):10-21.
5. Mozaffarian D, Marchioli R, Macchia A, et al. Fish oil and postoperative atrial fibrillation: the Omega-3 Fatty Acids for Prevention of Post-operative Atrial Fibrillation (OPERA) randomized trial. *JAMA*. 2012;308(19):2001-2011.
6. Heyland D, Muscedere J, Wischmeyer PE, et al. A randomized trial of glutamine and antioxidants in critically ill patients. *N Engl J Med*. 2013;368(16):1489-1497.
7. van Zanten AR, Sztark F, Kaisers UX, et al. High-protein enteral nutrition enriched with immune-modulating nutrients vs standard high-protein enteral nutrition and nosocomial infections in the ICU: a randomized clinical trial. *JAMA*. 2014;312(5):514-524.
8. Hegazi RA, Hustead DS, Evans DC. Preoperative standard oral nutrition supplements vs immunonutrition: results of a systematic review and meta-analysis. *J Am Coll Surg*. 2014;219(5):1078-1087.
9. Gustafsson UO, Scott MJ, Schwenk W, et al. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations. *Clin Nutr*. 2012;31(6):783-800.
10. Evans DC, Hegazi RA. Immunonutrition in critically ill patients: does one size fit all? *JPEN. J Parenter Enteral Nutr*. 2015;39(5):500-501.



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