Designing an evidence-based free-flap pathway in head and neck reconstruction

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Abstract

Background: The use of autologous free-tissue transfer is an increasingly utilized tool in the ladder of reconstructive options to preserve and restore function in patients with head and neck cancer. This article focuses on the evidence surrounding perioperative care that optimizes surgical outcomes and describes one tertiary center's approach to standardized free-flap care.

Data Sources: This article examines English literature from PubMed and offers expert opinion on perioperative free-flap care for head and neck oncology.

Conclusion: Free-flap reconstruction for head and neck cancer is a process that, while individualized for each patient, is best supported by a comprehensive and standardized care pathway. Surgical optimization begins in the preoperative phase and a thoughtful approach to intraprofessional communication and evidence-based practice is rewarded with improved outcomes.

KEYWORDS
facial plastics and reconstruction, free-flap tissue transfer, head and neck oncology

INTRODUCTION

Free-flap reconstruction is one of the most rewarding and challenging undertakings in the field of head and neck oncology. Free-flap surgery is fraught with challenges commensurate with the intricacy of this surgical feat. Structured clinical algorithms help mitigate these challenges by providing a framework for perioperative care that has been shown to positively impact outcomes and resource utilization in free-flap surgery.1 This study examines current literature on patient safety and quality improvement in free-flap care and describes our institution’s approach towards developing a care pathway for free-flap patients across all phases of care.

This study was initiated to review aspects of free-flap surgery which are amenable to standardization in the interest of improving clinical outcomes. As the literature is scattered on this topic, the aim of this review is to compile actionable patient safety measures that can be easily implemented to microvascular reconstruction programs.

TWO-TEAM SURGICAL APPROACH

The two-team approach to head and neck free-flap reconstruction is one that has been adopted by our center as well as many high-volume centers around the world.2 At our institution, this consists of early involvement of facial plastic and reconstructive surgery (FPRS) microvascular surgeons in each patient’s care. FPRS surgeons attend a weekly head and neck tumor conference and offer input on reconstructive options from the outset of preoperative planning.
Involving FPRS surgeons in this process shifts the burden of reconstructive planning to the reconstructive team, allowing head and neck surgeons to focus on oncologic outcomes. Previous authors have found that shifting reconstructive planning to a dedicated team resulted in wider surgical margins on pathologic analysis. At our institution, surgical subunits are evaluated and resected based on aesthetic and oncologic discussions among the two teams, allowing en bloc resection of these subunits with tumor margins when applicable.

Patient distress with cosmetic outcomes following head and neck reconstruction is common. Some studies have argued that the emotional burden of long-term disfigurement may rival that of long-term dysfunction. Similarly, up to 17% of head and neck cancer patients may be forced to change jobs or exit the labor force, based solely on concern for postoperative appearance. Multiple authors have demonstrated that cosmetic revision following head and neck surgery remains common, and it is our belief that upfront involvement of FPRS surgeons can reduce this burden for patients.

Within the operating room itself, a two-team approach may offer benefits to both patients and surgeons. When possible, it is our practice to perform simultaneous tumor resection and free-flap harvest to minimize operative time. Previous authors have demonstrated that longer operative times are predictive of postoperative complications. With regard to surgeon quality of life, microvascular surgeons have generally high rates of burnout relative to other otolaryngologic surgeons. Decreasing operative time and allowing for division of labor in these complex surgeries via a two-team approach may reduce burnout in microvascular surgeons.

**FREE-FLAP PLAN OF THE DAY**

Free-flap reconstruction of the head and neck requires close teamwork between anesthesiologists, surgeons, nurses, and clinical operative services. In an observational study of head and neck free-flap surgeries, 20% of operating room time was spent pre-incision, and an average of 270 entries and exits from the room occurred in each case, usually related to the need for supplies or communication purposes. Operating room communication failures have been reported to occur in up to 30% of all operating room exchanges, compromising patient safety by increasing cognitive load, causing interruptions, and increasing tension. Communication topics that increased operating room tension included: timing of elements of the procedure, safety and sterility, resources, and team roles; discussion of these topics have significant implications for team dynamics. Breakdown in communication between team members introduces delays to surgical starts and can be mitigated with improved communication strategies and improved accountability. Studies have demonstrated that systematic communication tools can be used to address anticipated communication errors. A pre- and postintervention study across 11 surgical specialties evaluated the impact of a pre-incision, interdisciplinary time-out where roles, antibiotics, critical steps in the surgery, and anticipated problems were discussed; this intervention resulted in a 31% reduction in unexpected delays and a 19% reduction in communication breakdowns leading to delays. Ibrahim et al. described a free-flap plan of the day for head and neck surgeries designed to address areas of operative inefficiency identified by observers trained in Lean methodology. This intervention improved in-room-to-incision times and total operating times. Longer operating times are associated with higher risk of early flap failure, pneumonia, blood transfusions, prolonged ventilat or requirement, wound dehiscence, and wound complications; however, causation cannot be extrapolated from these observations.

Our free-flap plan of the day (Table 1) was developed with input from anesthesia and nursing colleagues to anticipate critical information.

| Date of surgery | Procedure: list of all procedures including anticipated extirpation and all possible reconstructive options, including planned procedures by other consulting surgical teams such as general surgery |
|-----------------|------------------------------------------------------------------------------------------------------------------|
| Anesthesia | Recommended airway: nasotracheal/orotracheal/awake fiberoptic/ laterality |
| | Protect limb: arm/leg/laterality or both |
| | Paralytic ok?: yes/no |
| | Pressors ok?: no |
| | ERAS: yes/no |
| | Suggested temperature: normothermic 37°C/slightly hyperthermic 37.5°C–38°C |
| Position | Supine/left lateral decubitus/right lateral decubitus/prone |
| | No turn/90°/180° |
| Expected blood loss: <500 ml/>500 ml |
| Predicted postoperative airway: tracheostomy/intubated/extubated |
| Nursing | Underbody warmer: yes/no |
| | Number of setups: 1/2/3 |
| | Order of case: description of order of procedures in case |
| | Saw or drill: yes/no/both |
| | Plating (within H&N): yes/no |
| | Plating (extremity): yes/no |
| | Plating representative contacted?: yes/no |
| | Other services required: other surgical teams involved, product representatives, or neuromonitoring |
| | Split-thickness skin graft: yes/no |

Note: The free-flap plan of the day is filled out the day before surgery and placed in the electronic medical record. There are several embedded drop-down menus in the templated document here represented as different options separated by dashes. Abbreviation: ERAS, enhanced recovery after surgery.
required by all team members to improve efficiency. Similar to Ibrahim et al., our plan includes information pertinent to anesthesia such as type of airway, limb protection from lines, and anticipated blood loss volumes. In addition to this information, our plan includes whether or not paralysis and vasopressors are acceptable, and the anticipated postoperative airway. This information allows our anesthesia colleagues to prepare the materials required for the indicated airways and avoid placing lines in protected limbs. Although there is no consensus yet on whether intraoperative vasopressors are linked with free-flap failures, our experience and preference are that these medications are easily avoided. At our institution, the resident responsible for the case places a note with the completed free-flap plan of the day in the electronic medical record the day before surgery; many anesthesia colleagues have referenced this document as a helpful tool. The completion of this template often stimulates conversations with the surgical attendings the day before surgery, offering further opportunities for resident education and planning.

**TOPICAL VASODILATORS**

Maintaining vessel patency is critical to optimize perfusion during free-tissue transfer. Spasm of the donor or recipient vessel can restrict perfusion, stimulate thrombus formation, and lead to free-tissue ischemia, threatening viability of the flap. A number of factors may contribute to this phenomenon. First, the endothelium is of particular importance in regulating vasoconstriction via vascular smooth muscle activity. Endothelium-derived relaxing and hyperpolarizing factors such as nitric oxide, prostaglandins, and prostacyclins reduce calcium influx and inhibit smooth muscle contraction. On the contrary, endothelial damage stimulates smooth contraction via mediators such as endothelin-1, thromboxane A2, and adenosine diphosphate and also activates platelet function. In addition to endothelial damage, traumatic handling of vessels during raising, anastomosis, or inset can induce vessel spasm through direct myogenic responses to stretching or disruption of resting membrane potentials. Other factors that may contribute to vascular spasm are perioperative use of vasoactive medications, low core body temperature, and surgical catecholamine surge. The microvascular surgeon must recognize the above factors and attempt to mitigate their effects.

One of the most widely accepted strategies is the use of intraoperative topical vasodilators. Yu et al. found that 94% of microvascular surgeons implement topical vasodilators with the most common agents being papaverine, verapamil, and lidocaine. Papaverine is a phosphodiesterase inhibitor and acts as a smooth muscle relaxant via an incompletely known mechanism involving direct action on calcium channels along with increases in cyclic guanosine monophosphate (cGMP). In vitro studies have demonstrated up to 60% increase in vessel caliber with papaverine treatment. Drawbacks to papaverine include short duration of action (<2 h), dose-dependent endothelial toxicity, and acidic solution. Verapamil works via selective inhibition of the L-type voltage-gated calcium channels on smooth muscle thus inducing vasodilation. While the onset of action is slower than papaverine, verapamil has a half-life of 4.8 h. Lidocaine is an amide local anesthetic with activity against voltage-gated sodium channels. At low concentrations (2%) lidocaine may induce norepinephrine-mediated vasoconstriction while vasodilatory effects are seen at higher concentrations (20%). However, its use is limited by the risk of systemic toxicity with high dose lidocaine and thus it is less regularly implemented than papaverine or verapamil. Lastly, topical nitroglycerin has been implemented at some centers in the setting of recent papaverine national shortages. Nitroglycerin induces nitric oxide formation in smooth muscle cells and increases intracellular cGMP inhibiting downstream calcium release and resulting in vasodilation. However, the half-life is short and its isolated dilatory effect may be less than that of papaverine or verapamil alone.

The authors use a similar mixture to that recently published by Seth et al. which is presented in Table 2. In combination, verapamil and nitroglycerin are reported to provide a synergistic dilatory effect and the combination has both a fast onset and long-lasting effect. Seth et al. recently published the first series of 300 free-tissue transfers using this mixture with a flap failure rate of 1%. In our experience, application of this mixture results in a notable increase in vessel diameter and subjective decrease in spasm.

**FREE-FLAP CLOSURE TIMEOUT**

Despite high overall free-flap success rates, complications following head and neck free-flap reconstruction remain common. Of these, the most common surgical complications include dehiscence, fistula, infection, hematoma, and flap compromise. Additionally, intraoperative holdups remain a common cause for delay, adding to operative time, anesthesia time, and OR costs. Previous authors have estimated average operating room costs to equal $66 per min, which are likely to be even higher in complex surgeries such as head and neck free-flap reconstruction. At our institution, common delays at the termination of a case were secondary to calling for X-ray evaluation in the case of incorrect instrument counts, obtaining and placing enteral access, and locating doppler monitors with adequate functionality.

With patient safety and surgical efficiency in mind, our group implemented a simple mnemonic to be utilized just before final neck

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**TABLE 2 Components and ratios of topical vasodilator solution used during free-flap reconstruction**

| Component     | Dosage | Volume (ml) | Final concentration |
|---------------|--------|-------------|---------------------|
| Nitroglycerin | 2.5 mg | 0.5         | 8.3 mcg/ml          |
| Verapamil     | 5 mg   | 2           | 16.7 mcg/ml         |
| Sodium bicarbonate | 0.2 mEq | 0.2 | pH 7.4             |
| Heparin       | 500 U  | 0.5         | 1.6 U/ml            |
| Lactated ringers | -  | 296.8        |                     |
or recipient site closure (Table 3). To facilitate attention and multidisciplinary discussion during this final check, this mnemonic is applied as a formal timeout including input from anesthesia and nursing. We have found that performing this timeout has stimulated discussion of these critical aspects of free-flap care, and has altered operative or postoperative plans in nearly all cases.

**ENHANCED RECOVERY AFTER SURGERY PATHWAY**

An enhanced recovery after surgery (ERAS) pathway takes many forms, but fundamentally provides a set of standardized practices during the pre-, intra-, and postoperative phases of care to speed recovery, mitigate pain, and decrease the morbidity of surgery. In 2016, a panel of international experts developed ERAS consensus guidelines for head and neck surgery, recommending seventeen practices in the perioperative period. Many institutions have since adopted some version of ERAS although implementation varies widely. A recent systematic review of the literature on ERAS following head and neck free-flap surgery suggests ERAS protocols may decrease hospital length of stay by an average of 4.4 days, readmission rates, and the relative risk of wound complications without impacting reoperation rate, mortality, or intensive care unit length of stay.

At our institution, all patients undergoing major head and neck surgery, including all free-flap patients, are placed in the ERAS care pathway (Table 4). ERAS is explained by the physician during office consultation and reiterated by trained nurses who call patients the day before surgery to explain the preoperative steps patients will undertake. Patients on the ERAS pathway are identified to all perioperative staff by a marker on the surgical board, and specially trained nurses call patients. We have found that performing this timeout has altered operative or postoperative plans in nearly all cases.

**MANAGEMENT OF ANEMIA**

Management of perioperative anemia in patients undergoing free-tissue transfer has been widely debated in the literature with little consensus. The WHO defines anemia as hemoglobin less than 13 g/dl in males and 12 g/dl in females. Anemia is common in patients undergoing free-tissue transfer. Traditionally, perioperative hemoglobin goals were as high as 10 g/dl to maintain flap perfusion, possibly based on early animal studies demonstrating optimum oxygen-carrying capacity at this level. However, there is little evidence to support improved outcomes with transfusion to this level and many authors advocate free-flap transfusion thresholds as low as hemoglobin 7 g/dl or lower based on individual patient considerations. Risks of transfusion include acute and delayed hemolytic reactions, blood-borne infections,
| Elements                  | Preadmission                                      | Preoperative | Intraoperative                                                                 | Postoperative |
|--------------------------|---------------------------------------------------|--------------|--------------------------------------------------------------------------------|---------------|
| Two-team surgical        | H&N and FPRS teams discuss extirpative and        |              | Simultaneous head and neck resection and free-flap harvest                     |               |
| approach                 | reconstructive options at tumor board conference  |              |                                                                                  |               |
| Free-flap plan of the day| -                                                 | Resident places in electronic medical record the day before surgery | -             | -                           |
| Topical vasodilators     | -                                                 | -            | Vasodilator solution applied to anastomosis and pedicle                        |               |
| Free-flap closure time   | -                                                 | -            | Checklist led by attending before closing neck incisions                       |               |
| out                      | -                                                 | -            |                                                                                  |               |
| ERAS                     | Identification of patient for protocol            | Carbohydrate drink 3H before anesthesia | Prophylactic antibiotics before incision: ampicillin and sulbactam and clindamycin and gentamycin for penicillin allergic patients | Gabapentin 300 mg Q8H, celecoxib 200 mg Q12H, acetaminophen 975 mg Q8H |
|                          | Patient education on ERAS protocol                 |              | Fluid warmers and forced air warming device to maintain normothermia           | Ketorolac 15 mg or tramadol 50 mg Q6H for breakthrough pain |
|                          | Medical optimization visit                        |              | Lidocaine/propofol induction followed by volatile anesthetic                  | ICU for 48H for flap monitoring |
|                          | Laboratory testing                                |              | Goal-directed fluid therapy                                                   | Fentanyl PCA for opioid tolerant patients with pain management consult |
|                          | Evaluation by speech language pathologist and     |              | Ketonolac 30 mg and IV acetaminophen 1000 mg before completion                 | Ferrous sulfate 325 mg Q8H, vitamin C 500 mg daily, aspirin 81 mg daily |
|                          | dietician                                          |              | Antiemetic prophylaxis with ondansetron 4 mg                                  | Extubate POD1 if left intubated at end of case |
|                          | Preoperative nursing call reminds patient to take  |              | Avoid tracheostomy                                                            | Ambulate 5x a day and physical therapy and occupational therapy consults POD1 |
|                          | carbohydrate drink                                |              |                                                                                  | Dietician consult: start tube feeds POD1 and advance Urinary catheter removed POD1 |
|                          |                                                    |              |                                                                                  | Neck drains removed when output <30 ml/day |
|                          |                                                    |              |                                                                                  | Speech-language pathology evaluation before starting oral diet |
|                          |                                                    |              |                                                                                  | Discharge when patient afebrile, nutrition and pain control adequate with multimodal analgesia |

**Goal hemoglobin**

Limit transfusions for hemoglobin

>7 g/dl unless symptomatic

**Abbreviations:** ERAS, enhanced recovery after surgery; FPRS, facial plastic and reconstructive surgery; ICU, intensive care unit; POD, post operative day.
and important to consider in this population—immunomodulation or relative immunosuppression. While the exact mechanisms of transfusion-related immunomodulation (TRIM) are not fully recognized, there is thought to be a complicated pro-inflammatory state secondary to cytokine activation, residual leukocytes, and other intra/extracellular microparticles. TRIM was first reported when it was noted that solid organ transplant patients undergoing repeat blood transfusion demonstrated less rejection. This process may explain the poorer oncologic outcomes for cancer patients undergoing curative-intent surgeries who receive multiple transfusions. In head and neck patients undergoing free-tissue transfer, multiple intraoperative and postoperative transfusions have been associated with a higher rate of wound infections and lower overall survival. Therefore, at our institution 7 g/dl is a soft threshold for transfusion for asymptomatic patients. Patients are considered individually based on medical history and global clinical picture with many patients tolerating hemoglobin levels below 7 g/dl without transfusion. The introduction of intravenous iron as an “opt-out” to the postoperative order set in the electronic medical record can also decrease the incidence of transfusion.

CONCLUSIONS
Reconstruction for cancer of the head and neck is uniquely challenging in its requisite special consideration for the role this region plays in esthetics and crucial functions including breathing, eating, and speech. Towards this end, free-flap surgery is a powerful tool in the reconstructive arsenal. Free-flap reconstruction for head and neck cancer is arguably the most complex surgery performed by otolaryngologists; in our experience, this study is best supported by a two-team surgical approach and careful coordination between multidisciplinary team members. Intentional use of communication tools before and during free-flap surgeries can circumvent common pitfalls that lengthen operating room times and incur greater morbidity. The free-flap closure timeout is an easily implemented routine which has helped to coordinate communication between the multiple teams involved in caring for these complex patients. Overall, the authors advocate for the use of evidence-based comprehensive care pathways that can reduce variability of care and improve clinical outcomes.

CONFLICTS OF INTEREST
The authors declare no conflicts of interest.

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