American Society for Enhanced Recovery (ASER) and Perioperative Quality Initiative (POQI) Joint Consensus Statement on Nutrition Screening and Therapy Within a Surgical Enhanced Recovery Pathway

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Abstract:

Background: Perioperative malnutrition has proven to be challenging to define, diagnose, and treat. Despite these challenges, it is well known that sub-optimal nutritional status is a strong independent predictor of poor postoperative outcomes. Although perioperative caregivers consistently express recognition of the importance of nutrition screening and optimization in the perioperative period, implementation of evidence-based perioperative nutrition guidelines and pathways in the U.S. has been quite limited and needs to be addressed in surgery-focused recommendations.

Methods: The 2nd Perioperative Quality Initiative (POQI) brought together a group of international experts with the objective of providing consensus recommendations on this important topic with the goal of: 1) Developing guidelines for screening of nutritional status to identify patients at risk for adverse outcomes due to malnutrition; 2) Address optimal methods of providing nutritional support and optimizing nutrition status preoperatively and 3) Identifying when and how to optimize nutrition delivery in the post-operative period.

Discussion: Discussion led to strong recommendations for implementation of routine pre-operative nutrition screening to identify patients in need of pre-operative nutrition optimization. Post-operatively, nutrition delivery should be restarted immediately after surgery. The key role of oral nutrition supplements, enteral nutrition, and parenteral nutrition (implemented in that order) in most perioperative patients was advocated for with protein delivery being more important than total calorie delivery. Finally, the role of often-inadequate nutrition intake in the post-hospital setting was discussed, and the role of post-discharge oral nutrition supplements emphasized.

Keywords: Enhanced recovery pathway, enhanced recovery, enteral nutrition, oral nutrition supplements, parenteral nutrition, malnutrition, protein, oral intake, carbohydrate drink, sarcopenia,

Introduction

Perioperative malnutrition has proven to be challenging to define, diagnose, and treat. Despite these challenges, it is well-known that sub-optimal nutritional status is a strong independent predictor of poor postoperative outcomes [1]. Malnourished surgical patients have significantly higher postoperative mortality, morbidity, length of stay (LOS), readmission rates, and increased hospital costs [2-4]. It is estimated that 24-65% of patients undergoing surgery are at nutrition risk [5,6], [3,7]. Additionally, recent prospective observational data indicate undernourished patients OR patients at risk of malnutrition are twice as likely to be readmitted within 30 days following elective colorectal surgery[8]. As defined by the *National Surgical Quality Improvement Program* (NSQIP), malnutrition is among the few modifiable preoperative risk factors associated with poor surgical outcomes, including mortality, in surgical patients [9] [10]. This risk of malnutrition is often most significant following major gastrointestinal (GI) and oncologic surgery, groups commonly focused on in enhanced recovery pathways (ERPs) [2-4]. Further, appropriate perioperative nutritional therapy has been shown to specifically improve perioperative outcomes in GI/oncologic surgery, where the greatest risk of baseline malnutrition (~65%) occurs[3,6,11]. In surgical patients overall, perioperative nutrition interventions can improve surgical outcomes and reduce infectious morbidity and mortality [12]. There is a long history of randomized controlled trials (RCTs) and meta-analyses demonstrating preoperative nutrition (regardless of route of administration) in malnourished patients prior to GI surgery reduces postoperative morbidity by 20%.[13]. Postoperative nutritional support is vital in maintaining nutritional status during the catabolic postoperative period and underscored by evidence for early and sustained feeding following surgery as part of ERP protocols [14-16]. In fact, the advancement of oral intake has been identified as an independent determinant of early recovery following colorectal surgery [17]. Some of the most striking recent data on the role of nutrition delivery in the perioperative period has demonstrated in patients undergoing oncologic surgery in an ERP, delivery of nutrition on the first postoperative day is an independent predictor of postoperative survival at 5 years [18].

Unfortunately, recent evidence reveals significant deficiencies in nutritional screening and intervention in U.S. colorectal and oncologic surgical patients with only ~ 1 in 5 hospitals currently utilizing a formal nutrition screening process [19]. This is surprising as 83% of U.S. surgeons believe existing data supports preoperative nutrition optimization to reduce perioperative complications. However only ~20% of U.S. GI/Oncologic surgery patients receive any nutritional supplements in the pre-operative or post-operative setting. Overall U.S. surgeons recognized both importance of proper perioperative surgical nutritional support and the potential value to patient outcomes. Despite these beliefs, this data confirms poor implementation of evidence-based nutrition practices in major surgery [19].

A summary of the current challenges and known benefits of perioperative nutrition interventions are shown in **Figure 1.** The urgency of improving perioperative nutrition practices are underscored by strong recommendations from international nutrition society guidelines endorsing perioperative nutrition optimization [20-23]. However, limited surgical/perioperative society guidelines exist on how to optimally screen surgical patients for malnutrition and optimize nutritional status in the perioperative period, particularly within an ERP. Thus we sought to define and answer important questions related to perioperative nutrition in patients undergoing surgery within the context of an ERP.

Methods/Design

This consensus process utilized a modified Delphi method as described previously [24] and processes detailed by the National Institute for Health and Care Excellence (NICE) [25]. The Perioperative Quality Initiative (POQI) is a previously-described collaborative of diverse international experts in anesthesia, nursing, nutrition, and surgery tasked to develop consensus-based recommendations in ERP.[24,26] The participants in the POQI consensus meeting were recruited based on their expertise in the principles of ERAS/ERP and met in Stony Brook, New York on December 2-3, 2016.

Results

Key Perioperative Nutrition Questions Addressed in this Consensus are summarized in **Appendix #1. Comnsensus Recommendations are described in Table #1** *and key "take-away" recommendations are summarized in* **Table #2.**

I. Preoperative screening

Screening for malnutrition prior to major surgery is essential as it can identify patients at risk of malnutrition who may benefit from a nutritional intervention pre-operatively. Numerous screening tools have been validated for use in already hospitalized patients, yet there is no consensus related to the optimal screening tool in the preoperative patient. After literature review, we developed and proposed the Perioperative Nutrition Screen (PONS).

As shown in **Figure 2**, the PONS is a modified version of the Malnutrition Universal Screening Tool (MUST) [27] that has been altered for use perioperatively. The PONS determines the presence of nutrition risk based on a patient's body mass index (BMI), recent changes in weight, reported recent decrease in dietary intake, and preoperative albumin level. In addition, the PONS includes evaluation of preoperative albumin level, as this is a predictor of postoperative complications, including morbidity/mortality [28], [29], [27], [30], [31].

BMI assessment and recent unplanned weight loss are criteria used in several malnutrition screening tools [32], [33]. A BMI level indicative of underweight (< 18.5 kg/m^2 for adults < 65 years old) has been shown to increase post-operative complications in a variety of surgical patients [34], [35], [36], [33],[32]. The PONS uses a higher number (< 20 kg/m^2) for adults > 65 years old because research indicates that the risk for all-cause mortality increases starting at a BMI of 24 kg/m^2 for this age population and doubles when BMI is < 22 kg/m^2 for men and < 20 kg/m^2 for women [37]. While this research was not related to surgical risk, it suggests that higher BMI threshold should be used when evaluating weight status of older adults. Regardless of BMI, unintentional weight loss has been associated with morbidity, functional decline and negative postoperative outcomes [38,39] Reduced oral intake is determined by asking patients if they have been eating less than 50% of their normal diet in the preceding week. Similar questions related to reduced oral intake have been used in short nutrition screens with high sensitivity and specificity in validation studies [40], [41].

The PONS includes the use of albumin because it is inexpensive, commonly obtained in perioperative testing, and a strong predictor for surgical risk/mortality[10], [31]. While it has long utilized as an indicator of malnutrition, studies have shown that albumin is neither specific nor sensitive enough to be the optimal malnutrition marker in most patient populations[42]. Until a better marker is available we recommend its use as a component of the preoperative nutrition screen.

The PONS can be easily administered and incorporated into an electronic medical record for efficient communication. The intent is that the PONS can be administered quickly (< 5 minutes) by nursing staff in surgical/preoperative clinics and results will be instantly uploaded into EMR, automatically triggering a nutrition intervention if 1 or more positive responses on the PONS score are recorded. Patients who are identified as being at high nutrition risk upon screening should be referred to a Registered Dietitian Nutritionist (RDN) for a complete nutrition assessment and intervention. In situations where referrals to RDN's are not possible, oral nutritional supplements (ONS) are recommended and will be discussed in the following preoperative intervention section.

*Please see **Appendix #2** for discussion of future pre-operative assessment techniques for sarcopenia and role of vitamin D in surgery. Please see **Appendix #3** for discussion of obese patient considerations.*

II. PREOPERATIVE INTERVENTION

What is the role of achieving protein delivery goals in perioperative period?

Protein requirements are elevated in states of stress, such as surgery, to account for the added demands of hepatic acute phase proteins synthesis, the synthesis of proteins involved in immune function, and wound healing [43]. Although optimal protein intakes for surgery is currently not clearly defined, nonsurgical nutrition guidelines suggest stressed patients should consume at least 1.2–2.0 g protein/kg/day[21].

Whey protein and casein are among the best quality proteins overall for muscle synthesil [44] and to stimulate anabolism in patients with advanced cancer. [45] Several studies have identified that consuming 25-35 g of protein in a single meal maximally stimulates MPS [46]. Based on the evidence of this ceiling effect, an equal distribution of daily dietary protein across meals has been proposed. The idea being that the anabolic response to a single dose of amino acids can be compounded when repeated multiple times per day [47]. Given the emerging findings to support an even distribution of daily protein intake in healthy populations, and the evidence that substantive high quality amino acids are required to stimulate a typical anabolic response in cancer patients, it seems reasonable to suggest that daily protein requirements for cancer patients be met through moderate protein (~25-35g) consumption at every meal.

When should high protein oral nutrition supplements (ONS), enteral nutrition (EN), and parenteral nutrition (PN) be initiated preoperatively?

We recommend that patients who are screened as being at nutritional risk prior to major surgery receive preoperative ONS for a period of at least 7 days. This may be achieved with either of the following: Immunonutrition ((IMN) - containing arginine/fish oil) or High Protein ONS (2-3 x day, minimum of 18 g protein/dose). When oral nutrition supplementation via ONS is not possible, a dietician should be consulted and an enteral feeding tube be placed and home EN initiated for a period of at least 7 days. If neither oral nutrition supplementation via ONS or EN is possible, or when protein/kcal requirement (>50% of recommended intake) cannot be adequately met by ONS/EN, we recommend preoperative PN to improve outcomes.

These recommendations are consistent with existing nutrition societal guidelines from the European Society for Parenteral and Enteral Nutrition (ESPEN) guidelines indicating severely malnourished patients be supplemented via nutritional therapy prior to elective surgery[1]. The duration of preoperative support needed varies in published guidelines from 7-14 days [1] [20] . However, even 5-7 days of preoperative nutrition therapy can lead to a 50% reduction in postoperative morbidity in malnourished patients[48]. The optimal amount of time preoperative nutrition needed for malnourished patients and an objective measure of nutritional optimization needs further study. Intriguingly, recent consensus recommendations from the recent North American Surgical Nutrition Summit suggested "preventive" preoperative nutrition therapy and optimization involving "metabolic preparation" occur in all patients at risk of undernutrition, rather than simply just correcting deficiencies in severely undernourished patients [49]. This recommendation is based on the concept that preoperative nutritional care should be introduced early for malnourished and non–malnourished patients to maintain optimal nutritional status throughout the entire perioperative period [49]. Further, Kuppinger et al[50] showed that for patients undergoing abdominal surgery lower food intake before hospital admission was an independent risk factor for postoperative complications.

*Nutrition Pathway in low-nutrition risk perioperative patients (i.e. PONS < 1 & ALB > 3.0) (**Figure 3**):*

Patients should be encouraged to take in healthy high-protein (with high quality protein sources, such as eggs, fish, and lean meats/dairy) complex carbohydrate-rich diets preoperatively. However, many patients will not be able to meet optimal suggested perioperative energy goals of 25 kcal/kg/d and 1.5–2 g/kg/d of protein (~1 g/pound of ideal/adjusted body weight) from routine food intake[1,51]. Thus, we encourage patients to take high-protein ONS or IMN during perioperative period unrelated to nutritional status.

*Nutrition Pathway in Patients found to be at Nutrition Risk (i.e. PONS > 1 or ALB < 3.0) (**Figure 4**)*

In patients found to be at nutrition risk we recommend high-protein ONS or IMN be given prior to surgery. It is the consensus of the group that high-protein ONS should contain > 18 g/protein/serving in a balanced formula. Previous data utilizing preoperative ONS demonstrated benefits on reduction of surgical site infections in selected weight losing patients[52]. Again, because many patients do not meet their energy needs from normal food, especially malnourished patients, it is the consensus of this consensus group to encourage the use of high-protein ONS or IMN. As patient compliance with ONS intake (2-3 x day) is essential for benefit, it is vital to emphasize the key role of ONS in preoperative therapy [53]. Further, cost effectiveness of ONS in hospitalized patients has been shown in a recent large systematic review[54].

When oral nutrition is unable to meet the protein and calorie requirements in malnourished patients; enteral supplementation should be preferred over PN whenever possible. In 800 patients with gastric cancer undergoing gastrectomy and with severe nutritional risk according to ESPEN definitions the incidence of surgical-site-infections was significantly lower in the group receiving adequate energy support via oral, EN and/ or PN for at least 10 days than in group with inadequate/no support for <10 days (17.0% vs. 45.4%, p=0.00069). In multivariate analysis, nutritional therapy was an independent factor associated with fewer surgical site infections (OR 0.14, 95% CI 0.05 to 0.37, p=0.0002)[55]. Preoperative PN should only be utilized in patients with malnutrition or nutritional risk where energy requirement cannot be adequately met by E. A time period of 7-14 days of PN is recommended. If PN is required to meet energy needs, it should be combined whenever possible with EN or ONS. For surgical patients, the benefits of nutritional therapy have been consistently shown in cases of severe undernutrition [56-58] and confirmed by two meta-analyses [59,60]. PN was found to reduce the rate of postoperative complications in malnourished patients[56-59]. Patients in these studies were fed preoperatively for at least 7-10 days. The results of the meta-analysis by Braunschweig [61] also favour PN for malnourished patients. A significantly lower mortality with a tendency towards lower rates of infection was also found in malnourished patients receiving PN in the meta-analysis by Heyland et al [60]. In a later systematic review, which focused on patients undergoing gastrointestinal surgery, preoperative parenteral nutrition statistically significantly reduced risk for major complications from 45% to 28%. [62].

With regards to the timing of preoperative PN use, the benefits of preoperative PN for 7-15 days is most clearly shown in patients with documented malnutrition prior to major gastrointestinal surgery[56,57]. When PN is given for the 10 days preoperatively and continued for 9 days postoperatively the complication rate is 30 % lower and there is a reduction in mortality[57]. It is the opinion of the consensus group, that in patients with significant nutritional risk the potential for increased benefit will justify the preoperative extension of preoperative hospitalization or outpatient PN delivery length to 10-14 days of PN delivery. In order to avoid refeeding syndrome in severely malnourished patients, PN calorie delivery should be increased in a stepwise fashion (with dietician/pharmacist guidance) and laboratory and cardiac monitoring should be initiated with adequate precautions to replace potassium, magnesium, phosphate and thiamine [63].

III. Minimizing preoperative fasting and role of preoperative oral carbohydrate loading

Perioperative fasting can exacerbate surgical stress response, aggravate insulin resistance, exaggerate protein losses, and impair GI function. Additionally, preoperative fasting is associated with a number of patient-centered consequences including thirst, hunger, headaches, and anxiety. It is now known that preoperative overnight fasting is unnecessary in most cases; clear fluids taken up until 2 hr. before induction does not increase gastric volumes, therefore poses no risk for aspiration, and in fact has been found to stimulate gastric emptying. [49], [64].

Delivery of sufficient exogenous carbohydrate is considered the best method to induce a metabolically fed state pre-operatively . Carbohydrate loading is accomplished with the consumption of 50g carbohydrates as a clear liquid 2-3 hrs. pre-operatively and in some studies/centers 100g the evening before. The use of preoperative carbohydrate loading strategies have been associated with a statistically significant reduced length of stay (LOS), especially in major abdominal surgery (MD -1.66 days, 95% CI -2.97 to -0.34)[65]. For best results, the dose 2-3 h before surgery should be consumed within 5-10 minutes (not sipped over time) to enhance insulin secretion. The carbohydrate product most often studied contains maltodextrin as source of carbohydrate, and its low osmolality induces faster gastric emptying. Direct comparisons with more simple sugar containing solutions (glucose) are not yet studied. However, there are significant data suggesting the negative impact of high versus low glycemic index meal on response of glucose, insulin, and glucagon[66]. Overall, based on the low risk of harm, potentially improved nitrogen balance, better insulin sensitivity, and signal of reduced LOS in major abdominal surgery, we recommend the oral intake of carbohydrate-containing solutions preoperatvely and suggest solutions containing complex carbohydrates be used when available.

IV. Role of Perioperative Immunonutrition

Immunonutrition (IMN) has been proposed as a risk-reduction strategy in surgical patients for over twenty-five years. Arginine, omega-3-fatty acid, and antioxidants are delivered in combination at high levels in various EN and ONS formulas. Conditionally-essential arginine is rapidly depleted after surgical stress but can be supplemented with IMN.[67] Arginine is important for activation of T lymphocytes, promotion of T-helper cells, phagocytosis and respiratory burst generation.[68] Arginine serves as a precursor to nitric oxide and proline; both are important to anastomotic and wound healing—nitric oxide promotes vasodilation and tissue oxygenation while proline contributes to collagen deposition during healing. The omega-3 fatty acids DHA and EPA play a wide range of anti-inflammatory roles, reducing oxidative injury, down-regulating arachidonic acid, and generating resolvins.[69]

IMN ingredients, timing, dose, and duration vary from study to study. The clinical effect targeted to the aforementioned pathways appears most profound when the nutrients are used in combination. Most surgical IMN studies have applied either 5 days of preoperative supplementation and/or 7 days of supplementation postoperatively. Studies of single immunonutrients (i.e. arginine alone) have not demonstrated the same level of benefit, suggesting synergism of different components and complete nutrition delivery is crucial to IMN efficacy.[69]

Early studies strongly demonstrate that preoperative IMN reduced complications and LOS.[70] A Cochrane Library analysis reported decreased total and infectious complications with the use of preoperative IMN.[62] Evidence suggests that patients undergoing high-risk gastrointestinal surgery were the most likely to benefit—possibly due to the higher perioperative risk of complication.[71] Due to the large number of small to medium size trials, many conclusions have been drawn from meta-analyses. In their landmark meta-analysis in 2011, Drover et. al. demonstrated reduced a 40% reduction in perioperative infectious complications with IMN.[72] The effect observed in this analysis was similar whether the IMN was given pre-op only, pre- and post-operatively, or post-op alone. Much has been written on the value of pre- vs. post-operative IMN and there may be value to administration both before- and after-surgery. However, a recent meta-analysis suggested preoperative only IMN did not improve outcomes when compared to preoperative isonitrogenous ONS.[69] Additional meta-analyses have demonstrated that postoperative IMN reduces infectious complications [71,73-76], including the recent analysis from Ljungqvist, Lobo and colleagues [71,73-76]. One meta-analysis of early enteral postoperative IMN also demonstrated a reduction in anastomotic leaks.[77] Limitations of this data include many early IMN studies informing these meta-analyses were not balanced with an isocaloric, isonitrogenous controls. Further, some later small-randomized trials of IMN did not show benefit compared to isonitrogenous formulas.[78-80]

Two studies of perioperative IMN have occurred in the context of ERP and have suggested benefit. The larger was a RCT of 264 patients that demonstrated a reduction in infectious complications (23.8% vs.10.7%, $p = 0.0007$), particularly wound infections (16.4% vs. 5.7%, $p = 0.0008$) with the use of IMN when compared to standard high calorie supplements.[81]. In a separate study of IMN compared to dietary advice without supplementation by the same authors, wound infection rates in laparoscopic colectomy were significantly reduced with the use of IMN (11.5 vs. 0 %, $p = 0.006$).[82]

A major real-world quality improvement effort using preoperative IMN in 3375 patients in Washington State demonstrated a reduction of 23% in the number of patients with a prolonged length of stay ($p = 0.05$) in a covariate-matched analysis.[83]

The POQI-2 group was divided regarding the strength of their recommendation for IMN. Expert opinions based on interpretation of the evidence ranged from “recommend,” to “suggest,” and the finally agreed-upon consensus statement to “consider” IMN. Overall there were many concerns about the quality of the overall evidence, including the age of many seminal IMN studies published in the early 2000’s. There was also concern that older studies were not controlled with isocaloric, isonitrogenous formulas.[84] Overall, IMN study sample sizes are smaller, although a number of medium size trials (n=~200-300) are published. Concerns were raised regarding the level of industry sponsorship in the literature and the potential biases this can carry. Without question, additional definitive clinical trials comparing IMN to high protein ONS in the preoperative setting and pre-op IMN alone versus pre- and post-op IMN versus post-op IMN alone are needed.

V. Postoperative Nutrition

Early resumption of oral intake following surgery is now clearly realized to be safe[85] and vital for optimizing post-operative outcomes. Early oral feeding immediately following major surgery, including GI surgery, is associated with a decrease in postoperative complications, length of stay, and costs[86,87]. In fact, multiple meta-analyses now report that feeding within 24 h post–gastrointestinal surgery decreases mortality, as well as major morbidities[15,16,88]. Specifically, A systematic review and meta-analysis of the effects of early enteral feeding within 24 h of intestinal surgery (vs. no feeding within 24 h) demonstrated a significant reduction in mortality [relative risk (RR) 0.42 (95% CI 0.18–0.96)] and no benefit or harm related to anastomotic dehiscence [RR 0.62 (95% CI 0.3–1.28)] in the early fed group[88]. Overall, early postoperative feeding versus traditional withholding of feeding until return of bowel function, was not found to contribute to anastomotic breakdown or increase risk of nausea following surgery.

As earlier stated, anabolism cannot be achieved in the postoperative period when glucose is administered alone without adequate protein delivery [89]. Unfortunately, to this point, provision of calories alone has continued to be focused on in surgical nutrition messages [89]. It is well known, that inadequate protein intake is associated with loss of lean body mass, which impairs functional recovery and physical quality of life. Provision of protein, independent of whether energy or total calorie requirements, are met, can maintain lean muscle mass and reduce the risk of subsequent frailty in the elderly[90,91]. Finally, a key high-impact recent trial conducted in colo-rectal surgery patients within an ERAS/ERP pathway demonstrated in patients receiving high protein ONS post-operatively that consumption of > 60% of protein needs over first 3 post-operative days was associated with a 4.4-day reduction in length of stay ($p < 0.001$).[92]

Thus, the group was in full consensus recommending that a high protein diet (via diet or high protein ONS) be initiated on day of surgery in most cases, with exception of patients with bowel not in continuity, bowel ischemia, or persistent bowel obstruction. Traditional “clear liquid” and “full liquid” diets should not be routinely used as they typically do not provide adequate nutrition or protein delivery. Further, the group emphasized that reaching overall protein intake goal is more important than total calorie intake in the post-operative period.

Role of high protein ONS, EN, and PN in the post-operative period.

The type of nutrition support delivered in the postoperative setting is primarily determined by the patient’s ability to achieve calorie (25-30 kcal/kg/d) and protein (1.5–2 g/kg/d) goals and tolerance of oral intake[1,20,21,89]. A practical approach derived from recent publications[1,20,21,89,93] indicates patients tolerating 50%–100% of nutrition goals should receive high protein ONS (2-3 x day) to meet protein needs. In patients consuming < 50% via oral route, EN via tube feeds should be given. PN should be utilized if > 50% of protein/calories needs are not met via Oral/EN for > 7 days, even in well-nourished patients.

When oral nutrition is not tolerated or feasible, EN under guidance of a dietician should be initiated. Early EN within 24 h of surgery versus later feeding have been clearly shown to reduce morbidity and mortality in two meta-analyses (one Cochrane systematic review) [85,88] Another meta-analysis comparing EN within 24 hours of gastrointestinal surgery with traditional postoperative management demonstrated a 45% decrease in risk of overall postoperative complications. No differences in the incidence of anastomotic dehiscence were observed[15]. Thus, we recommend, in patients who meet criteria for malnutrition**,** who are not anticipated to meet nutritional goals (>50% of protein/kcal) through oral intake, we recommend early EN or tube feeding within 24 h. Further, in patients started on EN and/or PN, we recommend continuation of EN or PN support for patients who are not able to take in at least 60% of their protein/kcal requirements via the oral route. Finally, based on recent randomized clinical trial data and new clinical guidelines[21] we recommend when using gastric residual volume's as a marker of feeding tolerance, a cut-off of > 500 ml should be used prior to tube feeds being suspended or tube feed/EN rate reduced.

Role of PN in postoperative period:

In patients at risk for malnutrition (PONS > 1, or ALB < 3.0) where nutrition goals are not met via EN, we recommend early PN, in combination with EN if possible. This is based on data from meta-analysis incorporating 27 studies in a meta-analysis of PN in surgical patients. This data showed a lower complication rate in patients receiving PN, especially in patients found at risk for malnutrition.[60] An influence of PN on the mortality of surgical patients was not shown. Further, a meta-analysis by Braunschweig et al. showed in malnourished patients PN use resulted in a significantly lower mortality with a tendency towards lower rates of infection[61]. Traditionally, concerns for infection risk have limited the use of PN to achieve optimal nutrition delivery. However, three recent large randomized trials of PN in critical illness[94-96] (including a recent New England Journal of Medicine publication [95]) have clearly demonstrated that PN administration is no longer associated with any increased risk of infection.

Further, one of the recent large-scale multicentre studies investigated whether PN should be supplemented "early" (within 4 days) or "late" (after 7 days) in the event of impaired enteral tolerance[96]. Late infections (after day 9) were reduced in the PN group versus EN alone. The results provide arguments to initiate PN in malnourished patients and those at high illness risks on day 4 at the latest [97]. Overall, as stated recently by Awad and Lobo, "There is grade A evidence for use of PN in undernourished patients in whom EN is not feasible nor tolerated, and in patients with postoperative complications impairing gastrointestinal function[1]" [6]. This contributed to our recommendation to initiate early PN in patents at risk for malnutrition when goals are not met early via EN. Further we recommend continuation of PN support for patients who are not able to take in at least 60% of their protein/kcal requirements via the oral route. Finally, given the new availability of fish oil containing lipid formulations in the U.S. there is data supporting a benefit of utilizing fish oil containing balanced lipid formulations versus soy lipid alone in patients requiring post-operative TPN. This data from a recent systematic analysis in 23 RCTs, including 1502 surgical and ICU patients demonstrated fish oil containing lipids reduced length of stay and infectious complications versus traditional soy-only lipids[98].

VI. Role of nutrition in optimizing recovery from surgery post-hospital discharge?

Even with initiation of preoperative nutritional support, patients who develop postoperative complications will continue to lose weight and are at risk for serious further deterioration of nutritional status as was recently shown by Grass et al [99]. These patients identified via preoperative nutritional screening clearly require continuing nutritional follow-up post-discharge. Further in a considerable number of patients following major gastrointestinal surgery oral calorie intake will be inadequate for a prolonged period with a significant risk for postoperative malnutrition, especially after discharge. In patients after ICU discharge, an observational study demonstrated an average spontaneous calorie intake of 700kcal/d. This is far insufficient in the anabolic phase of rehabilitation, when a caloric intake of 1.2-1.5 x resting energy expenditure resting energy expenditure (REE) is recommended and thought to be required[100]. It also emphasizes the importance of closely observing food intake in post-operative patients. In patients who have lost significant weight following surgery/illness, a considerable period of significant increases in calorie and protein delivery is required for recovery[101]. As stated by Ansel Keys, principal investigator of the legendary Minnesota Starvation Experiment following World War II,

> "Enough food must be supplied to allow tissues destroyed during starvation to be rebuilt . . . our experiments show in an adult **no appreciable rehabilitation can take place on diet of 2000 calories/day. The proper level is more like 4000 kcal daily for some months".**

In this study of healthy, young men who sustained weight loss due to inadequate food intake (without the catabolic/hypermetabolic effects of a surgical insult) recovery to a normal weight took an average of 4000 kcal/d for an average of 6 months - 2 years. Hence, the post-hospital discharge period following major surgery is an essential period where nutrition support is required to optimize outcomes.

Thus, we must ask ourselves if our postoperative patients will be able to consume adequate protein and calories to optimally recover? As stated, data and experience has taught us in most cases the answer is no. Recovering postoperative patients, especially elderly individuals, are challenged by decreased appetites, persistent nausea and constipation from opiates, and lack of education about how to optimize their diet[102]. To address this, a large body of data demonstrates that oral nutrition supplement (ONS) should be a fundamental part of our postoperative discharge care plan. Meta-analysis data in a range of hospitalized patients, including surgery patients demonstrates ONS reduces mortality, reduces hospital complications, reduce hospital readmissions, shorten length of stay, and reduces hospital costs [54,103-105]. A large hospital database analysis of ONS use in 724,000 patients matched with controls not receiving ONS showed a 21% reduction in hospital LOS and for every $1 (U.S.) spent on ONS, $52.63 was saved in hospital costs[106]. Finally, a very recent large randomized trial of 652 patients and 78 centers studied the effect of high protein ONS with β-Hydroxy β-Methylbutyrate (HP-HMB) versus placebo ONS in elderly hospitalized patients at risk for malnutrition [107]. The data demonstrated that high protein HP-HMB reduced 90-day mortality by ~50% relative to placebo (4.8% vs. 9.7%; relative risk 0.49, 95% confidence interval [CI], 0.27 to 0.90; $p = 0.018$). [107] Further research focused on high-risk post-operative patients is needed in this critical period of recovery.

Future Research Questions: Please See Appendix #4 for full discussion.

Figure Legends:

Figure 1: Facts and Data For Perioperative Nutrition Screening and Therapy. Data drawn from [6,19,106]

Figure 2: Pre-Operative Nutrition Score (PONS) Assessment Tool

Figure 3: Example of Pre-Operative Nutritional Care Pathway for Low Nutrition Risk Patients (Currently Utilized by Duke University Peri-Operative Optimization Team (POET) Nutrition Clinic)

Figure 4: Example of Pre-Operative Nutritional Care Pathway for High Nutrition Risk Patients – as defined by any positive response on the PONS score. (Currently Utilized by Duke University Peri-Operative Optimization Team (POET) Nutrition Clinic)

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