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REVIEW ARTICLE

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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.[3] At our institution, surgical subunits are evaluated and resected based on esthetic 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.[4] 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.[5] 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.[6–9]

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 flap failure and other complications.[10,11] With regard to surgeon quality of life, microvascular surgeons have generally high rates of burnout relative to other otolaryngologic surgeons.[12] 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.[13] 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.[14] 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.[15] Breakdown in communication between team members introduces delays to surgical starts and can be mitigated with improved communication strategies and improved accountability.[16] Studies have demonstrated that systematic communication tools can be used to address anticipated communication errors.[17,18] 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.[17] Ibrahim et al.[18] 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.[18] 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.[19]

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

TABLE 1 Free-flap plan of the day

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.,[18] 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.[20] 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.[21] On the contrary, endothelial damage stimulates smooth contraction via mediators such as endothelin-1, thromboxane A2, and adenosine diphosphate and also activates platelet function.[21] 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.[21,22] Other factors that may contribute to vascular spasm are perioperative use of vasoactive medications, low core body temperature, and surgical catecholamine surge.[21,23,24] 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.[25] 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).[23,26] In vitro studies have demonstrated up to 60% increase in vessel caliber with papaverine treatment.[27] Drawbacks to papaverine include short duration of action (<2 h), dose-dependent endothelial toxicity, and acidic solution.[21,23,26] 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.[21] 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%).[28] 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.[23] Lastly, topical nitroglycerin has been implemented at some centers in the setting of recent papaverine national shortages.[23,26] Nitroglycerin induces nitric oxide formation in smooth muscle cells and increases intracellular cGMP inhibiting downstream calcium release and resulting in vasodilation.[21,23,26] However, the half-life is short and its isolated dilatory effect may be less than that of papaverine or verapamil alone.[21]

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	-

The authors use a similar mixture to that recently published by Seth et al. which is presented in Table 2.[23] 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.[21,23] Seth et al.[23] 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.[29,30] 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.[31] 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

TABLE 3 Free-flap closure timeout checklist is posted on the wall of the operating room and performed before closure of neck incisions

Letter	Discussion point	Description
A	Airway	Airway plan (intubated, extubated, tracheostomy, etc.)
B	Bleeding	Final check for hemostasis
C	Count	Nursing count performed early, with early call for X-ray if indicated
D	Drains	Donor site, recipient site. Ensure that drains hold suction
E	Enteral access	Nasogastric tube, gastrostomy tube, oral feeding plan
F	Flap checks	Plan for where to perform. Place doppler stitches away from confounding vessels. Baseline color
G	Geometry	Final check for vessel kinks or compression
H	Heparin	Prophylactic versus therapeutic anticoagulation. Aspirin plan. NSAID plan
I	Inset	Final inspection for gaps

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 rocovery 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.[32] Many institutions have since adopted some version of ERAS although implementation varies widely.[33] 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.[33]

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).[34] 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 developed pre- and postoperative order sets ensure that all aspects of ERAS are adhered to. With these interventions and investment by house staff and nursing we have found that with very few patient exceptions, the care that we provide to free-flap patients fulfills all 17 of the ERAS consensus recommendations.

One aspect of the ERAS pathway that has been particularly impactful to our practice is the use of perioperative multimodal analgesia. Studies have suggested that in the outpatient otolaryngology surgical setting, 75% of otolaryngology patients are prescribed excess opiate medications, and otolaryngologists wrote close to 1 million days' worth of opiate prescriptions to Medicare recipients alone in 2015.[35,36] The American Academy of Otolaryngology-Head and Neck Surgery Foundation recently published clinical guidelines on postoperative opiate prescribing practices and made a strong recommendation to avoid first-line opiates for analgesia.[37] The ERAS pathway institutes multimodal analgesia based on a combination of NSAIDs, acetaminophen, and gabapentin although the regimen varies by institution.[32] Chiu et al.[38] and Vu et al.[39] observed giving at least one dose of a non-opiate analgesic in the preoperative period significantly reduced postoperative opiate use. At our institution, we administer multimodal analgesia pre-, intra-, and postoperatively (Table 4). In our experience, multimodal analgesia reduces postoperative pain scores and morphine equivalent doses prescribed postoperatively and at discharge without increasing bleeding, emergency department visits, or readmissions.[40] Additionally we are able to avoid prescribing opiates in nearly all free-flap patients at discharge.

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.[41] Anemia is common in patients undergoing free-tissue transfer.[42,43] 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.[43,44] However, there is little literature 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.[42,43,45] Risks of transfusion include acute and delayed hemolytic reactions, blood-borne infections,

TABLE 4 A summary of the elements of a comprehensive care pathway for free-flap patients across all phases of care

Elements	Preadmission	Preoperative	Intraoperative	Postoperative
Two-team surgical approach	H&N and FPRS teams discuss extirpative and reconstructive options at tumor board conference	-	Simultaneous head and neck resection and free-flap harvest	-
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 out	-	-	Checklist led by attending before closing neck incisions	-
ERAS	Identification of patient for protocol Patient education on ERAS protocol Medical optimization visit Laboratory testing Evaluation by speech language pathologist and dietician Preoperative nursing call reminds patient to take carbohydrate drink	Carbohydrate drink 3H before anesthesia Preemptive analgesia with gabapentin 900 mg and acetaminophen 975 mg orally once before procedure Arterial line placed	Prophylactic antibiotics before incision: ampicillin and sulbactam or clindamycin and gentamycin for penicillin allergic patients Fluid warmers and forced air warming device to maintain normothermia Lidocaine/propofol induction followed by volatile anesthetic Goal-directed fluid therapy Ketorolac 30 mg and IV acetaminophen 1000 mg before completion Antiemetic prophylaxis with ondansetron 4 mg Avoid tracheostomy	Gabapentin 300 mg Q8H, celecoxib 200 mg Q12H, acetaminophen 975 mg Q8H Ketorolac 15 mg or tramadol 50 mg Q6H for breakthrough pain ICU for 48H for flap monitoring Fentanyl PCA for opioid tolerant patients with pain management consult Ferrous sulfate 325 mg Q8H, vitamin C 500 mg daily, aspirin 81 mg daily Extubate POD1 if left intubated at end of case Ambulate 5× a day and physical therapy and occupational therapy consults POD1 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.[46] TRIM was first reported when it was noted that solid organ transplant patients undergoing repeat blood transfusion demonstrated less rejection.[43,46] This process may explain the poorer oncologic outcomes for cancer patients undergoing curative-intent surgeries who receive multiple transfusions.[43,46] 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.[43] 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.[47]

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.

REFERENCES

1. Husbands JM, Weber RS, Karpati RL, et al. Clinical care pathways: decreasing resource utilization in head and neck surgical patients. *Otolaryngol Head Neck Surg*. 1999;121:755-759.
2. Ghazizadeh S, Kuan EC, Mallen-St Clair J, et al. It takes two: one resects, one reconstructs. *Otolaryngol Clin North Am*. 2017;50:747-753.
3. Garg A, Mair M, Singhavi H, et al. Adequacy of surgical margins in oral cancer patients with respect to various types of reconstruction. *South Asian J Cancer*. 2020;9:34-37.
4. Mast BA. Functional outcomes of microsurgical reconstruction of delayed complications following head and neck cancer ablation. *Ann Plast Surg*. 1999;42:40-45.
5. Liu HE. Changes of satisfaction with appearance and working status for head and neck tumour patients. *J Clin Nurs*. 2008;17:1930-1938.
6. Haddock NT, Saadeh PB, Siebert JW. Achieving aesthetic results in facial reconstructive microsurgery: planning and executing secondary refinements. *Plast Reconstr Surg*. 2012;130:1236-1245.
7. Hu J, Yin L, Tang X, Gui L, Zhang Z. Combined skeletal and soft tissue reconstruction for severe Parry-Romberg syndrome. *J Craniofac Surg*. 2011;22:937-941.
8. Parrett BM, Pomahac B, Orgill DP, Pribaz JJ. The role of free-tissue transfer for head and neck burn reconstruction. *Plast Reconstr Surg*. 2007;120:1871-1878.
9. Garg RK, Poore SO, Wieland AM, Mcculloch TM, Hartig GK. Elective free flap revision in the head and neck cancer patient: indications and outcomes. *Microsurgery*. 2015;35:591-595.
10. Brady JS, Desai SV, Crippen MM, et al. Association of anesthesia duration with complications after microvascular reconstruction of the head and neck. *JAMA Facial Plast Surg*. 2018;20:188-195.
11. Lin PC, Kuo PJ, Kuo S, Chien PC, Hsieh CH. Risk factors associated with postoperative complications of free anterolateral thigh flap placement in patients with head and neck cancer: analysis of propensity score-matched cohorts. *Microsurgery*. 2020;40:538-544.
12. Golub JS, Johns MM, 3rd, Weiss PS, Ramesh AK, Ossoff RH. Burnout in academic faculty of otolaryngology-head and neck surgery. *Laryngoscope*. 2008;118:1951-1956.
13. Bahethi RR, Gold BS, Seckler SG, et al. Efficiency of microvascular free flap reconstructive surgery: an observational study. *Am J Otolaryngol*. 2020;41:102692.
14. Lingard L, Espin S, Whyte S, et al. Communication failures in the operating room: an observational classification of recurrent types and effects. *Qual Saf Health Care*. 2004;13:330-334.
15. Lingard L, Reznick R, Espin S, Regehr G, DeVito I. Team communications in the operating room: talk patterns, sites of tension, and implications for novices. *Acad Med*. 2002;77:232-237.
16. Overdyk FJ, Harvey SC, Fishman RL, Shippey F. Successful strategies for improving operating room efficiency at academic institutions. *Anesth Analg*. 1998;86:896-906.
17. Nundy S, Mukherjee A, Sexton JB, et al. Impact of preoperative briefings on operating room delays: a preliminary report. *Arch Surg*. 2008;143:1068-1072.
18. Ibrahim A, Ndeti K, Bur A, et al. Association of a lean surgical plan of the day with reduced operating room time for head and neck free flap reconstruction. *JAMA Otolaryngol Head Neck Surg*. 2019;145:926-930.
19. Offodile AC, 2nd, Aherrera A, Wenger J, Rajab TK, Guo L. Impact of increasing operative time on the incidence of early failure and complications following free tissue transfer? A risk factor analysis of 2,008 patients from the ACS-NSQIP database. *Microsurgery*. 2017;37:12-20.
20. Ettinger KS, Arce K, Lohse CM, et al. Higher perioperative fluid administration is associated with increased rates of complications following head and neck microvascular reconstruction with fibular free flaps. *Microsurgery*. 2017;37:128-136.
21. Attaran S, John L, El-Gamel A. Clinical and potential use of pharmacological agents to reduce radial artery spasm in coronary artery surgery. *Ann Thorac Surg*. 2008;85:1483-1489.
22. Evans GRD, Gherardini G, Gürlek A, et al. Drug-induced vasodilation in an in vitro and in vivo study: the effects of nicardipine, papaverine, and lidocaine on the rabbit carotid artery. *Plast Reconstr Surg*. 1997;100:1475-1481.
23. Seth R, Badran KW, Cedars E, et al. Vasodilation by verapamil-nitroglycerin solution in microvascular surgery. *Otolaryngol Head Neck Surg*. 2021;164:104-109.
24. Hagau N, Longrois D. Anesthesia for free vascularized tissue transfer. *Microsurgery*. 2009;29:161-167.

25. Yu JT, Patel AJ, Malata CM. The use of topical vasodilators in microvascular surgery. *J Plast Reconstr Aesthet Surg*. 2011;64:226-228.
26. Ricci JA, Singhal D, Fukudome EY, Tobias AM, Lin SJ, Lee BT. Topical nitroglycerin for the treatment of intraoperative microsurgical vasospasm. *Microsurgery*. 2018;38:524-529.
27. Kerschner JE, Futran ND. The effect of topical vasodilating agents on microvascular vessel diameter in the rat model. *Laryngoscope*. 1996;106:1429-1433.
28. Gherardini G, Gürlek A, Cromeens D, Joly GA, Wang BG, Evans GR. Drug-induced vasodilation: in vitro and in vivo study on the effects of lidocaine and papaverine on rabbit carotid artery. *Microsurgery*. 1998;18:90-96.
29. Genden EM, Rinaldo A, Suárez C, Wei WI, Bradley PJ, Ferlito A. Complications of free flap transfers for head and neck reconstruction following cancer resection. *Oral Oncol*. 2004;40:979-984.
30. Every J, Subramaniam N, Dawson R, et al. Microvascular reconstruction of head and neck defects in the elderly. *ANZ J Surg*. 2021;91:969-974.
31. Shippert RD. A study of time-dependent operating room fees and how to save $100 000 by using time-saving products. *Am J Cosmet Surg*. 2005;22:25-34.
32. Dort JC, Farwell DG, Findlay M, et al. 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. *JAMA Otolaryngol Head Neck Surg*. 2017;143:292-303.
33. Chorath K, Go B, Shinn JR, et al. Enhanced recovery after surgery for head and neck free flap reconstruction: a systematic review and meta-analysis. *Oral Oncol*. 2021;113:105117.
34. Jandali DB, Vaughan D, Eggerstedt M, et al. Enhanced recovery after surgery in head and neck surgery: reduced opioid use and length of stay. *Laryngoscope*. 2020;130:1227-1232.
35. Pruitt LCC, Casazza GC, Newberry CI, et al. Opioid prescribing and use in ambulatory otolaryngology. *Laryngoscope*. 2020;130:1913-1921.
36. Svider PF, Arianpour K, Guo E, et al. Opioid prescribing patterns among otolaryngologists: crucial insights among the medicare population. *Laryngoscope*. 2018;128:1576-1581.
37. Anne S, Mims J, Tunkel DE, et al. Clinical practice guideline: opioid prescribing for analgesia after common otolaryngology operations executive summary. *Otolaryngol Head Neck Surg*. 2021;164:687-703.
38. Chiu TW, Leung CC, Lau EY, Burd A. Analgesic effects of preoperative gabapentin after tongue reconstruction with the anterolateral thigh flap. *Hong Kong Med J*. 2012;18:30-34.
39. Vu CN, Lewis CM, Bailard NS, Kapoor R, Rubin ML, Zheng G. Association between multimodal analgesia administration and perioperative opioid requirements in patients undergoing head and neck surgery with free flap reconstruction. *JAMA Otolaryngol Head Neck Surg*. 2020;146:708-713.
40. Eggerstedt M, Stenson KM, Ramirez EA, et al. Association of perioperative opioid-sparing multimodal analgesia with narcotic use and pain control after head and neck free flap reconstruction. *JAMA Facial Plast Surg*. 2019;21:446-451.
41. WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and mineral nutrition information system. World Health Organization. http://www.who.int/vmnis/indicators/haemoglobin.pdf
42. Motakef S, Mountziaris PM, Ismail IK, Agag RL, Patel A. Emerging paradigms in perioperative management for microsurgical free tissue transfer: review of the literature and evidence-based guidelines. *Plast Reconstr Surg*. 2015;135:290-299.
43. Danan D, Smolkin ME, Varhegyi NE, Bakos SR, Jameson MJ, Shonka DC, Jr. Impact of blood transfusions on patients with head and neck cancer undergoing free tissue transfer. *Laryngoscope*. 2015;125:86-91.
44. Messmer K, Lewis DH, Sunder-Plassmann L, Klövekorn WP, Mendler N, Holper K. Acute normovolemic hemodilution. *Eur Surg Res*. 1972;4:55-70.
45. Kim MJ, Woo KJ, Park BY, Kang SR. Effects of transfusion on free flap survival: searching for an optimal hemoglobin threshold for transfusion. *J Reconstr Microsurg*. 2018;34:610-615.
46. Goubran H, Sheridan D, Radosevic J, Burnouf T, Seghatchian J. Transfusion-related immunomodulation and cancer. *Transfus Apher Sci*. 2017;56:336-340.
47. McLean A, Lowe D, Rogers SN. Administration of intravenous iron and tranexamic acid in the management of postoperative iron deficiency anaemia following free flap reconstruction: re-audit. *Br J Oral Maxillofac Surg*. 2021;59:97-101.

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