12 Perioperative Nutrition in Head and Neck Free Flap Reconstruction

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Introduction

Nutritional optimization is a key but often overlooked aspect of the management of head and neck cancer (HNC) patients undergoing surgical resection and free flap reconstruction, both preoperatively and postoperatively. Due to a variety of physical factors, comorbidities, and metabolic perturbations associated with their disease process, HNC patients are at high risk for malnourishment prior to, during, and after treatment [1, 2]. While the prevalence varies with tumor site, stage, and assessment modality, overall >30% of HNC patients are malnourished prior to initiation of treatment [3]. As preoperative malnutrition has been associated with a variety of negative operative outcomes, the high rate of malnutrition in this patient population is both a challenge for head and neck surgeons and a target for improved interventions.

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Assessing Malnutrition

While specific definitions of malnutrition vary, it is generally agreed upon that malnutrition encompasses deficiencies in a patient's intake of energy, protein, and/or essential nutrients [4, 5]. Within a clinical setting, there is expert consensus that malnutrition as a diagnosis should be grouped by etiology in order to reflect underlying inflammatory state given the effect of inflammation on nutritional requirements, with categories of "starvation-related malnutrition," "chronic disease-related malnutrition," and "acute disease or injury-related malnutrition," with HNC patients generally falling into the middle category reflecting a chronic state of mild-to-moderate inflammation existing concurrently with their nutritional compromise [6].

A variety of different metrics are used in practice to assess for malnutrition, each with their own strengths, limitations, and ideal use cases. These assessment modalities include clinical and anthropometric characteristics such as body mass index (BMI) and weight loss, biologic markers such as serum albumin level, and several validated composite scoring systems designed for holistic, multidisciplinary evaluation.

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Clinical Markers

Clinical characteristics such as BMI and weight loss are widely accepted as markers of malnutrition and are easily measured in a clinical setting. The WHO organization defines "underweight" as a BMI <18.5, a cutoff that has been widely adopted [7]. However, as obesity increases worldwide, there has been a push to raise BMI cutoffs in order to capture patients who may fall within clinically "normal" BMI but have significant disease-related weight loss. The European Society of Clinical Nutrition and Metabolism (ESPEN) consensus statement advocates for a screening cutoff of 20 for patients <70 years old and 22 for 70 years and older, as long as the patient also experienced weight loss [8].

Besides BMI, the other widely accepted screening modality is unintentional weight loss. Compared to BMI, which provides a static measurement at a point in time, unintentional weight loss provides a dynamic measurement of a patients nutritional status and has been found to have better sensitivity and specificity in identifying malnutrition in cancer patients compared to BMI [9]. While cutoffs differ somewhat between organizational guidelines, generally unintentional weight loss ≥5% within 1–3 months or ≥10% within 6 months qualifies a patient as being at risk for malnutrition [6, 8, 10].

From a research perspective, it is useful to have a common definition of malnutrition in order to allow for easier comparison between studies. Within the head and neck surgical literature, the most frequently used definition of malnutrition is unintentional weight loss ≥5–10% within 6 months along with a BMI <20 [10].

A variety of other clinical characteristics have been used as proxies for malnutrition. Fat free mass index (FFMI) is a composite height-weight metric similar to BMI; however, it only incorporates lean body mass rather than total body mass. As such, FFMI better reflects the loss of lean body mass seen in cancer-related malnutrition and is less affected by patient obesity [11, 12]. However, objective measurement of FFMI requires specialized equipment, making it less convenient than BMI. For malnutrition screening purposes, an FFMI of <15 for women and <17 for men has been suggested. Other metrics used include hand grip strength, arm and leg circumferential measurements, and skeletal muscle mass as calculated from imaging measurements [8, 13, 14]. However, these metrics also all require specialized training or equipment, making them more difficult to implement clinically compared to BMI or weight loss.

Biologic Markers

A variety of serum markers are sometimes used as proxies for malnutrition, most commonly serum albumin and prealbumin levels. The use of biomarkers to evaluate nutritional status is appealing, as they are objective, routinely obtained, and easily followed over time. Albumin and prealbumin levels in particular have also been correlated with a number of clinical outcomes of interest in HNC surgical patients including overall survival, disease-free survival, and wound infection [15–23]. Albumin, the most common protein in blood plasma, acts as a transport protein and regulates oncotic pressure. Prealbumin also acts as a transport protein and, though less well validated as a biomarker compared to albumin, is frequently used as its much shorter half-life (2–3 days vs. 20 days for albumin) means that it may better reflect acute changes in patient status [1]. Other biomarkers that have been used include transferrin, total serum protein, and composite markers such as prognostic nutritional index, which combines albumin and lymphocyte count [1, 10, 24].

The use of any of these biomarkers is controversial due to their activity as acute-phase reactants, meaning that perturbations in their levels may more accurately reflect systemic inflammatory status than nutrition. While systemic inflammation predisposes patients to malnutrition, albumin and prealbumin levels are not correlated to weight loss in noninflammatory etiologies of malnutrition. In the context of significant systemic inflammation, providing nutrition support will oftentimes not correct low albumin and prealbumin [25, 26]. As such, expert consensus assigns limited relevance to biomarkers as indicators of malnutrition and cautions against their use as a primary screening or diagnostic modality for malnutrition [8, 13].

Composite Assessment

In addition to the individual clinical and biologic markers described previously, a number of validated instruments have been developed to provide a holistic assessment of nutritional status. The most commonly used of these assessments is the Patient Guided Subjective Global Assessment (PG-SGA). The PG-SGA was first developed in the 1990s as a scored, patient-reported extension of the Subjective Global Assessment—a physician-generated evaluation of patient nutritional status first published in 1987—and is comprised of two segments [27]. The first segment, known as the PG-SGA short form, is completed by the patient and assesses weight loss, food intake, activity level, and associated symptoms affecting eating [28]. The second segment, completed by a provider, further assesses relevant aspects of the patient's history and evaluates multiple physical characteristics including metabolic demand, muscle wasting, fat stores, and fluid balance [28]. At the end of the evaluation, patients are assigned to one of the three global assessment groups (well nourished, moderate/suspected malnutrition, severely malnourished), and the total score is used to triage patients to appropriate nutritional interventions.

Though not specifically developed for oncologic purposes, it is well validated in cancer patients and for evaluation of cancer cachexia and is frequently used in HNC both clinically and for research purposes [29–33]. PG-SGA scores are associated with a variety of clinical outcomes in oncologic patients including length of stay, postoperative complications, and overall survival [34, 35]. The PG-SGA is especially valuable in that it not only serves as a nutritional screening and assessment tool, but also triages patients and can be used to monitor the success of nutritional interventions [36]. While the physical components of the provider segments require time and some expertise to administer, the patient-completed PG-SGA short form alone has high sensitivity and specificity in detecting malnutrition compared to the complete PG-SGA and so can act as an easier screening tool [37–39].

A variety of other composite scoring systems have been validated for screening and assessing malnutrition. The Nutritional Risk Screening, 2002 (NRS 2002), was designed to identify who are malnourished or at nutritional risk and who would benefit from nutritional interventions [40]. Derived from a retrospective analysis of randomized control trials examining the effects of malnutrition and nutritional interventions, the NRS 2002 is a simple, provider-administered tool which generates a composite score based both on nutrition status as measured by BMI, weight loss, and food intake and on severity of underlying disease process. A score of 3 or greater out of 7 indicates that a patient is malnourished and that nutritional support should be started. The NRS 2002 has been well validated as a measure of malnutrition including in HNC, where it performs comparably to the PG-SGA while being quicker and simpler to perform [40–43]. Other scoring systems include the Malnutrition Universal Screening Tool (MUST), the Academy of Nutrition and Dietetics/American Society for Enteral Nutrition (AND/ASPEN) criteria, and the recently developed Global Leadership Initiative on Malnutrition (GLIM) criteria [13, 38, 43, 44]. While these systems vary somewhat in their specific assessments, they all evaluate multiple history and physical findings of malnutrition as well as underlying disease states.

Mechanisms of Malnutrition in Head and Neck Cancer

Rates of malnutrition and nutritional risk are very high in HNC patients, with greater than 30% of patients with significant weight loss at initiation of treatment, a number which is even higher in certain subgroups of patients including those with late-stage disease and tumors of the upper aerodigestive tract [3]. The reason for this is multifactorial, encompassing physical factors associated with HNC and its treatments, common characteristics of HNC patients, and systemic metabolic perturbations associated with malignancies referred to as cancer cachexia.

Physical Mechanisms

As suggested by the higher rates of malnutrition in patients with aerodigestive tract tumors compared to other head and neck locations, HNC can contribute to malnutrition via mechanical barriers to appropriate oral intake [1, 3, 45]. Patients with aerodigestive tract tumors experience varying levels of dysphagia, odynophagia, and trismus, all of which can contribute to the development of malnutrition via insufficient oral intake. This is further compounded in patients requiring salvage surgery, as prior radiotherapy, chemotherapy, or surgery can compromise oral intake via alteration of normal anatomy, fibrosis, xerostomia, dysgeusia, and loss of dentition among other mechanisms [45, 46].

Patient Characteristics

Several of the behavioral and demographic characteristics frequently seen in the HNC patient population also contribute to malnutrition. Alcohol and tobacco use are well established as major risk factors for the development of HNC, and rates of alcohol and tobacco use are high among HNC patients [47]. Heavy alcohol use is associated with malnutrition due to micronutrient deficiencies and lifestyle disruption, with high levels of malnutrition seen in patients undergoing treatment for alcohol abuse [48, 49]. Likewise, tobacco use is associated with decreased oral intake and lower body weight, potentially due to appetite-suppressing effects of nicotine [50]. Alcohol and tobacco use are also both associated with perturbations in taste, which may further contribute to decreased oral intake [51]. HNC cancer patients also tend to be older, with more than 50% of patients over the age of 60 [52]. These older patients are also at risk for sarcopenia, age-related loss of muscle mass that further contributes to the loss of lean muscle seen in malnutrition [53].

Cancer Cachexia

Per consensus guidelines, cachexia is defined as "a multifactorial syndrome characterized by ongoing loss of skeletal muscle (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment" [54]. It is frequently seen in cancer patients, occurring in over 80% of patients with advanced-stage disease [54–56]. While a detailed review of cachexia pathophysiology is beyond the scope of this chapter, cancer cachexia results from complex interactions between tumor and host cells via humoral factors leading to perturbations in metabolism and organ system function, resulting in the loss of skeletal muscle [56]. Factors contributing to muscle loss include decreased anabolism via reduction in anabolic hormone secretion and sensitivity and amino acid availability, as well as increased catabolism due to chronic proinflammatory stimulation and increased oxidative stress [2, 56, 57]. Cytokine-mediated disruption of the neuroendocrine axis also leads to perturbations in orexigenic and anorexigenic pathways, resulting in decreased appetite and oral intake, which further contributes to loss of muscle mass [1, 2, 57]. Recent evidence also implicates a variety of other organ systems in the pathogenesis of cancer cachexia, including conversion of white adipose tissue to brown adipose tissue, abnormalities in liver metabolism, and changes in gut microbiota [1]. Compared to the other factors contributing to malnutrition, cancer cachexia is particularly difficult to address, as it is only partially responsive to conventional nutritional support.

Effects of Malnutrition on Head and Neck Free Flap Reconstruction

Within the general surgical literature, preoperative malnutrition is well established as a negative surgical prognostic factor, having been associated with increased length of stay (LOS), delayed wound healing, and increased rate of complications among other undesirable outcomes [58, 59]. Though there are only a few studies examining the effects of malnutrition on head and neck free flap reconstruction specifically, the available evidence supports that it is likewise associated with poorer postoperative outcomes.

In the largest study to date, a retrospective review of 977 patients undergoing resection of HNC with free flap reconstruction, patients who were malnourished as measured by Nutrition-Related Index (a composite score of albumin level and body weight) had significantly higher 30-day mortality compared to matched controls, along with higher rates of pulmonary complications, bleeding, and venous thromboembolism [60]. Similarly, another large retrospective study found a significant association in multivariate analysis between preoperative albumin and overall survival in patients with upper aerodigestive tract squamous cell carcinoma undergoing resection and free flap reconstruction [23].

Looking at other postoperative outcomes after head and neck free flap reconstruction, separate retrospective studies found an increased rate of wound infections and increased rate of major postoperative complications in patients with low BMI and history of malnutrition, respectively [61, 62]. Likewise, in two retrospective studies which calculated the volume of skeletal muscle mass from CT imaging as a measure of malnutrition, decreased muscle mass at L3 was associated with a variety of postoperative complications including higher rates of wound infection, fistula, wound breakdown, and flap-specific complications [14, 63]. Finally, outside of head and neck reconstruction, a retrospective study of extremity free flap reconstruction found a significant association on multivariate analysis between malnutrition as measured by a composite score of albumin and lymphocyte count and rate of flap failure [24]. Some caution must be taken in interpreting these results as there is a lack of prospective studies, which limits preoperative nutrition assessment to regularly collected data such as BMI and albumin rather than more robust assessments such as PG-SGA. Nonetheless, based on existing data, there is a clear association between preoperative malnutrition and poor outcomes after head and neck free flap reconstruction.

Nutritional Interventions

Given the high prevalence of malnutrition in HNC patients and the negative surgical outcomes associated with preoperative malnutrition, there is a clear need for nutritional intervention in this patient population. However, implementing these interventions successfully—including nutrition screening and supplementation prior to hospitalization, in the immediate preoperative period, and postoperatively—requires a well-defined clinical pathway with close collaboration between an interdisciplinary team and institutional buy-in. A possible framework for addressing these challenges can be found in Enhanced Recovery After Surgery (ERAS) protocols.

ERAS Protocols

ERAS protocols are "patient-centered, evidence-based, multidisciplinary team-developed pathways for a surgical specialty and facility culture to reduce the patient's surgical stress response, optimize their physiologic function, and facilitate recovery" [64]. ERAS protocols were initially developed to improve patient recovery and outcomes after open GI surgery, where there is strong evidence that implementation reduces LOS and results in fewer major postoperative complications [65]. ERAS protocols have subsequently been developed for a variety of other surgical fields including head and neck surgery, for which consensus ERAS guidelines were published in 2017 [66–68]. ERAS protocols address all aspects of the perioperative process including non-nutrition factors such as standardized multimodal anesthesia and intraoperative fluid management. However, a significant portion of the protocols focus on nutrition optimization—prehospital, preoperative, and postoperative—and as such serve as an evidence-based example for implementing nutritional support in head and neck free flap reconstruction [66].

ERAS in Head and Neck Surgery

In 2017, an international working group of head and neck surgeons, anesthesiologists, intensivists, and nutritionists published a consensus, evidence-based ERAS protocol specifically for head and neck surgery with free flap reconstruction [66]. Based on existing ERAS protocols, the group identified best practices for 17 areas of perioperative care, many of which are nutrition focused. These include comprehensive nutritional assessment with preoperative nutrition intervention as indicated, minimization of preoperative fasting with carbohydrate loading, and initiation of postoperative feeding within 24 h with oral diet if possible. In a subsequent systematic review of 2630 head and neck free flap patients, enrollment in ERAS protocols was associated with significant decreases in hospital LOS, readmissions, and wound complications [69]. While these improvements cannot be solely attributed to the nutrition interventions in the protocols, they nevertheless illustrate the potential of improved perioperative nutrition management in this patient population.

Prehospital Patient Assessment

The first step in successfully implementing nutrition interventions is identifying patients who are malnourished or at nutritional risk. As such, all patients being evaluated in clinic for possible head and neck surgery with free flap reconstruction should undergo nutritional screening as a routine part of their preoperative workup. Simple, patient- or nursing-performed screening tools such as the PG-SGA short form or NRS 2002 are well suited for this purpose and should be integrated into the workflow of a standard clinic appointment. Any patient identified as malnourished or at nutritional risk should then be referred to a clinical nutritionist for a comprehensive nutritional assessment. This assessment should include patient history, anthropometry, biochemistry, dietary intake, and a clinical examination of body composition [66]. Based on this evaluation, a personalized nutrition plan should be created, including patient-specific adaptations such as enteric access and feeding in patients unable to tolerate an oral diet. There is wide consensus for preoperative screening and assessment including National Comprehensive Cancer Network, Cancer Council Australia, and UK National Multidisciplinary Guidelines [70–72].

Prehospital Nutritional Support

Given the strong evidence for worse surgical outcomes, there is consensus agreement that HNC patients assessed to be malnourished should receive nutritional support prior to surgery [59, 66]. Within the general surgical literature, preoperative nutritional support has been associated with lower rates of postoperative complications and shorter LOS [73–75]. Unfortunately, there is a lack of prospective studies specific to head and neck surgery; however, in one small RCT, preoperative nutrition support in HNC patients was associated with improved preoperative quality of life scores [76]. Consensus surgical nutrition guidelines strongly recommend that severely malnourished patients receive support—with time ranging from 5–7 to 10–14 days—prior to major surgery, even if surgery has to be delayed [59, 77]. Particularly in the case of oncologic surgery, the benefits of optimal nutrition support must be weighed against potential negative outcomes associated with delaying definitive surgery. However, in general, there is at least some delay between when the decision to operate is made and when surgery occurs due to logistical and administrative realities, giving time for appropriate support in most cases as long as evaluation by clinical nutrition and initiation of treatment are performed promptly.

The appropriate form of nutritional support is determined with the clinical nutritionist based on their comprehensive assessment and the patient's individual needs. Whenever possible, sufficient nutrition is maintained with an oral diet with high caloric and protein content. Symptomatic barriers to nutrition such as pain or xerostomia can be addressed with topical or systemic medications. Diet consistency can be modified, and intake can be augmented with supplements such as nutritional shakes. However, if a patient is unable to maintain sufficient oral caloric intake even with support, enteral nutrition should be initiated.

Enteral and Parenteral Nutrition

Access for enteral nutrition can be established either with a nasogastric tube (NGT) or with a gastrostomy tube. Gastrostomy placement is accomplished either percutaneously under endoscopic (PEG) or radiologic (PRG) guidance or with an open surgical procedure if patient anatomy is not conducive to minimally invasive access. Though tumor seeding to the gastrostomy site following PEG placement has been reported, newer techniques utilizing direct transabdominal placement rather than the traditional method of advancing the tube transorally may minimize this possibility [78]. In HNC patients undergoing radiotherapy or chemoradiotherapy, a systematic review of RCTs found no difference in overall patient satisfaction or complications between NGT and PEG [79]. However, in practice, NGTs are generally used when enteral nutrition is required for less than 4 weeks, while gastrostomy tubes are used for longer term feeding, as NGTs are more cumbersome and easier to dislodge [1, 10, 80].

A number of standard tube feed formulas are commercially available, as are a variety of specialty feeds such as low glycemic index feeds for diabetic patients and free amino acid feeds for patients with impaired GI function [1]. Depending on a patient's ability to tolerate PO, enteral feeding can be used as a supplement to oral feeding or as a sole source of nutrition. Type and volume of feeding are determined based on the results of the comprehensive nutritional assessment by clinical nutrition.

In the rare instances where an HNC patient cannot receive enteral nutrition, such as when enteral access cannot be established or with comorbid intestinal failure, parenteral nutrition can be provided preoperatively. In malnourished general surgical patients, preoperative parenteral nutrition is associated with improved postsurgical outcomes including decreased complications and LOS [58]. However, compared to enteral nutrition, parenteral nutrition is more expensive, is more complicated to administer, and may be associated with higher rates of infectious complications [81]. As such, parenteral nutrition should only be utilized when oral or enteral nutrition is not possible.

Immunonutrition

One of the defining features of cancer cachexia is the inability to fully reverse it with conventional nutritional support [54]. This is due to the metabolic, inflammatory, and immune perturbations associated with cancer cachexia, with patients exhibiting a chronic systemic inflammatory state with a shift from anabolism to catabolism [56]. As such, significant research has gone into the development of oral and enteral diets supplemented with specific nutrients thought to have a beneficial immune- and inflammation-modulating effects, known as immunonutrition or immune-modulating diets [82].

A variety of nutrients have been utilized in these dietary formulas based on their known physiologic roles, the most widely used of which are glutamine, arginine, omega-3 fatty acids, and ribonucleotides [81, 82]. Arginine is an amino acid involved in wound healing and immune function via its role in numerous synthetic and metabolic pathways including nitric oxide metabolism, collagen production, and normal T-cell, B-cell, and macrophage activity [83, 84]. Arginine is considered a conditionally essential amino acid, in that in can be synthesized de novo by the body, but can be depleted in times of metabolic stress or rapid tissue turnover as seen in cancer cachexia [82, 84]. Glutamine—another conditionally essential amino acid for which demand increases during catabolic disease states—serves as oxidative fuel for immune cells and rapidly replicating cells such as GI mucosal cells and is involved in gluconeogenesis [85, 86]. Omega-3 fatty acids, specifically eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), competitively inhibit the production of proinflammatory arachidonic acid and decrease the expression of proinflammatory cytokines and adhesion molecules [87]. Ribonucleotides, as the constituent elements of DNA and RNA, are required for essentially all cellular processes and, like arginine and glutamine, require exogenous supplementation during times of metabolic stress [86]. A number of commercial immunonutrition formulas are available, containing varying combinations and concentrations of these elements.

The use of perioperative immunonutrition in general surgery is well established, with a number of systematic reviews of RCTs showing a decreased rate of postoperative complications and LOS [81, 88, 89]. Use of immunonutrition is also cost effective [90]. As such, multiple consensus guidelines strongly recommend perioperative immunonutrition in patients undergoing major cancer surgery [81, 91, 92]. However, there is no consensus on the ideal timing of immunonutrition, or if preoperative immunonutrition alone is more effective than standard nutritional supplementation [81, 93].

The use of immunonutrition in head and neck surgery is less well studied. A 2018 systematic review of 19 head and neck-specific RCTs examining the efficacy of perioperative immunonutrition found a significant decrease in the rate of postoperative fistula but no decrease in wound infections or LOS [94]. Most included studies were small, at high risk of bias, or both. Conversely, in a recent prospective study of HNC patients undergoing salvage surgery after radiotherapy—a group at increased risk for poor wound healing—use of preoperative immunonutrition was associated with decreased postoperative complications and LOS [95]. Large, well-designed studies are necessary to further elucidate the efficacy of immunonutrition in head and neck surgery as well as answer the questions regarding ideal timing, formulation, and use in certain patient subgroups.

Preoperative Nutrition

Avoidance of Preoperative Fasting

Traditionally, patients are instructed to fast starting at midnight before major surgeries due to concerns for aspiration during induction of anesthesia, meaning that they may go without nutrition or even fluids for eight or more hours prior to surgery even without taking into account any delays or changes in surgical scheduling. However, this is not supported by current evidence. In a meta-analysis of RCTs, a shortened fluid fast that allows clear fluids up to 2 h before surgery was not associated with increased aspiration, regurgitation, or morbidity [96]. This is reflected in the newest best practice guidelines from both US and international anesthesia societies, which allow for clear liquids up to 2 h before surgery and light meals up to 6 h before surgery [97, 98].

Conversely, fasting for even a short period of time prior to surgery is associated with undesirable physiologic changes. Fasting induces a catabolic state. This further contributes to metabolic stress and increases postoperative insulin resistance, making glycemic control more difficult [99, 100]. Postoperative hyperglycemia in HNC patients undergoing free flap reconstruction has been associated with higher rates of surgical site infection [101]. Preoperative fasting is also associated with increased inflammation, decreased immune functioning, and increased patient discomfort and anxiety [102–105]. Because of this, there is strong expert consensus that preoperative fasting should be limited as much as possible including in head and neck surgery [66, 81, 91].

Carbohydrate Loading

Given the deleterious effects of preoperative fasting, ERAS protocols advocate for carbohydrate loading in patients prior to surgery with a carbohydrate-rich drink [65, 81]. While exact protocols vary, patients are commonly given 800 mL of a 12.5% carbohydrate drink at midnight prior to surgery and another 400 mL 2 h before surgery [59, 65]. A variety of commercial formulations are available to patients over the counter. In several systematic reviews of RCTs, use of preoperative carbohydrate loading was associated with increased insulin sensitivity and improved postoperative discomfort [106–108]. Effect on LOS is equivocal, with the most recent review finding a small decrease in LOS compared to fasting but not to water or placebo [108]. No difference was seen in postoperative complications, and notably, no aspiration events were seen in any of the included studies. Other individual RCTs have associated carbohydrate loading with improved preoperative comfort, decreased postoperative inflammation, enhanced immune function, and better retention of muscle strength both 1 week and 1 month after surgery [102–105, 109]. The overall quality of existing trials is low, and there is a lack of head and neck surgery-specific trials. Nevertheless, the ERAS head and neck protocol offers the option for preoperative carbohydrate loading given the low cost, minimal associated risks, and well-established benefit to patient comfort, if nothing else [66, 81].

More recent studies have also examined the efficacy of adding whey protein to preoperative carbohydrate drinks, theorizing that it may further decrease inflammation and improve postoperative recovery [110–112]. In an RCT of HNC patients undergoing surgery, the addition of whey protein to standard preoperative carbohydrate loading was associated with decreased postoperative complications and no instances of aspiration [113]. However, given the small size of the trial, more evidence is needed to make informed recommendations regarding preoperative whey protein use.

Postoperative Nutrition

Postoperative Feeding

Optimal nutritional management of HNC patients undergoing free flap reconstruction does not end at the time of surgery, but rather continues through the postoperative period. A major topic of investigation within the surgical nutrition literature has been the appropriate timing for resuming feeding after surgery. Though there is a lack of head and neck-specific studies, multiple systematic reviews of RCTs from the GI surgery literature found that resumption of feeding—either enteral or oral—within 24 h of surgery resulted in shorter LOS and potentially a decrease in postoperative infections and other complications [114, 115]. Early feeding was also not associated with any increased morbidity. As such, there is wide consensus among surgical nutrition guidelines and ERAS protocols—including for head and neck surgery—that feeding should be resumed within 24 h of surgery [65, 66, 81, 91].

Early Oral Feeding

As discussed above, there is clear evidence that early feeding in general is beneficial to postoperative recovery. In line with the principle that oral feeding is always the preferred route of nutrition when feasible, there is also evidence that early oral feeding specifically may convey additional benefits compared to early enteral or parenteral nutrition. In a systematic review of trials comparing early oral feeding to traditionally timed feeding ± early enteral or parenteral nutrition in 2112 patients undergoing upper GI surgery including esophagectomy, early feeding was associated with a decreased LOS [116]. No increase was seen in mortality or in postoperative complications including anastomotic leak.

However, early postoperative oral feeding in HNC patients is more controversial. Per the ERAS head and neck protocol, after free flap reconstruction, "oral diet is the first choice for all patients tolerating it" [66]. Yet, there are a number of reasons why these patients may not be able to tolerate oral feeding in the early postoperative period. Fundamental changes in upper aerodigestive tract anatomy resulting from surgery and reconstruction may render patients unable to safely tolerate an oral diet. Patients who will be able to tolerate an oral diet in the long term may nevertheless be unsafe for an oral diet in the early postoperative period due to swelling and a need to learn compensatory swallowing techniques. Finally, there has traditionally been a concern that early oral feeding may compromise the surgical site, leading to flap dehiscence, poor wound healing, or fistula formation.

Early oral feeding has been best studied after total laryngectomy. In a systematic review of 14 studies (4 RCTs, 10 cohorts, 1886 total patients) comparing the rate of fistula formation in patients started on oral feeding on or before postoperative day (POD) 5 versus after POD 5, no increased rate of pharyngocutaneous fistula formation was seen in the early feeding group [117]. The early feeding group also had a decreased LOS in the two studies which used it as an outcome measure. There was also no increased fistula rate with early feeding in a subgroup analysis of studies in which >40% of patients were undergoing salvage surgery, an important finding for clinical practice given an increasing percentage of salvage surgeries due to increasing rates of primary treatment with nonsurgical therapies [118, 119]. However, another systematic review published around the same time found an increased risk of fistula with early feeding, though no increase was seen when only including RCTs [120].

Among other head and neck subsites, a number of studies have examined early feeding after oral cavity free flap reconstruction [121–124]. In the largest study, 400 patients (212 with previous radiotherapy or chemoradiotherapy) were either given nothing per mouth until POD 5 or evaluated for oral fluids ± soft diet on POD 1 [124]. In the early feeding group, 46% were able to tolerate oral fluids and 30% were able to tolerate a soft diet on POD 1, which increased to 94% and 84% by POD 3. In line with prior studies, there was no increase in fistulas, flap dehiscence, or other complications in the early feeding group, while LOS was significantly reduced [121, 122, 124].

Overall, while available evidence supports that early feeding after total laryngectomy or oral cavity free flap reconstruction is likely safe and may reduce LOS, there is a lack of large, randomized trials. As such, appropriate caution should be taken in implementing early feeding, with patients assessed on an individual basis. A team-based approach with collaboration between surgeon, dietician, and speech language pathologist should be used to determine the optimal timing for restarting oral intake [66].

Comprehensive Nutrition Management Pathway

Successfully implementing comprehensive nutrition management for HNC patients undergoing free flap reconstruction requires a multidisciplinary team and institutional support. The following section outlines the key steps of a head and neck free flap nutrition pathway based on the current evidence and best practice guidelines previously discussed in this chapter, and how these steps fit into clinical practice.

All patients should undergo nutrition screening at their initial visit with their head and neck surgeon, and those found to be malnourished or at risk for malnutrition should be referred to clinical nutrition for comprehensive assessment and initiation of appropriate nutritional support. It is critical that referred patients are seen by a nutritionist in a timely manner in order to give sufficient time for support without delaying surgery. Patients can also be referred to IR or GI at this time for PEG placement if it is anticipated that they will require more than a month of enteral nutrition. In the immediate preoperative period, patients should be allowed to have clear liquids by mouth until 2 h preoperatively, with a carbohydrate drink given 6 h and 2 h preoperatively. Implementation of these preoperative interventions must be done in close collaboration with anesthesia in order to ensure that they are implemented safely and do not result in cases being delayed. Postoperatively, feeding should be resumed within 24 h of surgery, either orally or via enteral access. Early oral feeding can be considered in patients who underwent total laryngectomy or oral cavity resection; however, the decision on optimal timing and need for supplementary tube feeds should be made in collaboration with clinical nutrition and speech language pathology. Diet supplementation with immune-modulating nutrients can also be considered throughout the perioperative period, particularly in patients at high risk for poor wound healing.

Conclusion

HNC patients are at high, multifactorial risk for preoperative malnutrition due to the nature of their disease process. Malnourishment, in turn, is associated with a variety of negative outcomes following head and neck surgery with free flap reconstruction including higher rates of major complications and increased 30-day mortality. As such, it is critical that malnutrition be identified and interventions initiated prior to surgery, and that nutrition monitoring and appropriate nutritional support are continued throughout the entire perioperative period. ERAS protocols, which have been increasingly adopted across surgical fields, provide a multidisciplinary, evidence-based framework for the implementation of comprehensive perioperative nutritional management. Larger prospective, randomized trials are necessary to better assess the effectiveness and safety of nutrition interventions in HNC patients undergoing free flap reconstruction, particularly regarding immunonutrition and early oral feeding.

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