**Supplemental Appendix**

**#1- Key Perioperative Nutrition Questions within context of an ERAS/ERP Program**

Based on both pre-conference discussions and key literature, the following questions were considered most relevant to perioperative nutrition management:

**Prior to Surgery:**

i) What are the optimal methods to routinely incorporate preoperative nutritional evaluation into an ERP to predict surgical risk and identify patients in need of preoperative nutritional optimization?

ii) What are the key goals of pre-operative nutritional optimization? Specifically, what is the role of achieving protein delivery goals in perioperative nutrition?

iii) When should high protein oral nutrition supplements (ONS), enteral nutrition (EN), and parenteral nutrition (PN) be initiated in the pre-operative setting?

iv) What is the appropriate practice to minimize preoperative fasting and what is the role of preoperative oral intake of clear carbohydrate loading solutions up to 2 h prior to the induction of anesthesia?

**Before and After Surgery:**

v) What is the role of immunonutrition (IMN) in optimizing patient outcomes when utilized before and after surgery?

**After Surgery:**

vi) When should feeding be initiated after surgery? What should the goals of post-operative nutritional optimization include? Specifically, what is the role of protein delivery in postoperative nutrition?

vii) What is the role of specific interventions such as high protein oral nutrition supplements (ONS), enteral nutrition (EN), and parenteral nutrition (PN) in the post-operative setting and when should these therapies be initiated?

viii) What nutrition intervention(s) should be utilized to optimize recovery from surgery following hospital discharge?

**#2- Future Pre-Operative Assessments: Sarcopenia and Vitamin D**

Sarcopenia is traditionally defined as age-related loss of muscle mass though newer definitions include the loss of muscle strength as well. 1 Low muscle mass has been shown to predict perioperative morbidity and mortality after a wide range of surgical procedures.2 3, 4, 5, 6, 7. Additionally, sarcopenia is associated with higher payer costs and negative margins after surgery. 8 It has been advocated as an additional factor to consider for preoperative risk assessment, as sarcopenic patients can have normal and even high BMIs. Skeletal muscle mass has traditionally been quantified using computed tomography (CT) scans at the third lumbar vertebra, as this area correlates with whole-body muscle mass. 9. In surgical patients, a rapidly growing body of literature demonstrates low baseline skeletal muscle mass may be an independent risk factor for surgical complications in patients undergoing colorectal 10,11, diverticular12, and pancreatic13 oncological surgery. Muscle mass loss pre-post oncological surgery is an additional risk factor for complications14 and mortality15,16. Thus, we suggest evaluation of lean body mass via CT scan, when available, to assist with nutritional risk prediction prior to surgery.

Further studies on the role of objective measures of sarcopenia, such as CT scan or lean body mass ultrasound, are needed. A major limitation of these studies is their retrospective nature. While evidence from observational studies of baseline muscle mass and quality continues to grow, sufficient data to justify intervention development based on these measures exists and is desperately needed. Primary outcomes should likely focus on function and/or complications as opposed to mortality17.

Finally, increasing data demonstrates a significant portion of the U.S. population is Vitamin D deficient18 and data in surgical patients shows that Vitamin D Deficiency has a significant relationship to postoperative complications19. Further, a recent randomized controlled trial published in JAMA showed in ICU patients with Vitamin D levels < 12 ng/ml experienced a significant improvement in hospital survival when vitamin D was aggressively supplemented20. Thus, it is possible to consider checking vitamin D levels prior to all major surgery and repletion of 50,000 units once weekly for the period prior to surgery in patients found to be deficient (< 30 ng/ml). More data is needed on the role of vitamin D supplementation on surgical outcomes.

**#3 – Special Populations: Obesity**

For patients that are found to have a BMI > 40 or a BMI > 35 with weight related co-morbidity such as diabetes, hypertension, sleep apnea or gastroesophageal reflux disease, referral for weight management, including surgery should be considered to minimize overall morbidity and mortality21.  In such patients, pre-operative weight reduction may have a positive impact on outcomes in patients presenting for elective procedures such as hernia surgery22,23. A large number of obese patients (especially elderly obese) suffer from significant sarcopenic obesity and needs for optimal protein delivery in the perioperative setting is paramount 24.

**#4- Future Research Questions:**

Question #1: The PONS scoring system was created due to a need for a simple, objective definition of surgical malnutrition. The questions in the score are based on previously well-validated nutrition risk variables. However, prospective validity and reliability testing along with a usability assessment needs to be performed to evaluate the utility the PONS score as a clinical and research tool.

Question #2: Further research is needed to identify a gold standard point-of-care (POC) and/or laboratory test that can assist in determining malnutrition/nutrition risk. POC tests for anemia, diabetes, and other chronic conditions have been developed yet there is no reliable POC indicator for malnutrition. Albumin, which is clearly correlated to surgical outcomes,25 has been used to quickly and inexpensively measure nutritional risk has unfortunately been misconstrued as a universal marker of malnutrition. It is well-known thatAlbumin is an acute-phase reactant that gets depleted during inflammation 26, shifts from vascular to interstitial spaces in response to sepsis/trauma 27, and does not change in simple starvation conditions28. The utility of albumin as a *modifiable* risk factor has not been thoroughly explored and deserves further research. Further, although albumin is a very useful of surgical risk, which may be related to malnutrition, a more specific, objective laboratory marker is needed. The development of a cost-effective perioperative marker of nutritional status will also assist in addressing the question of potential endpoints of nutritional therapy prior to surgery. This will be essential in order to provide the most “cost-effective” and timely perioperative nutritional therapy, where the goal is not likely to be “normalization” of nutritional status pre-operatively, but an attempt to define optimal nutritional “readiness” for surgery.

Question #3: The role of IMN was an area of great controversy in our discussions. 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. Further, additional trials of IMN within ERAS pathways are needed. Ultimately, a definitive, adequately-powered, randomized, multi-center trial of IMN is needed to finally define the previously observed benefits of perioperative IMN in many smaller trials.

Question #4: As stated, much of the perioperative nutrition literature is based on studies conducted outside the context of ERAS. Thus, the role of nutritional assessment and intervention in patients who receive care in a structured pathway are needed. Trials on the role of preoperative and postoperative optimization with PN, when indicated, can now be conducted more confidently in ERPs, given the newly described safety and lack of infectious risk with PN. Further, the ideal amount of protein to optimize surgical outcomes and post-operative physical functional in ERPs need to be better determined. Recent trials, such as the study demonstrating receiving > 60% of protein needs over first 3 post-operative days associating with a 4.4-day reduction in length of stay are encouraging29. Without doubt, additional trials examining effect of specific nutrition therapy in ERP/ERAS pathways should be a focus of future research.

Question #5: The role of protein versus total caloric delivery and potential combination with exercise to improve perioperative outcomes will need continued exploration. Our recommendation to prioritize protein intake over consumption of calories in the pre-operative period is based on studies showing that the addition of protein to a diet can has an anabolic effect30, as does consumption of food sources that consist primarily of protein31. There is at least one prospective randomized controlled trial in critically ill surgical patients demonstrating that a hyperproteineic hypocaloric diet leads to improved sequential organ failure assessment (SOFA) scores despite receiving similar amounts of calories prior to surgery32. Further as described previously 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).29 In non-surgical patients, the addition of a structured exercise regimen to a high protein diet increases both lower extremity muscle mass and strength33. Two randomized controlled trials conducted have found that protein supplementation improves physical performance but does not affect muscle mass in frail, elderly subjects, whereas resistance training in combination with a high protein diet improves both physical strength and muscle mass34,35 Interestingly, the timing of protein consumption may be as important as the amount. A prospective randomized controlled trial of elderly inpatients found that a protein “pulse” diet improved lean body mass when compared to a standard diet containing 1.3 g/kg/d protein spread throughout the day36. Reconciling this data with the protein “ceiling effect” described above will take additional research.

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