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# Optimal Perioperative Care in Major Head and Neck Cancer Surgery With Free Flap Reconstruction
## A Consensus Review and Recommendations From the Enhanced Recovery After Surgery Society

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**IMPORTANCE** Head and neck cancers often require complex, labor-intensive surgeries, especially when free flap reconstruction is required. Enhanced recovery is important in this patient population but evidence-based protocols on perioperative care for this population are lacking.

**OBJECTIVE** To provide a consensus-based protocol for optimal perioperative care of patients undergoing head and neck cancer surgery with free flap reconstruction.

**EVIDENCE REVIEW** Following endorsement by the Enhanced Recovery After Surgery (ERAS) Society to develop this protocol, a systematic review was conducted for each topic. The PubMed and Cochrane databases were initially searched to identify relevant publications on head and neck cancer surgery from 1965 through April 2015. Consistent key words for each topic included "head and neck surgery," "pharyngectomy," "laryngectomy," "laryngopharyngectomy," "neck dissection," "parotid lymphadenectomy," "thyroidectomy," "oral cavity resection," "glossectomy," and "head and neck." The final selection of literature included meta-analyses and systematic reviews as well as randomized controlled trials where available. In the absence of high-level data, case series and nonrandomized studies in head and neck cancer surgery patients or randomized controlled trials and systematic reviews in non–head and neck cancer surgery patients, were considered. An international panel of experts in major head and neck cancer surgery and enhanced recovery after surgery reviewed and assessed the literature for quality and developed recommendations for each topic based on the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system. All recommendations were graded following a consensus discussion among the expert panel.

**FINDINGS** The literature search, including a hand search of reference lists, identified 215 relevant publications that were considered to be the best evidence for the topic areas. A total of 17 topic areas were identified for inclusion in the protocol for the perioperative care of patients undergoing major head and neck cancer surgery with free flap reconstruction. Best practice includes several elements of perioperative care. Among these elements are the provision of preoperative carbohydrate treatment, pharmacologic thromboprophylaxis, perioperative antibiotics in clean-contaminated procedures, corticosteroid and antiemetic medications, short acting anxiolytics, goal-directed fluid management, opioid-sparing multimodal analgesia, frequent flap monitoring, early mobilization, and the avoidance of preoperative fasting.

**CONCLUSIONS AND RELEVANCE** The evidence base for specific perioperative care elements in head and neck cancer surgery is variable and in many cases information from different surgerical procedures form the basis for these recommendations. Clinical evaluation of these recommendations is a logical next step and further research in this patient population is warranted.

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Malignant abnormalities of the head and neck often require complex, labor intensive surgery such as composite oral cavity resections, skull base surgeries, or large pharyngectomy and/or laryngectomy resections, often in the setting of salvage surgery after failed attempts at radiation and chemotherapy. Free flap reconstruction is often required for extensive defects, thereby adding to the length and complexity of these procedures. These extended procedures require a coordinated multidisciplinary team to deliver care before, during, and after surgery. Optimal perioperative patient care is of the utmost importance to ensure that the recovery period is efficiently and effectively managed in an effort to provide the best possible outcome for the patient. Enhanced Recovery After Surgery (ERAS) was introduced as a way of optimizing perioperative care for a variety of surgical procedures. Initially ERAS recommendations were developed for patients undergoing colorectal surgery[1]; evaluation of these recommendations has shown that patients in whom the ERAS interventions are applied experience significant improvements in function after surgery.[2] In turn, when the ERAS guidelines are implemented patients have demonstrated reduced morbidity and shorter length of hospital stay.[2] The ERAS protocols have revolutionized the way perioperative care is provided and measured.

An ERAS protocol for head and neck cancer surgery with free flap reconstruction has not been published previously. Therefore, an international expert panel of head and neck clinicians (surgery, anesthesiology, critical care, and nutrition), working collaboratively with the ERAS Society (http://www.erassociety.org), developed a consensus-based ERAS protocol for the perioperative treatment of patients undergoing head and neck cancer surgery with free flap reconstruction. The best available evidence for each intervention was considered when developing the recommendations. Evidence levels and recommendation grades are provided for all interventions. The purpose of this protocol is to improve patient well-being in the postoperative period by reducing procedure-related morbidity and complications. Evidence from previous ERAS protocols suggest that implementation of this protocol will also improve efficiency of care, with improvements in overall resource use and cost of care.

### Key Points

**Question** What is optimal perioperative care, as defined by an enhanced recovery after surgery (ERAS) approach, for patients undergoing head and neck cancer surgery with free flap reconstruction?

**Findings** In this systematic review, best practice includes several elements of perioperative care. Among these elements are the provision of preoperative carbohydrate treatment, pharmacologic thromboprophylaxis, perioperative antibiotics in clean-contaminated procedures, corticosteroid and antiemetic medications, short acting anxiolytics, goal-directed fluid management, opioid-sparing multimodal analgesia, frequent flap monitoring, early mobilization, and the avoidance of preoperative fasting.

**Meaning** Recovery following surgery for head and neck cancer with free flap reconstruction can be enhanced through the use of evidence-based elements of perioperative care.

## Methods

### Development of Consensus Recommendations

In February 2015, an international panel of content experts in major head and neck cancer surgery with free flap reconstruction, representing the nations of Australia, Canada, Sweden, Switzerland, and the United States, was assembled. Following a review of existing ERAS Society guidelines, the panel was consulted for appropriate items to include in the protocol. Final decisions were made by the lead authors (J.D. and J.H.) and approved by the ERAS Society in March 2015. Items were assigned to individual authors, based on areas of expertise and interest. A researcher (M.S.B.) with expertise in oncology systematic reviews and cancer recommendation development provided content expertise, methodological support, and coordination. The panel met monthly from May 2015 through November 2015.

### Literature Search and Study Selection

The PubMed and Cochrane databases were initially searched to identify relevant publications on head and neck cancer surgery from 1965 through April 2015. Consistent key words for each topic included "head and neck surgery," "pharyngectomy," "laryngectomy," "laryngopharyngectomy," "neck dissection," "parotid lymphadenectomy," "thyroidectomy," "oral cavity resection," "glossectomy," and "head and neck." Additional key words were added to the search strategy, as appropriate, based on the particular topic. Reference lists of all eligible articles were hand-searched for additional relevant studies. Conference proceedings were not included in the search.

The resulting list of abstracts was initially screened to identify potentially relevant articles for each topic. Each section author reviewed the resulting literature and search strategies were expanded or refined, as appropriate. The final selection of literature included meta-analyses and systematic reviews as well as randomized controlled trials wherever possible. In the absence of high-level data, case series and nonrandomized studies in head and neck cancer surgery patients or randomized controlled trials and systematic reviews in non-head and neck cancer surgery patients, were considered. Section authors thoroughly reviewed this literature to form the basis for the recommendations. Any discrepancies in the interpretation of the literature were discussed and resolved during monthly conference calls with panel members.

### Quality Assessment and Data Analyses

Criteria developed by the Centre for Evidence Based Medicine (Oxford, England)[3] were used to assess the overall quality of the evidence. Possible levels of evidence included "high" (ie, systematic reviews, meta-analyses, or robust randomized controlled trials), "moderate" (ie, smaller randomized controlled trials or prospective cohort data), or "low" (ie, retrospective data). The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system[4] was used to assign a level of strength to each recommendation. Briefly, "strong" recommendations were based on high-quality evidence alone or on weaker quality evidence where there is a high likelihood of benefit and low risk of harm; "weak" recommendations were based on low-quality evidence alone or on higher quality evidence where the likelihood of benefit is uncertain; "conditional" recommendations were based on low-quality evidence where the desirable effects probably outweigh the undesirable effects. Any conflicts in the assigned strengths of evidence and grading of recommendation statements were resolved through discussions with all authors during panel meetings.

## Results

A total of 17 topic areas, spanning preoperative, intraoperative, and postoperative care, were identified for inclusion in the protocol. The literature search, including a hand search of reference lists, identified 215 relevant publications that were considered to be the best evidence for the topic areas. Presented in the **Table** are the recommendations for each of the 17 ERAS items, along with the level of evidence that was used to inform each recommendation and the strength (grade) of each recommendation. The evidence base is described in the discussion with additional references included as an online supplement (eg, see Additional References in the Supplement).

## Discussion

### Preadmission Education

Preparing patients and families for surgery is believed to be a worthwhile endeavor. Preoperative education is thought to be an important step in the surgical journey, particularly when major surgery is planned. Despite these widely held beliefs, there is limited evidence demonstrating the beneficial effects of preoperative education on patient outcomes. Evidence from the pediatric literature suggests preoperative counseling, regardless of how it is provided, is a useful educational intervention and that the shorter the time between counseling and the procedure, the greater the retention of information.[5] A randomized study in patients undergoing parotidectomy and thyroidectomy found that a preoperative educational intervention improved recall of operative risks.[6]

Preoperative education is probably a useful intervention because the psychosocial aspects of undergoing major head and neck cancer surgery are believed to have an important impact on clinical outcomes. However, the details of the timing and nature of such education has not been well described; there are no high quality studies specifically focused on the impact of preoperative education on clinical outcomes in patients undergoing major head and neck cancer surgery. A small 2015 study[7] concluded that head and neck patients who had a preoperative social worker visit felt better prepared for their surgical procedure and its aftermath. A 2002 descriptive study[8] looked at care pathway development in patients undergoing major head and neck cancer surgery and anecdotally reported beneficial effects from a patient education brochure. We recommend that further research be conducted in this important area.

### Perioperative Nutritional Care

Enhanced recovery after surgery protocols routinely include elements of perioperative nutritional care, such as reduced fasting time, avoidance of dehydration, and carbohydrate loading preoperatively followed by early progression to oral feeding postoperatively, however, evidence specific to enhanced recovery practices in relation to nutritional care of patients with head and neck cancer is limited.[9] Where deemed safe, and while taking into account the considerations unique to this patient group, perioperative nutrition care recommendations may be extrapolated from existing enhanced recovery protocols in other cancer surgical populations[1,10] and draw on existing comprehensive evidence-based guidelines for nutritional care of adult patients with head and neck cancer.[11]

### Preoperative Nutritional Status

Malnutrition is prevalent in patients with head and neck cancer, is influenced by multiple factors, and is associated with adverse clinical, cost, and patient-centered outcomes. Mechanical obstruction arising from tumor location contributes to progressive and/or prolonged dysphagia, predisposing patients to detrimental sequelae of malnutrition and subsequently greater susceptibility to postoperative complications, such as compromised wound healing, increased risk of infection, increased length of stay, and risk of refeeding syndrome. Existing guidelines suggest preoperative nutrition intervention in malnourished patients may lead to improved outcomes through a reduction in malnutrition-related adverse events.[10,11] Patients with a high risk of dysphagia and refeeding syndrome may need an adapted nutrition plan. Nutrition assessment tools validated for use in the oncology population should be considered standard practice in modern surgical care with comprehensive evaluation of anthropometry, biochemistry, dietary intake, and clinical examination of body composition in conjunction with medical and social histories.[12]

### Nutritional Formulae

Immunonutrition has been explored in the surgical setting. Potential benefits of oral or enteral formulae enriched with nutrients purported to have an immune modulating effect, typically arginine, glutamine, ω-3 fatty acids, or ribonucleic acids, have been investigated. Systematic reviews suggest an association between reduced length of stay and postoperative administration of immunonutrition support[13,14]; however, the mechanism is not fully understood. Preoperative immunonutrition does not seem to have any additional benefits in comparison with standard nutrition support in patients undergoing head and neck cancer surgery. Investigations of immunonutrition administered in the perioperative period have produced mixed results in the head and neck cancer population, largely arising from variations in study design, nutritional formula administration protocols, and definitions of perioperative period make drawing definitive conclusions challenging.[11] Despite the possible benefits of immunonutrition, particularly in the postoperative setting, further investigation through well-designed clinical studies is warranted.

### Preoperative Fasting and Preoperative Treatment With Carbohydrates

Fasting from midnight prior to surgery originates from historical, institutional, and clinician-driven practices. Despite evidence of poorer outcomes and delayed recovery with prolonged fasting, outdated surgical fasting practices persist.[15]

In enhanced recovery protocols for other patient groups, the rationale for preoperative carbohydrate (CHO) loading arises from the hypothesis that ingestion of CHO-rich fluids attenuates both insulin resistance and catabolism, promoting better glucose control and lean tissue preservation.[16] High quality studies evaluating the potential benefits of preoperative CHO treatment are limited, particularly in patients undergoing head and neck cancer surgery. Systematic reviews and meta-analyses consistently confirm that although preoperative CHO loading appears to be safe, published trial quality has been poor and larger, more rigorous randomized clinical trials (RCTs) are required.[17,18] A recent systematic review[19] of preoperative CHO treatment after elective surgery evaluating 1976 participants across 27 RCTs found that, although the intervention was associated with a 1.5-day reduction in length of hospital stay in major abdominal surgery, there was no difference in postoperative complication rates. The review also

Table. Enhanced Recovery After Surgery Recommendations for Perioperative Care in Head and Neck Cancer Surgery With Free Flap Reconstruction

| Item | Recommendation | Evidence | Recommendation |
|---|---|---|---|
| Preadmission education | All patients undergoing major head and neck cancer surgery with free flap reconstruction should receive structured teaching from a qualified health practitioner. | Low | Strong |
| Perioperative nutritional care | All patients undergoing major surgery for head and neck cancer should undergo preoperative comprehensive nutritional assessment, with a special focus on dysphagia and risk for refeeding syndrome. Preoperative nutrition intervention is recommended for those identified as malnourished. | High | Strong |
| | A standard polymeric enteral nutrition formula should be considered suitable for use in patients requiring preoperative nutrition support. | Low | Weak |
| | A standard polymeric enteral nutrition formula should be considered suitable for use in patients requiring postoperative nutrition support. There are insufficient data to provide a recommendation on the use of immunonutrition | Moderate | Conditional |
| | Preoperative fasting should be minimized. In patients suitable for oral intake and with appropriate screening and management for those presenting with dysphagia or risk of refeeding syndrome, clear fluids should be permitted for up to 2 hours and solids for up to 6 hours prior to anesthesia. Preoperative CHO treatment may be offered to head and neck cancer patients. | High (fluids), low (solids), low (CHO) | Strong (fluids), strong (solids), conditional (CHO) |
| | Oral diet is the first choice for all patients tolerating it. In patients for whom oral feeding cannot be established postoperative tube feeding should be initiated within 24 hours. Nutrition interventions should be developed in consultation with the multidisciplinary team and individualized according to nutritional status and surgical procedure. | Moderate | Strong |
| Prophylaxis against thromboembolism | Patients undergoing head and neck cancer surgery with free flap reconstruction are at increased risk of VTE and should undergo pharmacologic prophylaxis; however, the risk of bleeding must be weighed against the benefits on an individualized basis. | High | Strong |
| Antibiotic prophylaxis | Perioperative antibiotics are not indicated for short clean head and neck oncologic procedures. In clean-contaminated procedures, perioperative antibiotics should be given 1 hour prior to surgery and continued for 24 hours. | High | Strong |
| Postoperative nausea and/or vomiting prophylaxis | Patients undergoing head and neck cancer surgery should receive preoperative and intraoperative medications to mitigate Postoperative nausea and/or vomiting. A combination of corticosteroid and antiemetic should be considered. | High | Strong |
| Preanesthetic medications | Patients should receive short acting anxiolytics, given intravenously and titrated to required effect. Long acting anxiolytics and opioids should be avoided. | High | Strong |
| Standard anesthetic protocol | The anesthetic protocol should not only prevent awareness, but also minimize adverse effects and allow patients to awaken and recover rapidly; therefore, avoidance of too deep anesthesia, especially in elderly patients, is recommended. | Low | Strong |
| Preventing hypothermia | Normothermia should be maintained intraoperatively. Temperature monitoring is necessary to ensure normothermia is maintained. | High | Strong |
| Perioperative fluid management | Fluids should be managed in a goal-directed manner, avoiding over and under hydration. | Moderate | Strong |
| Routine postoperative intensive care admission | Routine intensive care unit admission to facilitate an immediate postoperative period of deep sedation and artificial respiration is not necessary. A subset of low-risk uncomplicated patients may be treated safely after recovery from anesthesia in a high dependency unit or specialist ward, provided adequate skilled nursing and medical coverage is provided. | Low | Weak |
| Pain management | Opioid-sparing, multimodal analgesia, utilizing NSAIDs, COX inhibitors, and paracetamol, are preferred for patients undergoing head and neck cancer surgery. Patient-controlled analgesia can be considered if multimodal analgesia approaches are insufficient. No recommendation can be made on the role of additional nerve blocks. | High | Strong |
| Postoperative flap monitoring | Free flap monitoring should be performed at least hourly for the first 24 hours postoperatively. Monitoring should be continued for the duration of the patient's stay with tapering of intensity after the first 24 hours. Method of monitoring should include, at a minimum, clinical examination by staff experienced with free flap monitoring. Adjunct monitoring techniques should be considered. | Moderate | Strong |
| Postoperative mobilization | Early mobilization, within the first 24 hours of surgery is recommended for patients undergoing major head and neck cancer surgery. | Moderate | Strong |
| Postoperative wound care | Vacuum assisted closure is recommended for complex cervical wounds. | High | Strong |
| | Vacuum assisted closure may be considered for free flap donor site. | Moderate | Strong |
| | Polyurethane film or hydrocolloid dressings should be used for skin graft donor site treatment. | High | Strong |
| Urinary catheterization | Urinary catheters should be removed as soon as the patient is able to void, ideally less than 24 hours after completion of surgery. | High | Strong |
| Tracheostomy care | Decannulation after tracheostomy and stoma closure is recommended. | High | Strong |
| | Surgical closure of the tracheostomy site is recommended. | Moderate | Strong |
| Postoperative pulmonary physical therapy | Pulmonary physical therapy should be initiated as early as possible after head and neck reconstructions to avoid pulmonary complications. | High | Strong |

Abbreviations: CHO, carbohydrate; COX, cyclooxygenase; NSAID, nonsteroidal antiinflammatory drug; VTE, venous thromboembolism.

highlighted a lack of adequate blinding resulting in biases that may have influenced the observed treatment effects. As such, recommendations for routine use of preoperative CHO treatment in patients undergoing head and neck cancer surgery require extrapolation from other patient groups. The data on patients with diabetes are still sparse but available information suggests that gastric emptying is similar to controls in well controlled diabetics.[20] Well-designed trials should be considered to reduce this evidence-gap.

## Early Postoperative Diet and Artificial Nutrition

There is large variation in the degree of functional deficit anticipated following surgery for head and neck cancer, depending on the extent of surgical resection and reconstruction that may be required. Hence, some patients may be able to resume oral intake with relatively little impact on nutrition, while for others, nil by mouth with enteral nutrition support is indicated.

The literature examining the early introduction of postoperative oral diet is limited to the post primary total laryngectomy cohort and is controversial. An RCT[21] of early vs delayed oral feeding in this subgroup found no significant difference in length of stay or fistula rates. A systematic review[22] including 4 RCTs examined the safety of initiating early oral feeding in 180 patients and found no increase in pharyngocutaneous fistula rates in those patients who received early oral feeding following total laryngectomy. However, given the limited number of publications, care should be taken in its application and patient suitability should be evaluated on an individual basis. Consultation with the surgical team, dietitian, and speech pathologist regarding optimal timing of the reintroduction of oral intake is advised.

Postoperative enteral nutrition support in the form of nasoenteric tube feeding is commonly required for those patients undergoing major ablative and reconstructive surgery of the upper aerodigestive tract. In cases where adjuvant therapies are planned, insertion of a feeding gastrostomy tube may need to be considered at the point of diagnosis when prolonged nutrition support is anticipated.[23] Few studies have explored timing to initiation of postoperative tube feeding specifically in patients with head and neck cancer; however, existing guidance can be used to guide routine clinical practice.[11]

Parenteral nutrition (PN) support is indicated in the absence of normal gut function and when enteral access is not possible. In rare instances when PN is commenced in patients with head and neck cancer, published guidelines on PN following surgery may be used to guide practice.[24]

## Prophylaxis Against Thromboembolism

Both cancer and surgery are individual risk factors for venous thromboembolism (VTE); however, patients with both factors are at high risk.[25] The rates of deep vein thrombosis and fatal pulmonary embolism range from 15% to 30% and 0.2% to 0.9%, respectively, in general surgery patients without prophylaxis; however, advanced age (>40 years) and the presence of cancer increases these rates to 40 to 80% and 0.2% to 5%, respectively.[26] Controlled trials[27,28] provide compelling evidence for the use of perioperative VTE prophylaxis in properly selected surgical patients. Validated scoring systems to determine the need for and nature of VTE prophylaxis consistently place patients undergoing major head and neck resections with free flap reconstruction at moderate to high risk for VTE.[29] Readers are cautioned against heeding contrary recommendations from smaller retrospective studies in the otolaryngology–head and neck cancer surgery literature that suggest that this population may be at lower risk than expected, as retrospective studies are well known for underestimating the incidence of deep vein thrombosis.

There is a demonstrable reduction in VTE when pharmacologic prophylaxis (ie, low-molecular-weight heparin) is used in patients undergoing head and neck cancer surgery with free flap reconstruction.[30] However, there is also a demonstrable increase in bleeding complications if VTE prophylaxis includes anticoagulants.[31] Therefore, the use of anticoagulants in patients undergoing major head and neck cancer surgery with free flap reconstruction must be individualized based on both the risk of VTE and the risk of bleeding. Combined use of antiplatelet agents and anticoagulant VTE prophylaxis may increase the risk of bleeding above the risk of VTE events.

There are no pharmacologic measures that have been proven to reduce free flap anastomotic thrombosis or flap necrosis.[32] Although some animal studies demonstrate the efficacy of antithrombotic agents, human studies have failed to confirm these findings.

## Antibiotic Prophylaxis

Clean head and neck oncologic cases have a low baseline perioperative wound infection rate and do not benefit from prophylactic antibiotics.[33] However, clean contaminated head and neck oncologic cases have an unacceptably high rate (ie, up to 80%) of perioperative wound infections.[34] Perioperative antibiotics, given 1 to 2 hours prior to surgery and continued for 24 hours have consistently demonstrated a significant reduction in wound infections in randomized controlled trials.[35] Longer courses of antibiotics of 3 to 5 days have not shown benefit over 24 hours in either wound infection rates or pneumonia rates.[36] These findings have held in most series looking at larger cases requiring pedicle or free flap reconstruction.[37]

The use of topical decontamination of the upper aerodigestive tract with mupirocin and 0.2% chlorhexidine has been shown to reduce pneumonia rates and nosocomial infections in patients in the intensive care unit (ICU).[38] Studies[39] specific to head and neck oncology patients have not demonstrated significant differences in wound infection rates with topical decontamination. However, a recent study[40] demonstrated a trend toward fewer and less severe infections.

## Postoperative Nausea and Vomiting Prophylaxis

Especially after free flap reconstructions, vomiting can have detrimental effects on outcomes by causing suture dehiscence, wound infection, fistula, and consecutive flap loss.[41] Postoperative nausea and vomiting (PONV) can also impair early mobilization. Postoperative nausea and vomiting prophylaxis should be considered for all patients undergoing head and neck cancer surgery, because they are at moderate to high risk.[42] A combination of 5-hydroxytryptamine-3 (5-HT3) receptor agonists and corticosteroids has been proven efficacious.[43] When rescue therapy is required, the antiemetic should be chosen from a different therapeutic class than the drugs used for prophylaxis.[44] A newer class of antiemetics, NK1 receptor agonists, have demonstrated equivalent control of PONV compared with 5-HT3 agonists.[45] Randomized clinical trial data on the incidence of PONV in association with propofol or sevoflurane strongly favor the use of these agents for maintenance of anesthesia.[46]

## Preanesthetic Medications

Not all patients experience preoperative anxiety, but some data suggest an incidence rate as high as 80%.[47] Anxiety can be relieved by nonpharmacological means, including a preoperative visit by an anesthesiologist,[48] preoperative music chosen by the patient,[49] or a CHO drink.[50] Medications, such as benzodiazepines, can be effective in reducing anxiety and do not increase discharge time in outpatients, though some patients may have short-term impairment of psychomotor function.[51] Alternatively, comparable anxiolytic effects can be achieved with nonbenzodiazapines, such as dexmedetomidine.[52]

## Standard Anesthetic Protocol

The airway of all patients undergoing head and neck cancer surgery should be carefully examined preoperatively with particular attention being paid to airway assessment, since previous irradiation can lead to lymphedema and fibrosis, causing difficulties with intubation.[53] In addition, any tumor, especially an obstructing one, may be challenging and require the use of special airway devices such as a Glidescope or fiberoptic intubation.[54] Fiberoptic assessment of the airway preoperatively can provide useful information.[55]

There is no literature indicating that a specific standard anesthetic protocol or drugs for patients undergoing head and neck cancer surgery should be employed. Therefore, the general recommendations on anesthesia practice from the ERAS Society have been elected to serve as guidance.[56]

## Preventing Intraoperative Hypothermia

Hypothermia, defined here as a core temperature less than 36°C, is associated with a number of perioperative complications.[57] In general, these include morbid cardiac events, bleeding, and wound infection.[58] Hypothermia is associated with increased morbidity, increased length of stay, and increase in cost.[59] More recently increased complications in hypothermic patients have been shown in those having surgery for head and neck cancer.[60] Intraoperative hypothermia can also pose considerable risk of free flap infection with no benefits to anastomotic patency.[61] Hypothermia in the recovery room can lead to shivering, which can increase wound pain and the metabolic rate (and associated heat production), owing to increased oxygen consumption.[62,63] Compliance with a surgical care improvement project for body temperature management (SCIP Inf-10) is associated with improved clinical outcomes, specifically a reduced incidence of hospital-acquired infection, ischemic cardiovascular events, mortality and reduced length of stay.[64]

Avoiding hypothermia at any stage in the perioperative process is therefore important. Warming patients preoperatively with a warm air cover has been shown to increase core temperature and thus reduce intraoperative hypothermia.[65] Intraoperatively it is important to continuously measure central temperature. The site of surgery my well preclude the usual monitoring sites of the nasopharynx, esophagus, or tympanic membrane. The urinary bladder thermistor catheter has been shown to correlate well with pulmonary artery thermistors[66] and can be used if necessary. Maintaining normothermia intraoperatively can be achieved by forced air warming, circulating water garment, underbody electrical mattress,[67] or resistive heating blankets.[68] Insulating blankets alone may not be sufficient to prevent hypothermia.[69] Warming intravenous fluids keeps patients warmer with less shivering than fluids at room temperature, though it was not shown that warming wash out fluids made a significant difference.[70]

## Perioperative Intravenous Fluid Management

The use of vasoconstrictors for the management of hypotension in free flap surgery is controversial. Animal studies have shown that their use can lead to vasoconstriction in the flap microcirculation[71]; yet, intraoperative use of vasoconstrictors has not been shown to affect flap outcomes in head and neck cancer surgery[72] or other microsurgical procedures.[73] An alternative to vasoconstrictors is certain inotropes, such as dobutamine, which has been shown to improve mean and maximum blood flows through arterial anastomoses in head and neck cancer surgery.[74]

Intraoperative fluid management has been studied mainly in patients undergoing intraabdominal surgery. The available head and neck literature indicates that in patients undergoing head and neck cancer surgery large amounts of intraoperative fluids are associated with increased complications.[75] However, fluid under resuscitation may put patients at risk for postoperative flap thrombosis.[76] An optimum fluid load is possible.[77] The ERAS literature concentrates on near zero balance, where the aim is to maintain the preoperative weight in the immediate perioperative period, or goal directed fluid therapy.[78] The latter is based on determining whether a patient is fluid responsive, as measured by cardiac output, stroke volume, or pulse pressure variation.[79,80] The aim is to push the patient's blood toward the peak of the Frank Starling curve[81] and maximize cardiac output and oxygen delivery,[82] which can be measured invasively with an arterial line, semiinvasively using a Doppler, or noninvasively using bioreactance technology. Zero-balance and goal directed therapy have similar outcomes.[83] The use of central venous monitoring in major head and neck cancer surgery is not useful.[84]

Blood transfusion in head and neck free flap patients does not affect flap survival, but is associated with increased perioperative complications.[85] Significantly increased wound infection rates and death were shown in a retrospective study[86] of blood transfusion controlled for age, preoperative hemoglobin and albumin, cancer stage, and adverse pathologic features. These recent studies support consideration of a restrictive transfusion policy in free flap patients.[87] Nevertheless, recent data have suggested that a liberal transfusion strategy may improve outcomes perioperatively in adult cardiac surgery patients.[88] The trigger for transfusion remains a moving target. A transfusion trigger of 7 g/dL has been suggested for routine patients with adaptation for patients with asymptomatic coronary disease (8 g/dL) and patient with ongoing ischemia (10 g/dL).[89]

## Routine Postoperative Intensive Care Admission

There are no prospective randomized trials investigating the usefulness of routine ICU treatment following head and neck cancer surgery. However, a growing body of literature, including retrospective studies examining the practice of routine ICU admission following major head and neck cancer surgery, suggest that ICU admission could be avoided. An immediate postoperative period of deep sedation and artificial ventilation in an ICU has been associated with prolonged time to weaning from mechanical ventilation and an increase in the frequency of respiratory insufficiency and pneumonia, as compared with allowing patients to breathe spontaneously without sedation in a recovery room; furthermore, there was no difference in the number of flaps lost or ICU readmissions.[90] Other studies[91,92] in patients undergoing head and neck cancer surgery have demonstrated no difference in general morbidity between patients cared for in an ICU and those cared for in a specialist ward, suggesting that it is possible to nurse these patients outside of the ICU environment, provided there is close medical support and an appropriately trained nurse allocated to care for these patients.

A retrospective analysis[93] revealed low use rates of critical care services by patients undergoing head and neck cancer surgery and did not identify any causes of complications leading to use of critical care services. Risk factors for complications include bilateral neck dissection, an APACHE II score greater than 10, massive blood transfusion, early postoperative complications requiring further operation under general anesthesia, smoking history, and perioperative antibiotic choice.[94] In absence of these factors, there are no data to support the use of routine ICU care. Funding issues, ICU work load, standing costs (in the ICU and elsewhere), and the availability of skills and resources outside of the ICU must be considered in the determination of optimal postoperative location of care and this needs to be individualized to each health care facility.

## Pain Management

The pretreatment of patients with analgesic drugs to reduce postoperative pain, also known as preemptive analgesia, has become part of a multimodal pain therapy that has been applied to numerous types of surgery,[95] including head and neck cancer surgery.[96] The timing of analgesia does not appear to affect postoperative pain quality.[96,97] However, premedication with nonsteroidal antiinflammatory drugs (NSAIDs) and local wound infiltration has been shown to delay time to first analgesia and reduce total analgesic use.[97] Clinicians should rely on a multimodal approach combining strong opioids, nonopioid analgesics, and peripheral or neuraxial local anesthetics acting on different sites of the pain pathway.[98] Paracetamol is effective for postoperative analgesia[99]; for reliable blood levels perioperatively the intravenous route may be preferable.[100] Celecoxib has also been shown to be effective for postoperative pain relief after different surgeries[101] and has no deleterious effect on free flap survival or wound healing.[102] Although celecoxib, unlike COX-1 inhibitors, has been shown to have essentially no inhibitory effects on platelet aggregation,[103] there have been case reports of associated surgical bleeding[104] and so its use should be individualized. Although the efficacy of preoperative gabapentin seems variable,[105] it has been shown to be effective for patients having tongue reconstruction with a thigh flap.[106]

Most head and neck tumor resections imply large resection defects, frequently combined with free flap reconstruction and prolonged operation times. This results in specific challenges regarding postoperative analgesia. Several randomized studies on tumor resection and flap harvesting showed a benefit with patient-controlled analgesia (PCA) by morphine pump.[107] The use of PCA does not appreciably increase nausea or vomiting.[108] However, multimodal analgesia using combinations of narcotic and nonnarcotic analgesics have also shown promising results. Numerous high-quality studies indicate that multimodal analgesia is effective, reduces narcotic induced side effects, and facilitates rapid recovery after surgery.[109]

Several randomized studies have addressed the effects of additional nerve blocks on postoperative pain. Of special interest is the (bilateral) superficial cervical plexus block (SCPB), which has been shown in most studies to result in reduced postoperative pain scores following thyroidectomy with or without parathyroid surgery.[110] Use of the SCPB also resulted in reduced need for intraoperative analgesics and reduced length of hospital stay.[111] A meta-analysis[112] of 799 patients concluded that a combination of bilateral SCPB and general anesthesia reduces pain after surgery to a statistically significant, but clinically insignificant, magnitude.

## Postoperative Flap Monitoring

Postoperative free flap monitoring protocols are highly variable between both surgeons and institutions. Multiple methods of monitoring have been described, from simple clinical examination for evidence of adequate arterial and venous flow to invasive monitoring techniques, such as implantable Doppler or pO2 monitors.[113,114] Each technique has been shown to be effective, but there are advantages and disadvantages for each of the approaches. To date, no universally acceptable approach to monitoring has been defined. Similarly, the ideal timing for postoperative flap monitoring, in terms of both frequency and duration, is variable and best practices have been hard to define from an evidentiary basis. Most evidence suggests that vascular complications will occur within the first 24 hours in most patients, thus the need for intensive monitoring in the first 24 hours.[115]

It seems that the most widely accepted approaches for postoperative flap monitoring include bedside clinical examination for color, capillary refill, surface temperature monitoring, and, in some cases, pin prick testing performed at frequent intervals, usually hourly, for at least 24 hours postoperatively.[116] Many centers use other monitoring technology in addition to these basic approaches, with some reporting improvements in flap salvage rates relative to other published series.[117] However, there are no randomized controlled trials in this area and most publications present retrospective or prospective case series.[118]

## Postoperative Mobilization

Data on early mobilization in patients undergoing major head and neck resection with free flap reconstruction are limited. A single retrospective cohort study[119] found that early mobilization was associated with fewer pulmonary complications in patients undergoing major head and neck resection with free flap reconstruction. Most data on early mobilization are from patients undergoing major abdominal procedures, which showed that early mobilization, as part of a comprehensive treatment protocol, reduced complications and overall length of stay.[120] A secondary analysis of the randomized Laparoscopy in Combination with Fast Track Multimodal Management (LAFA) study[121] showed that early mobilization was a significant independent predictor of good outcome. The independent contribution of early mobilization on postoperative clinical outcomes seems to be favorable.

The timing of mobilization is clearly important, because early mobilization has been shown to be better than late mobilization.[119,121] However, the impact of "dose" of mobilization has not been studied. Data on the number of minutes per day of patient activity have been inconsistently reported across studies.[122] There are challenges to getting patients to mobilize early after surgery and a multipronged approach that includes control of postoperative pain and nausea is required,[123] because failure to adequately address these factors leads to delayed mobilization.

## Postoperative Wound Care

In evaluating best evidence for postoperative wound care, consideration must be given to both the resection site and the donor site for free flap reconstruction. In most cases primary closure with drain placement is performed for cervical incisions. A systematic review[124] suggested there is no compelling evidence to support any particular wound dressings for wounds healing by primary intention and in general these may be left open for healing. There is limited evidence that topical antimicrobials may reduce surgical site infections.[125] There is considerable evidence that active drains are more effective than passive drains and reduce drain-related complications.[126]

The evidence for vacuum-assisted closure for complex open cervical wounds demonstrates a potential benefit,[127] however, there is less evidence for the routine use of these systems for free flap or skin graft donor sites, although case-series have been positive.[128] There is strong evidence to support polyurethane film for use at skin graft donor sites with reductions in patient pain and discomfort relative to other dressing types.[129] However, a large RCT[130] suggested that hydrocolloid dressings had the most rapid wound healing and polyurethane film resulted in the least patient satisfaction with scar appearance.

## Urinary Catheterization

Patients undergoing major head and neck cancer surgery with free flap reconstruction universally require postoperative urinary catheterization. When prolonged, urinary catheterization results in urinary tract infection (UTI) in 5% to 43% of patients, which can result in prolonged hospital stay and other hospital-related complications.[131] A UTI in head and neck patients is associated with higher postoperative complication rates and prolonged hospital length of stay.[132]

Although there are no studies of catheterization duration in head and neck cancer surgery patients, evidence from other surgical disciplines is illustrative. Randomized trials[131,133] in postoperative gynecologic patients show clear reductions in UTI rates and reductions in hospital length of stay in patients who have shorter duration of catheterization. These findings are supported by a large meta-analysis[134] of postoperative gynecologic patients. Findings are similar in patients undergoing thoracic and abdominal surgery.[135] Results from studies of infection rates in patients having transurethral vs suprapubic catheterization are conflicting. However, a high quality meta-analysis[136] suggests that suprapubic catheterization results in fewer bladder infections when prolonged catheterization is required.

### Postoperative Tracheostomy Care

Airway management in patients undergoing major head and neck procedures with free flap reconstruction is important. This includes the protection of the airway in the early postoperative phase from obstruction via oropharyngeal edema, swelling of the flap, or bleeding and in the later postoperative phase during swallowing rehabilitation.

Surgical tracheotomy is in general a low-morbidity procedure with rare severe complications.[137] However, it has the potential to prolong hospital stay considerably.[138] Certain patients may not require tracheotomy after free flap reconstruction and instead the airway could be treated by overnight or, if needed, longer oro or nasotracheal intubation.[138-141] These patients include selected oral cavity resections without bony reconstruction and certain maxillary reconstructions.[138-140] The decision to perform a tracheotomy is dependent on the presence of severe comorbidities, tumor stage and location, alcohol consumption, extent of resection, and whether or not a bilateral neck dissection was performed.[139,140]

Decannulation after tracheostomy and closure of the stoma is important for respiratory and swallowing rehabilitation of the patient. Various protocols are proposed in the literature to help determine the timing of decannulation. However, all protocols usually advise a capping trial of varying duration prior to decannulation.[142] Finally, surgical closure of the tracheostomy site after decannulation may speed up recovery. Data suggest that surgical closure results in shorter hospital stay, faster swallowing recovery, cost savings, and eventually fewer long-term tracheal complications.[143] In most cases patients can be safely decannulated within 1 week following surgery.

### Postoperative Pulmonary Physical Therapy

Pulmonary complications have the potential to jeopardize recovery of patients after major head and neck ablative and reconstructive procedures. Pneumonia may delay mobilization, swallowing exercises, and also has a negative impact on wound healing. Increased pulmonary secretions may delay decannulation and closure of the tracheostomy site and thus increase overall length of stay.[143] Therefore, postoperative pulmonary physical therapy for patients after major head and neck resection and reconstruction is in general felt to be of great benefit.

Although there are no data from patients undergoing major head and neck cancer surgery, a large body of evidence has been gathered on patients after other procedures (ie, abdominal procedures) demonstrating a clear benefit of pulmonary physical therapy after the intervention to avoid pulmonary complications. The type of physical therapy consists usually of incentive spirometry (IS), intermittent positive pressure breathing (IPPB), and deep breathing exercises (DBE).[144] Each type of physical therapy was found to be beneficial in avoiding pulmonary complications, but between the various types (IS vs IPPB vs DBE) no explicit advantage of 1 or the other technique could be identified.

## Conclusions

Improving perioperative surgical care in an evidence-based and structured manner is the primary goal of enhanced recovery after surgery protocols. The ERAS guidelines for a number of surgical disciplines have reduced surgical complications, overall length of stay, and costs of care.[145] Major head and neck surgical procedures with free flap reconstruction are among the most complex areas of surgical endeavor and require careful preoperative preparation, intraoperative care, and coordinated postoperative care. Although many centers around the world provide excellent care to head and neck cancer patients, there is still tremendous variation in the application of perioperative care elements provided to this patient population. We have assembled an international expert panel and carefully employed the ERAS Society approach to protocol development. We collected and evaluated the best available evidence and, using a formal consensus based approach, formulated clear recommendations for the major elements of perioperative care in the major head and neck cancer patient population. Our approach used several of the key elements described by Rosenfeld, et al[146] in *Clinical Consensus Statement Development Manual Otolaryngology*. In some cases, a paucity of literature specific to head and neck cancer surgery was available and, as a result, several of the recommendations are based on data extrapolated from other patient populations, particularly those undergoing colorectal surgery. We have adapted the recommendations, where appropriate, to better fit the needs of patients undergoing head and neck cancer surgery and have used the considerable expertise of the working group to make those adaptations. We believe the end result is a set of consensus recommendations and a proposed measurement framework that will provide a baseline for future clinical effectiveness research and outcomes evaluation in a very important patient population. The proposed consensus recommendations may also have an impact on the quality, safety, and cost of care offered to patients undergoing major head and neck cancer surgery with free flap reconstruction.

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Invited Commentary

# Evidence-Based Perioperative Treatment After Free Tissue Reconstruction

## Moving From Alchemy to Data

Samir S. Khariwala, MD, MS, FACS

**The use of free tissue transfer** (FTT) in the head and neck has made considerable strides since the first procedures were performed nearly 40 years ago.[1] Free tissue transfer began as a risky and extremely time-consuming procedure, yet through improved instrumentation and accumulated experience, head and neck defects are now routinely treated with FTT. Furthermore, the expansion of indications for FTT has resulted in surgeons tackling cases of increasingly greater difficulty with regularity.

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For example, it is not uncommon for patients who have been doubly radiated and/or had prior neck dissections to receive second, third, or even fourth free flaps,[2] which may require vein grafting and accessing the internal mammary vessels.[3] Free flap failure will almost invariably increase the length of hospital stay and cost of care. In addition, free flap failure may be associated with open wounds that result in decreased quality of life for patients. Free flap surgeons often rely on patient treatment techniques handed down from experienced surgeons, which may lack a sound scientific basis. Because of their concern about serious complications, free flap surgeons are frequently reluctant to try new and untested techniques or engage in controlled randomized trial designs. Whether the technique in question is anticoagulation, antibiotics, vasoactive agents, or free flap monitoring, too often the rationale for decision making is: “I’ve always done it this way…” or “This is how Dr. X did it.” Given the serious consequences of flap loss, this reaction by free flap surgeons, most of whom are habitually meticulous and suspicious, is certainly understandable. Still, the era of evidence-based medicine is well upon us and we must seek to base our practice on the strongest data available.

In this issue of *JAMA Otolaryngology–Head & Neck Surgery*, Dort et al[6] propose recommendations for perioperative treatment of patients receiving major head and neck cancer surgery with free flap reconstruction. This effort is based on the mission of, and endorsed by, the Enhanced Recovery After Surgery (ERAS) Society. Based on a finding that ERAS recommendations developed for patients undergoing colorectal surgery resulted in functional improvements after surgery, the authors sought to apply a similar approach for patients receiving free flaps. To accomplish this, they performed an extensive literature search and attempted to coalesce a series of of-