Complex Head and Neck Microvascular Surgery

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Editors

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Comprehensive Management and Perioperative Care

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Preface

Modern surgical capabilities continue to develop and improve at an accelerating rate. Whereas less than 50 years ago a diagnosis of head and neck cancer or a devastating injury destined patients to lifelong disfigurement and severe functional deficits, in the recent decades, with the advent of microvascular free tissue transfer, the prognosis for these patients is no longer that grim. Even more fascinating, recent developments in the field of personalized surgery with computer-aided surgical planning and custom-made hardware allow us to perform devastating surgery with exceptional esthetic and functional outcomes due to outstanding reconstructive capabilities. We are fortunate to enjoy success rates well above 90% for microvascular tissue transfer. However, every single head and neck microvascular surgeon is keenly aware of the disastrous implications affecting patients' life expectancy and quality of life if reconstruction failure occurs. The remarkably technically challenging surgery carried out successfully is just half the battle, however. Consideration of various perioperative aspects is essential to ensuring overall satisfactory patient outcomes.

As the field of microvascular surgery is still relatively new, there are countless opportunities to continue to develop our understanding on how to improve patient care and surgical outcomes.

A single source that addresses all aspects of perioperative management of head and neck patients who underwent microvascular reconstruction does not exist. There is a generalized effort to improve overall quality of surgical care with initiatives such as the National Surgical Quality Improvement Program (NSQIP) and surgical patient recovery with efforts of Enhanced Recovery After Surgery (ERAS). These initiatives have shown significant reduction in complications and costs associated with the management of surgical patients in other specialties. Most recently, in 2017, ERAS published guidelines on the management of head and neck patients and highlighted paucity of data regarding optimal perioperative care. Perioperative management varies widely between hospitals and individual surgeons, and no standard guidelines aimed at optimization of patient outcomes currently exist. It has been shown in other specialties that standardization of perioperative management results in reduced complication rates, hospital stays, and cost.

In the following chapters, some of the world's most experienced head and neck microvascular surgeons share their knowledge, experience, and latest available scientific evidence on how to avoid pitfalls in the preparation for surgery, manage challenging intraoperative situations, and provide the most

effective postoperative care to our patients so that they can enjoy timely hospital discharge and return to their life.

Deepest gratitude goes out to my colleagues across the United States and the globe for their initiative and valuable contributions.

Sincerely

West Palm Beach, FL, USA Anastasiya Quimby

Contents

Part I

Pre-operative Considerations

Medical Assessment

1

Caitlin McMullen and Marianne Abouyared

Introduction

The advent of microvascular free tissue transfer has allowed many patients with complex head and neck defects to regain form and function in ways that previously may not have been possible. With a greater than 90% success rate, and some highly experienced surgeons even citing a greater than 99% success rate, free tissue transfer has become a powerful reconstructive option for most patients with head and neck oncologic ablative defects, benign tumor ablative defects, traumatic defects, or secondary complications of prior treatments such as osteoradionecrosis [1, 2].

An optimized patient is essential to prevent fistula and life-threatening wounds, to maximize postoperative function and aesthetics. Due to the risk factors that may lead to the need for head and neck free flap surgery, these patients commonly have a high burden of comorbidities that can affect their wound-healing abilities and recovery. The surgeon must undertake careful consideration of each patient including a full medical, surgical, and social history to determine the patient's candidacy.

There are few definitive contraindications to a surgical approach. Ultimately, those that would contraindicate any major surgery are strict contraindications for head and neck microvascular reconstruction (HNMVR) such as MELD >12, severe aortic stenosis, severe cardiac or pulmonary disease, and unresectable disease. Relative contraindications include surgery that will irreparably destroy basic essential functions, surgery that would render them unable to ever leave the hospital, and an inability to consent to surgery.

The surgeon's doorway exam or "eyeball test" should be strongly considered; however, this must be reinforced with objective data. An analysis of medical, surgical, nutritional, and psychosocial factors preoperatively is critical. Fortunately, with advanced planning, many conditions can be managed to minimize perioperative risk. While the literature is scant regarding medical considerations specifically for HNMVR, one can generally extrapolate the data from studies focused on any major surgical intervention. The patient's own medical history is also important to consider, and tightly intertwined with this

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is their current substance use, nutritional status, and mental health. The surgeon is encouraged to enlist available multidisciplinary consultants such as primary care physicians, cardiologists, pulmonologists, endocrinologists, social workers, nutritionists, speech language pathologists, dentists, and anesthesiologists to exercise their expertise and help optimize complex patients prior to these major surgeries. The head and neck microvascular surgeon plays a key role in coordinating care among these team members, and open and early conversation with anesthesia colleagues is critical.

In this chapter, we review important modifiable and nonmodifiable considerations when evaluating a patient for surgical readiness for HNMVR.

Medical Comorbidities and Their Preoperative Management

A thorough medical, surgical, and social history is essential when assessing a patient prior to surgery. Preoperative checklists and guidelines can be helpful to ensure that specific conditions have been assessed [3, 4]. An example of a preoperative checklist for a head and neck free flap patient that addresses many of their common issues is depicted in Table 1.1. In addition to careful questioning of the patient and caregivers, a review of referring records and primary care notes may provide essential information. Diagnoses, prior hospitalizations, medications, and prior surgeries all play an important role when determining surgical candidacy and reconstructive options. Preoperative blood work including comprehensive blood count (CBC), basic metabolic panel (BMP), international normalized radio (INR), prothrombin time (PT), and partial thromboplastin (PTT) should be obtained preoperatively routinely. Other laboratory studies may be relevant depending on the clinical scenario and past medical history including liver function tests (LFTs), thyroid-stimulating hormone (TSH), prealbumin, and others. Important considerations for the physician exam are listed in Table 1.2.

Table 1.1 An example of a preoperative checklist for a head and neck free flap patient to assess common and important considerations

Category	Considerations
Diagnosis/pathology	Pathology-confirmed diagnosis if applicable
Available imaging	Imaging and dates
Donor-site evaluation/selection	Examine and specify donor site
Preoperative labs	CBC, CMP, PT, PTT, INR, type, and screen
History of hypothyroidism or radiation	TSH level
Current feeding access	Oral/gastrostomy tube
Nutrition assessment	Dietician appointment, prealbumin, ferritin
Social work consultation	Perioperative support, discharge needs
Tobacco, alcohol, and substance use screening	Smoking cessation, preparation for withdrawal
Swallow assessment	Preoperative speech language pathology consult
Dental assessment	Dentition/occlusion
Current anticoagulation	Instructions for preoperative discontinuation
History of DVT/VTE	Use of mechanical compressive devices and chemical prophylaxis
History of urinary issues or prostate hypertrophy	Foley placement
Preoperative consultations/risk assessments	Anesthesia, cardiology, pulmonology
Perioperative pain management	Current pain medications, plan inpatient

As with any complex and prolonged operation, comorbidity burden affects medical outcomes after HNMVR [5–9]. Comorbidity burden is strongly associated with postoperative emergency department visits, unplanned readmission, and cardiac complications [10–13]. Patients with a heavy comorbidity profile that do not have any specific contraindications to surgery may benefit from the involvement of the primary care physician and anesthesia colleagues to ensure that the patient is optimized.

Risk calculation tools and scales are useful to estimate the perioperative risk of complications and functional decline. These tools may help in determining if the estimated risks for a particular

Table 1.2 Important aspects of the physical exam prior to HNMVR

Factor/site	Considerations
General exam	Ambulatory assist devices Nutritional status Evidence of substance use/abuse
Neurologic/ psychiatric	Comprehension Ability to consent Ability to participate in care and rehabilitation
Primary site assessment	Ability to restore reasonable function Resectability
Dental assessment	Number and quality of teeth Occlusion
Neck assessment	Evidence of prior treatment or surgery Adequate skin for closure Presence of recipient vessels
Upper extremity donor sites	Evidence of prior surgery Allen's test and reverse Allen's test Evidence of prior axillary dissection
Lower extremity donor sites	Evidence of lymphedema Evidence of PVD (smooth skin, hair loss, pulses) Evidence of prior surgery such as vein graft harvest

patient are unacceptably high, contraindicating surgery, and at minimum to counsel patients about what to expect after surgery. The American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) is a highly practical and free online tool that can provide patient-specific information using 20 patient predictors and the procedure code to calculate various outcomes including cardiopulmonary complications. Other tools include the Charlson Comorbidity Index (CCI) and the American Society of Anesthesiology (ASA) score.

Older age is not a specific contraindication to surgery. Older adults must be individually assessed for surgical fitness. A number of evaluation tools exist to estimate perioperative risk in this population, such as sarcopenia measurements [14, 15], comprehensive geriatric assessment, modified frailty index [16], and Fried's frailty score [17], among others [18, 19].

Though not a contraindication to surgery, prior treatment including radiation, particularly over 60 Gy, and chemotherapy may impact outcomes postoperatively. Prior treatment has been associated with fistula formation, worse functional outcomes, flap viability, and infection—likely related to treatment-induced tissue fibrosis, inflammation, and a prothrombotic state [7, 20–24]. While a priori knowledge of prior treatment does not necessarily affect surgical candidacy, the additional risks should be discussed with the patient. Detailed perioperative considerations for patients who have been previously treated with radiation and chemotherapy will be discussed in a subsequent chapter.

Cardiac Comorbidities

Cardiac risk assessment preoperatively can identify modifiable and nonmodifiable factors that are critical to prepare for HNMVR. Symptomatic severe aortic stenosis, poorly controlled symptomatic tachyarrhythmia or bradyarrhythmias, acute ischemic heart disease, and decompensated congestive heart failure may contraindicate major surgery [25]. Coronary artery disease in itself is not associated specifically with free flap failures [26].

There are several tools available to determine a patient's specific risk. Basic initial assessment with functional capacity such as inability to climb more than two flights of stairs (metabolic equivalent tasks) may indicate that further assessment is warranted. If the patient cannot perform four metabolic equivalent tasks (METs) or greater, their risk for perioperative cardiovascular complication is doubled [25]. The Lee Cardiac Risk Index (LCRI) is a short assessment that is predictive of cardiovascular complications [27]. Other scores previously discussed that can be implemented include the ASA score and Adult Comorbidity Evaluation (ACE-27) score.

In conjunction with anesthesia, primary care, and/or cardiology, some interventions may reduce perioperative risk. Perioperative beta-blockers and

statins may be protective. Routine use of aspirin preoperatively for low-risk patients undergoing noncardiac surgery is not associated with reduced risk of perioperative events but may be associated with bleeding events [28]. Anticoagulation medications for atrial fibrillation are discontinued from 2 to 5 days preoperatively depending on the agent pharmacokinetics [25]. A study assessed the risk of perioperative arterial thromboembolism (ATE) in atrial fibrillation randomizing patients to bridging with low-molecular-weight heparin or placebo. ATE was not lower with bridging for atrial fibrillation patients, but bleeding rates were higher (3.2% vs. 1.3%, $p = 0.005$) [29]. Patients on warfarin for mechanical mitral or aortic valves may require bridging. Patients with cardiac stent placement within the past 1 year are at increased risk of perioperative events [25]. Non-emergent surgery should be delayed at least 30 days after bare metal stent placement and at least 3–6 months after drug-eluting stent placement [25].

The surgeon should involve a patient's cardiologist and the anesthesiologist to determine which tests and interventions may be warranted to minimize perioperative cardiac risks. Routine testing is not indicated for low-risk patients with good functional status.

Coagulation Disorders

Both hypercoagulable conditions and anticoagulated states must be carefully considered and actively managed when preparing for surgery. Patients with a malignant diagnosis are fundamentally in a hypercoagulable state. Other conditions that the surgeon may encounter include prior venothromboembolism (VTE), factor V Leiden, antiphospholipid syndrome, and other diagnoses associated with a hypercoagulable state. Occasionally, these can be contraindications to free flap surgery.

A recent study of 1061 patients undergoing HNMVR demonstrated that a history of VTE was independently associated with free flap pedicle thrombosis (OR 95% CI = 3.65 (1.12–11.90), $P = 0.032$). Prior pulmonary embolism specifically was associated with greater than seven times higher risk of flap failure [30].

Anticoagulation medications typically must be interrupted prior to surgery to prevent major bleeding risks. Tools are available to estimate the risk of thrombosis with cessation of therapeutic anticoagulation relative to the risk of perioperative bleeding with the medications. Any procedure longer than 45 min is considered a high-bleeding-risk procedure [31]. If the risk of interrupting these medications is unacceptably high, this may be a contradiction for HNMVR. Patients with a very recent VTE who require surgery may benefit from placement of an inferior vena cava filter in order to safely interrupt anticoagulation. Other patients with a congestive heart failure, hypertension, older age, diabetes, and previous stroke/transient ischemic attack (CHADS2) score of 5 or greater may require bridging anticoagulation.

Rarely, the surgeon may encounter a patient with a bleeding disorder such as von Willebrand disease or hemophilia. While there is no specific data in head and neck free flap surgery about these issues, one can extrapolate management from other high-bleeding-risk procedures. A hematologist consultation is essential to determine the exact timing and agent administered to minimize perioperative bleeding risk.

Involvement of the primary care physician or hematologist may be helpful to determine the optimal perioperative management of these patients to minimize microvascular thrombosis, other thromboembolic complications, and bleeding complications.

Peripheral Vascular Disease

While PVD may not be a direct contraindication to HNMVR, this diagnosis is heavily considered when choosing a donor site especially from the lower extremity. Arterial changes associated with this disease may make microvascular anastomoses more technically challenging to perform. Donor site considerations will be discussed in detail in subsequent chapters.

PVD is associated with several other serious medical conditions such as coronary artery disease, which may affect anesthesia tolerance. While peripheral vascular disease may be associ-

ated with anesthesia complications, the association with free flap loss is unclear [26, 32, 33]. Patients with PVD warrant subsequent cardiac risk assessment prior to surgery, but PVD in itself is not necessarily a contraindication for HNMVR.

Pulmonary Dysfunction

Many patients with head and neck cancer have a history of heavy smoking and potentially associated lung disease. Major pulmonary comorbidities, especially those that are actively symptomatic and require home oxygen therapy, may result in significant medical complications intraoperatively and perioperatively with prolonged surgeries. Unexplained dyspnea or symptoms of untreated pulmonary dysfunction should be elicited in the patient history. Other patients who may be at risk of pulmonary complications perioperatively include those with obesity, poor overall health, and asthma [34]. Limited exercise capacity may also be indicative of pulmonary dysfunction and perioperative risk [35]. A diagnosis of chronic obstructive pulmonary disease (COPD) (Fig. 1.1) portends a relative risk of 2.7–4.7 for postoperative pulmonary complications [34, 36, 37]. Patients with this diagnosis should be optimized with inhaled medications, incentive spirometry, or oral corticosteroids [34].

Selective assessment with preoperative pulmonary risk stratification may be warranted, but this test is potentially of limited value for decision-making in non-pulmonary surgeries. Patients with poor outcomes on PFTs may still undergo surgery with acceptable risk [34, 36–39].

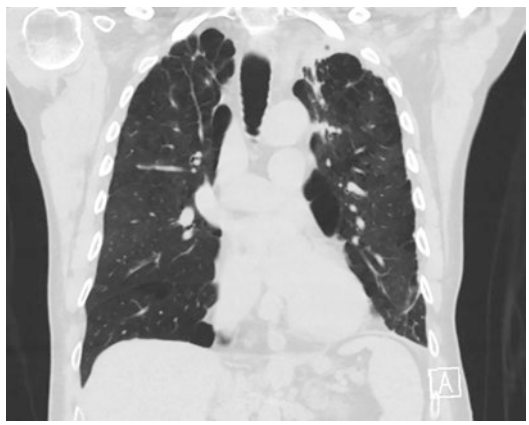

Fig. 1.1 Computed tomography demonstrating radiographic findings of chronic obstructive pulmonary disease

Diabetes

Though not a definitive contraindication to surgery, poorly controlled diabetes contributes to worse outcomes, and this condition should be optimized prior to surgery to reduce risk. Diabetes is associated with a higher rate of perioperative complications, up to five times more likely for patients undergoing free flap surgery [40–43]. An analysis of the NSQIP database reported that patients with diabetes were significantly more likely to have complications including postoperative ventilator dependence, reintubation, cardiac complications, and surgical complications [44]. A systematic review and meta-analysis including 7890 patients reported that diabetic patients have a 1.76 times increased risk of complications with free flap surgery [45]. Similar findings have been reported in other studies [11, 40, 41].

Preoperative optimization for diabetic patients can mitigate risks related to major operations [46–48]. Preoperative diabetes optimization programs that utilize multiple practitioners such as endocrinologists and nutritionists may be helpful to comprehensively manage these patients [49]. Fortunately, guides are available to aid in the preoperative assessment and management of these patients [50]. Hemoglobin A1c levels over 8% may escalate the situation, and severe hyperglycemia with a glucose >250 mg/dL contraindicates elective surgery [50]. Involvement of the patient's primary physician or endocrinologist is essential for patients with poor glycemic control.

Hypothyroidism

While routine screening for thyroid dysfunction prior to major surgery is not indicated, patients with symptoms and risk factors may benefit from assessment prior to surgery. Prior radiation treat-

ment to the head and neck is a risk factor for hypothyroidism and has been reported in up to 32% of patients within the first year after therapy [51]. Because the consequences of poorly controlled hypothyroidism are significant in HNMVR cases, preoperative testing of TSH is advisable for patients with prior head and neck treatment with radiation, prior diagnosis of hypothyroidism, or history and physical exam evidence of hypothyroidism.

The multisystem effects of hypothyroidism can result in reduced cardiac output, decreased clearance of medications, gastric outlet slowing and postoperative ileus, increased susceptibility to anesthetics and narcotics, and electrolyte abnormalities. Relevant to free flap surgery, hypothyroid patients have an increased risk of intraoperative hypotension when compared to euthyroid patients [52]. Poorly controlled hypothyroidism is associated with major wound-healing complications postoperatively [53–55]. It is also associated with a significantly increased risk of fistula formation [54, 56], postoperative sepsis [57], and increased readmission rates [53].

Ideally, a patient is euthyroid or mildly hypothyroid prior to proceeding with surgery. Checking a thyroid-stimulating hormone (TSH) level and free T4 level when first evaluating the patient for surgery may allow some time to initiate treatment preoperatively with thyroid hormone. Oral levothyroxine can be prescribed at a typical initial dose of 1.6 mcg/kg/day, with a recheck of TSH in approximately 6 weeks. If surgery is urgent or emergent, intravenous levothyroxine is given at a loading dose of 200–500 micrograms followed by a daily IV dose of approximately 50% of the weight-based oral dosage. Oral or intravenous liothyronine can also be added in severe, nonresponsive cases. Involvement of an endocrinologist in these cases is encouraged. The physician should proceed with caution prescribing these medications in patients with cardiac ischemic disease.

Renal Disease

Renal diseases such as chronic kidney disease and end-stage renal disease should be carefully considered prior to surgery but are not strict contraindications to proceeding. Chronic kidney disease has been associated with an increased perioperative risk of bleeding [58]. End-stage renal disease (ESRD) is especially challenging as it is associated with a number of issues such as cardiovascular function, coagulation, electrolyte abnormalities, fluid management challenges, and pharmacokinetic/pharmacodynamic alterations. The risk of 30-day mortality is four times higher in those with ESRD undergoing elective vascular procedures [59]. Active involvement of the nephrologist with dialysis the day before surgery and clear communication with anesthesiologist are required to minimize complication risk such as electrolyte abnormalities and cardiopulmonary complications of fluid overload.

Hyponatremia

Hyponatremia, a prevalent issue in cancer patients, is a common finding in head and neck cancer patients. This electrolyte abnormality may be caused by decreased oral intake, pain, alcohol abuse, syndrome of inappropriate antidiuretic hormone, hypothyroidism, and systemic chemotherapies. In a review of over 800,000 patients, preoperative hyponatremia (<135 mEq/L) was associated with a higher risk of 30-day mortality (5.2% vs. 1.3%), greater risk of perioperative major coronary events, wound infections, and pneumonia [60]. In head and neck surgery patients specifically, preoperative hyponatremia was associated with a 60% overall risk of complications including cardiac, renal, and respiratory complications and increased length of stay [61]. It has also been associated with increased rates of 30-day readmission [62]. Involvement of a nephrologist may be appropriate to investigate causes and administer appropriate treatment. Overly rapid correction of hyponatremia can rarely result in cerebral edema and mortality from rapid osmotic shifts. If the patient's hyponatremia is subacute/acute, hyponatremia <125 mEq/L is a contraindication to surgery, and correction is required prior to a prolonged anesthetic and any elective major head and neck operation.

Soft Tissue, Connective Tissue, and Dermatologic Diseases

Rarely, the surgeon may encounter patients with severe soft tissue and connective diseases or extensive dermatologic conditions such as scleroderma or severe psoriasis that may be challenging for cutaneous tissue harvesting and successful wound healing. Though there is limited evidence in this particular area, severe disease with high risk of poor wound healing or contracture may be a contraindication to surgery as this would result in unacceptable outcomes. These patients may also be on immunosuppressant medications, which may increase the risk of postoperative wound infection and breakdown. Patients with these diagnoses should be carefully considered on an individual basis based on severity and in conjunction with the patient's primary treating physician.

Preoperative Considerations for Substance Use

Smoking and tobacco use are major risk factors for the development of head and neck cancer, and as a result, many surgical patients would have previously smoked heavily or are active smokers. It is well known that smoking perioperatively has risks specifically related to head and neck surgical sites and medical complications. Complication rates in current and former smokers have been reported to be as high as six times higher than nonsmokers undergoing head and neck surgery (Hatcher 2016) such as wound breakdown and reoperation [63]. The literature is mixed if cessation truly improves surgical complication rates [64–66]. Medical complication rates after surgery are improved with cessation including mortality, pulmonary complication, and intensive care unit stays [67]. Four weeks may be the optimal minimum time frame to observe some improvement in outcomes [68, 69]. Though smoking is not a contraindication to surgery, some surgeons may delay elective HNMVR such as repair for osteonecrosis until the patient has quit smoking in order to minimize the risk of additional wound complications. Fortunately, there are many publicly available, and sometimes free, resources to aid patients in cessation such as nicotine replacement therapy.

Heavy alcohol use is not a contraindication to surgery, with few exceptions. Active intoxication without the ability to consent to surgery is a contraindication to surgery. In addition, heavy alcohol use may result in decompensated medical issues such as hyponatremia and liver failure, which may be a contraindication to a general anesthetic. Patients with chronic heavy alcohol use are at elevated risk for postoperative complications including flap failure [70–72] and should be counselled accordingly. Patients should be encouraged to wean slowly prior to surgery.

Active cocaine and/or methamphetamine may be a contraindication to anesthetics and HNMVR. Patient metabolism of anesthetic drugs may be altered, and patients may be unable to consent for surgery. However, existing literature supports that recent cocaine use may not be associated with certain anesthetic or medical complications postoperatively [73]. These substances do cause vasoconstriction, which may affect flap microcirculation.

Nutritional Assessment and Intervention

A careful assessment of the patient's medical history and a general physical examination, as noted above, importantly help prepare the patient for their reconstructive surgery. However, this patient population also often faces significant nutritional challenges preoperatively. These challenges may range from undernutrition and malnutrition to sarcopenia, cachexia, and overall frailty. Identifying these conditions and possible intervention and preventive measures will be outlined throughout this section.

Nutritional management may not seem like a relevant skill for the microvascular free flap surgeon; however, free flap outcomes are greatly intertwined with the patient's nutritional status [74]. Thus, screening for malnutrition is a vital part of these patients' preoperative management.

The surgeon may benefit from pairing with a registered dietician or nutritionist to help augment this aspect of the patient's care, or they may choose to screen the patient themselves prior to deciding on a referral.

Defining Malnutrition

To begin, it is important for the surgeon to consider the patient's risk factors for malnutrition. For example, a patient with a malignant tumor may have marked pain precluding their ability to take in enough food by mouth, or their tumor may have grown to such an extent that they have lost appropriate function to swallow. Difficulties with oral intake are very frequently reported in our head and neck cancer patients, and while these symptoms may worsen after surgery, chemotherapy, and/or radiation therapy, the patients often experience these symptoms even before beginning their treatment [75, 76]. These symptoms are collectively termed nutritional impact symptoms (NISs). However, aside from the usual symptoms experienced by most cancer patients (pain, anxiety/depression, nausea/vomiting), head and neck cancer patients' tumors directly can result in additional NIS such as dental pain, trismus, and restricted tongue mobility, to name a few [76, 77]. Even those without a head and neck cancer may experience significant NIS due to the location of their injury or surgical defect. For example, a patient who has suffered a trauma or a fracture from necrosis of the mandible may require an altered diet due to their severe discomfort. These NISs typically result in significant weight loss in our patients and are an important part of the patient's history to make note of during the presurgical assessment.

In general, weight loss is due to either increased energy expenditure or decreased caloric intake, and both are very multifactorial in our cancer patients. As little as an involuntary 5% loss of body weight in a 6-month period is associated with increased complications and longer hospital stays [78]. However, when assessing weight alone, the most reliable definition of malnutrition is a greater than 10% unintended weight loss [79]. This assessment of change in weight can be expeditiously done at the patient's preoperative appointment or at a dedicated nutritional consultation. Furthermore, at a minimum, the patient's vital signs, including their body mass index (BMI), are likely recorded and calculated at each office visit. BMI is often used as a defining feature of malnutrition, with some studies citing BMI <20 or BMI <18.5. However, BMI alone is not a reliable marker of malnutrition, as even those with high BMI are at risk for malnutrition [79]. To clarify, those who originally had a higher BMI may still be malnourished if they have lost a significant amount of weight and muscle mass in a short time frame. This loss of muscle mass is termed "sarcopenia" and will be reviewed later in this section.

Cachexia

Cachexia is a multifactorial syndrome that includes weight loss and increased energy expenditure, and in the setting of cancer, this increased expenditure is due to the metabolic demands the tumor exerts on the patient. Thus, when related to cancer, this is termed cancer cachexia syndrome. Numerous proinflammatory cytokines are upregulated in these patients, with interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF)-alpha playing key roles [80]. Treating cancer cachexia is thus complicated and multifactorial and should ideally focus on improving nutritional intake/caloric intake, improving muscle mass through physical therapy and strength training, and possibly including pharmacologic intervention to decrease inflammation, for example.

Sarcopenia

Sarcopenia is a progressive loss of muscle mass and is highly prevalent in our head and neck cancer patients. This is again due to the location and nature of the patients' tumors, but it is also due to the proinflammatory state underlying their cancer. Where BMI is lacking in its ability to identify body compositional differences, assessing sarcopenia prevails. Assessing for sarcopenia in the presurgical setting is arguably

extremely important, as numerous studies have identified an association between sarcopenia and decreased survival in cancer patients [14, 81]. In head and neck cancer patients specifically, sarcopenia is reportedly present in anywhere from 30% to 60% of patients and is a poor prognosticator [82, 83]. In one study of 260 patients undergoing major head and neck surgery, sarcopenia was a significant negative predictor of both 2-year and 5-year overall survival on multivariate analysis [14]. Specific to patients undergoing complex head and neck reconstruction, sarcopenia was associated with an increased rate of intraoperative blood transfusions and postoperative complications, including wound disruption, fistula, prolonged ventilation, and flap-specific complications [15]. Thus, identifying and attempting to mitigate sarcopenia and malnutrition preoperatively are extremely important.

Sarcopenia can be identified by assessing the patient's muscle mass, muscle strength, and physical performance. Low muscle mass alone reveals a probable chance of sarcopenia being present, with low muscle mass plus decreased muscle strength being a defining feature [84]. The gold standard for assessing muscle mass and sarcopenia is by assessing skeletal muscle index (SMI) via imaging. While whole-body skeletal muscle volumes would be ideal, this would be extremely time consuming and not practical in a clinical practice. Thus, cross-sectional measurements of skeletal muscle index (SMI) at the L3 vertebral level are most commonly performed and correlate with whole-body SMI. At this level, sarcopenia is often defined as SMI $\leq$41.6 cm^2/m^2 in men and $\leq$32.0 cm^2/m^2 in women [15]. However, in head and neck cancer patients, it is far more common to have imaging at the cervical spinal level rather than of the abdomen. Studies evaluating images at the C3 vertebral level have revealed promising results, with SMI at C3 correlating to L3 SMI [85, 86]. Head and neck reconstructive surgeons thus commonly have these images available to assess for sarcopenia in their patients and should strive to identify these patients for presurgical intervention whenever possible.

Medical optimization for sarcopenic patients is often focused on exercise interventions, with an improvement in muscle strength often more readily achieved than an increase in muscle mass [87]. However, the issue in our head and neck patients is that many do not have the luxury of time to implement a presurgical exercise program prior to their surgery, especially if they are pending surgery for cancer. It is thus clear that while assessing for sarcopenia is beneficial to our surgical patients and is associated with important clinical outcomes, it is often not an easy feat to identify or to mitigate.

Additional Nutritional Screening Methods

As preoperative imaging assessment of SMI is time consuming and requires specialized training, it is admittedly not the most accessible way for the microvascular surgeon to assess for malnutrition in the preoperative setting. The Patient-Generated Subjective Global Assessment (PG-SGA) is a valid screening tool used to assess malnutrition in cancer patients and is particularly attractive as it realistically assesses the patient's nutritional status as a dynamic and changing process throughout their cancer treatment [88]. Head and neck cancer patients have found the PG-SGA to be beneficial in increasing their own self-awareness regarding their nutritional status [89]. The PG-SGA specifically assesses the patient's weight history, food intake, symptoms, and activities/function and combines these four patient-reported categories with additional variables input by the provider, which include metabolic demand (presence of fever, use of corticosteroids) and physical examination (muscle and fat status). The patient then receives both a numeric and letter score, with the numeric score acting as a continuous variable that assists the clinician with categorizing the patient into specific triage categories (Table 1.3).

Laboratory markers have additionally been historically used to assess for malnutrition, specifically albumin and prealbumin. However, both are acute-phase reactants that have altered synthesis in times of inflammation and thus have limited use in the setting of active cancer and acute surgery. Thus, more useful is combining

Table 1.3 Nutritional triage recommendations based on PG-SGA scores

0–1	No intervention currently required. Reassess on routine basis during treatment
2–3	Patient and family education by dietician, nurse, or others
4–8	Requires intervention by dietician
≥9	Critical need for improved symptom management or intervention

Table 1.4 Tools for calculating nutritional indices

Prognostic nutritional index	[10 × serum albumin (g/dL)] + [0.005 × total lymphocyte count]
Geriatric nutritional risk index	[1.489 × serum albumin (g/L)] + [41.7 × (body weight/ideal body weight)]
Ideal body weight	Men: 50 + (0.91 × [height in cm—152.4] Women: 45.5 + (0.91 × [height in cm—152.4]

these laboratory markers into aggregate scores, which may predict nutritional status and outcomes, such as the prognostic nutritional index (PNI) and geriatric nutritional risk index (GNRI).

The PNI is calculated using the serum albumin level and total lymphocyte count, and a score less than or equal to 40 has reportedly been associated with a high complication rate and poor prognosis. Furthermore, when used in patients undergoing head and neck surgery with free tissue transfer reconstruction, PNI less than or equal to 40 was a significant risk factor for adverse surgical outcomes, postoperative complications, and prolonged hospitalization (Imai 2020). The geriatric nutritional risk index (GNRI), which has somewhat of a misnomer as it is beneficial in more than just a geriatric population, similarly has been shown to be a promising prognostic tool in patients with advanced head and neck cancer [90]. The GNRI is calculated with the serum albumin, patient's current body weight, and their ideal body weight. Ideal body weight is a standard calculation measured differently for men and women based on their height. These tools and calculations are summarized in Table 1.4.

Nutritional Intervention

Ensuring adequate enteral nutrition in any form is of utmost importance. Thus, carefully identifying which patients may require a preoperative percutaneous endoscopic gastrostomy (PEG) tube may be key in ensuring that the patient receives adequate nutrition.

Newer, immune-enhancing formulas, termed immunonutrition, are gaining traction in the cancer world and as an important supplement in the perioperative setting. Immunonutrition contains arginine, omega-3 fatty acids, and dietary nucleotides and promotes an attractive anti-inflammatory and immune environment [91]. Use of these formulas for as little as 5 days preoperatively, and ideally continuing their use through the patient's hospitalization and initial postoperative period, is associated with improved wound healing, decreased complications, and shortened hospital stay [92, 93].

Aside from specifically using immunonutrition, oxandrolone is an interesting pharmacologic agent thought to improve cachexia. Oxandrolone is an anabolic-androgenic steroid approved by the Food and Drug Administration (FDA) for weight gain following disease-related weight loss and has been shown to improve weight in cancer patients [94]. In 18 head and neck cancer patients treated perioperatively twice daily, oxandrolone resulted in an improvement in prealbumin levels and in subjective wound healing [95]. However, additional larger scale studies with more rigid end points are needed to define which patient more clearly would benefit from its use preoperatively.

Mental Health Assessment

Just as a thorough examination of the patient's physical and nutritional well-being is extremely important preoperatively, the head and neck patient's mental health and psychological well-being should also be assessed. These patients are facing a surgery which will potentially be physically disfiguring and functionally result in difficulties in speech and swallowing, all of which are essential for social interaction and maintaining

relationships. Thus, it is not surprising that approximately 40% of head and neck patients report depression, and patients with oral cavity, pharynx, and larynx cancer are among the greatest at risk for suicide [96, 97].

There are numerous tools available for screening for depression in the outpatient setting. Some may be concerned that there is insufficient time in an already busy consultation or presurgical visit to also screen for depression; however, the very simple question "Do you often feel sad or depressed?" is surprisingly effective at screening for depression [98]. To take this one step further, the patient health questionnaire (PHQ) 2 question screen is highly efficient at identifying those at risk for depression and when coupled with the 9-question version (PHQ-9) its specificity for identifying depression increases to 94%, with a sensitivity of 97% [99].

For those looking for and able to perform a more detailed screen, the Quick Inventory of Depressive Symptoms is available for use both by the clinician and for self-reporting from the patient (QIDS-C versus QIDS-SR, respectively). The self-report method is particularly appealing to some of our head and neck patients who have difficulty with verbal communication, and those who score greater than 4 are at a higher risk of developing moderate-to-severe depression during their treatment [100].

With these tools and the known risk of depression in our patients, it is thus extremely important to consider screening each preoperative patient. Especially in patients with cancer who are undergoing head and neck reconstruction, screening for and diagnosing depression can hopefully improve compliance with treatment and survival [101].

Conclusion

Surgical readiness for HNMVR, a major operation, reflects an interplay of external modifiable factors and inherent, non-modifiable factors. To avoid catastrophic outcomes and complications, mitigation of modifiable factors and management of non-modifiable factors may be undertaken in a multidisciplinary fashion.

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