Published in final edited form as:

Laryngoscope. 2021 March ; 131(3): E792–E799. doi:10.1002/lary.28768.

ERAS for Head and Neck Tissue Transfer Reduces Opioid Usage, Peak Pain Scores, and Blood Utilization

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Additional supporting information may be found in the online version of this article.

The authors have no funding, financial relationships, or conflicts of interest to disclose.

Level of Evidence: 3

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Abstract

Objectives: We implement a novel enhanced recovery after surgery (ERAS) protocol with pre-operative non-opioid loading, total intravenous anesthesia, multimodal peri-operative analgesia, and restricted red blood cell (pRBC) transfusions. 1) Compare differences in mean postoperative peak pain scores, opioid usage, and pRBC transfusions. 2) Examine changes in overall length of stay (LOS), intensive care unit LOS, complications, and 30-day readmissions.

Methods: Retrospective cohort study comparing 132 ERAS vs. 66 non-ERAS patients after HNC tissue transfer reconstruction. Data was collected in a double-blind fashion by two teams.

Results: Mean postoperative peak pain scores were lower in the ERAS group up to postoperative day (POD) 2. POD0: 4.6 ± 3.6 vs. 6.5 ± 3.5 ; $P = .004$ (POD1: 5.2 ± 3.5 vs. 7.3 ± 2.3 ; $P = .002$) (POD2: 4.1 ± 3.5 vs. 6.6 ± 2.8 ; $P = .000$). Opioid utilization, converted into morphine milligram equivalents, was decreased in the ERAS group (POD0: 6.0 ± 9.8 vs. 10.3 ± 10.8 ; $P = .010$) (POD1: 14.1 ± 22.1 vs. 34.2 ± 23.2 ; $P = .000$) (POD2: 11.4 ± 19.7 vs. 37.6 ± 31.7 ; $P = .000$) (POD3: 13.7 ± 20.5 vs. 37.9 ± 42.3 ; $P = .000$) (POD4: 11.7 ± 17.9 vs. 36.2 ± 39.2 ; $P = .000$) (POD5: 10.3 ± 17.9 vs. 35.4 ± 45.6 ; $P = .000$). Mean pRBC transfusion rate was lower in ERAS patients (2.1 vs. 3.1 units, $P = .017$). There were no differences between ERAS and non-ERAS patients in hospital LOS, ICU LOS, complication rates, and 30-day readmissions.

Conclusion: Our ERAS pathway reduced postoperative pain, opioid usage, and pRBC transfusions after HNC reconstruction. These benefits were obtained without an increase in hospital or ICU LOS, complications, or readmission rates.

Keywords

Enhanced recovery after surgery; ERAS; head and neck cancer; free tissue transfer; total intravenous anesthesia; restricted blood transfusion

INTRODUCTION

Head and neck cancer (HNC) is the ninth most common cancer in the United States with an estimated 117,480 new cases diagnosed annually.^{1,2} Patients with advanced HNC often require both tumor resection and free or regional tissue transfer reconstruction with or without skin grafting, tracheostomy, and enteral tube placement. Modern reconstructive techniques improve functional and aesthetic outcomes but are complex, time intensive, and expensive. As such, patients incur significant acute and long-term morbidity from them.³⁻⁸ Improving the tolerability of these surgeries would positively affect patient experience.⁹

Enhanced recovery pathways (ERPs) were first described over 20 years ago.¹⁰ These approaches combine several interventions to improve peri- and intraoperative stressors to

reduce pain and morbidity while promoting an early return to function. The first formal protocol was released by the Enhanced Recovery After Surgery (ERAS) Society in 2012 for colorectal surgery.¹¹ A HNC pathway was introduced in 2017 by the ERAS Society.¹²

Studies investigating the effects of ERAS protocols in patients who undergo HNC tissue transfer reconstruction are limited and outcomes vary.^{12,13} The aim of this initiative was to implement a standardized, multi-disciplinary peri- and intraoperative protocol founded on evidence based practices to improve patient comfort, reduce morbidity, and accelerate recovery after surgery. We hypothesized that our protocol would decrease opioid utilization, peak pain scores, and blood utilization.^{14,15}

MATERIALS AND METHODS

Study Population

Under a protocol approved by the Institutional Review Board at the University of Southern California (USC), we conducted a retrospective cohort study of patients undergoing HNC surgery with tissue transfer reconstruction from August 2018 to October 2019. One hundred and thirty-two consecutive patients were enrolled in ERAS. For comparison purposes, we retrospectively included 66 consecutive patients from July 2017 to July 2018 who received the same procedure at our institution but did not follow a formal recovery program (non-ERAS). All patients were operated upon by one of four microvascular trained otolaryngologists at Keck Medical Center of USC. Operating suites, intensive care units (ICU), and surgical wards were the same between the two groups.

All subjects were over the age of 18 and underwent free tissue transfer or pedicled flap reconstruction for major HNC defects in between July 2017 and October 2019. Pregnancy was an exclusionary criterion. Patients with prior exposure to opioids and those who required patient-controlled anesthesia (PCA) after surgery were included.

ERAS Protocol

The departments of otolaryngology, anesthesiology, and nursing at Keck Medical Center of USC created an ERAS protocol. Please refer to Figure 1 for a summary of the protocol. Gabapentin dosage was adjusted for age (patients older than 70 years were given 100 mg every 8 hours). Celecoxib dosage was halved for patients with cirrhosis defined as Child-Pugh Class B or greater and avoided in patients with sulfa drug allergy or history of coronary artery disease. Anesthesiologists delivered total intravenous anesthesia (TIVA). Methadone was given during induction due to its long half-life and activity at both the opioid and NMDA receptor. Liposomal bupivacaine (1.3% 260 mg total) was injected at both the flap and skin graft harvest sites prior to closure and before grafting, respectively, to further mitigate postoperative pain. Vasoactive agents such as dopamine, dobutamine, and norepinephrine were used to limit packed red blood cell (pRBC) transfusions. Volume administration was capped at 5 L total. With the exception of patients who were kept intubated for airway protection, every opportunity was taken to wake the patient and discontinue ventilator dependence at the end of surgery.

Compliance was ensured through the use of standardized order sets and weekly inter-departmental ERAS meetings comprised of surgeons, anesthesiologists, nursing supervisors and dedicated hospital ERAS personnel. ERAS patients wore specially colored wristbands throughout their hospitalization and ERP specific signs were posted on doors and in rooms. Supplemental documents used to educate patients and clinical providers to promote compliance can be reviewed online (see Supporting Information, Appendix 1–3, in the online version of this article).

All ERAS patients after discharge were prescribed acetaminophen 650 mg every 6 hours and celecoxib 200 mg twice daily for 1 week. They also received a 3-week long gabapentin taper (300 mg thrice daily for 1 week, 300 twice daily for the second week, and 300 daily for the third week) and a prescription for tramadol 50 mg to be taken every 6 hours for breakthrough pain for up to 5 days.

Non-ERAS Protocol

Immediately before surgery, similar to ERAS, all patients received 325 mg of oral aspirin. Arterial lines were placed in all patients. Fluid, blood, and vasoactive products were given intra-operatively at the discretion of the anesthesiologist. To minimize flap complications in the ICU, systolic blood pressure was closely maintained between 110 mm and 160 mm of mercury with the use of crystalloids, colloids, and vasoactive agents. Thromboembolic prophylaxis was started 1 day after surgery with aspirin 81 mg and 40 mg enoxaparin daily.

Patients were transferred to an intermediate, non-ICU unit after they were no longer ventilator dependent. Indwelling catheters and invasive lines were removed at the discretion of the primary team. Blood products were administered if hemoglobin (Hg) was less than 10 grams per deciliter (g/dL). Enteral nutrition commenced when patients expressed hunger. Prophylactic broad-spectrum antibiotics were given for a minimum 7 days.

Postoperative pain was controlled with opioids. Morphine or hydromorphone PCAs were typically used during the immediate postoperative period. Oral and parenteral opioid medications were given at varying doses to treat moderate and severe pain. Intravenous morphine was used to control breakthrough pain. Non-opioid adjuncts were not used routinely. Patients in the non-ERAS path-way were not discharged on a standardized pain regimen. Commonly used home medications in this population included hydrocodone, hydrocodone-acetaminophen, and oxycodone.

Fit to Discharge Criteria

All patients were deemed fit for discharge using the same criteria. All surgical sites were considered stable or well healing by the primary team. The patient was afebrile, tolerating a diet, and pain was controlled with oral medications. Both occupational and physical therapists assessed each patient and determined final discharge disposition. Surgeons and nurses provided education on wound, tracheostomy, and feeding tube care where applicable. Patients or their caretakers demonstrated expertise in these areas. Facility placement, home health supplies and visiting nursing care were arranged as necessary. All patients received follow-up appointments with their HNC surgeon within 1 week of discharge.

Data Collection

Patient characteristics, surgical variables, and clinical outcomes were anonymized and collected from electronic medical records in a double-blind fashion by two data entry personnel teams. Each team's identity was concealed from the other. Both teams collected the same data for identical patient sets. Their collected data was compared against each other for discrepancies. Discrepancies were reviewed and settled by a third party. Any missing values left after corrections were filled using forward-fill or group mean-fill imputation methods. All outliers were checked and included in statistical analysis.

We assessed pain using the critical care pain observation tool and the numeric rating scale. These methods are validated, sensitive, and reliable methods of assessing pain.^{16,17} Education on pain measurement and administration of analgesics was provided to nursing staff during weekly interdepartmental meetings and reinforced during shift changes. All patients recovered in the same intensive care unit and otolaryngology-specific surgical step-down unit. This universality in postoperative care helped minimize variation in assessment protocols.

Opioid requirements were converted to morphine milligram equivalents (MME) via previously published methods.¹⁸ To avoid overestimation, the lowest conversion ratios were used. Complications were divided into the following categories: flap compromise, wound (dehiscence, fistula, partial or total skin graft loss, and gastrostomy tube complication), cardiopulmonary (stroke, myocardial infarction, unplanned intubation, or tracheostomy), infectious (UTI, sepsis, pneumonia), and hematologic (deep vein thrombosis, hematoma, hemorrhage).

Study data was collected and managed using REDCap electronic data capture tools hosted at USC (National Institutes of Health grant UL1TR001855).^{19,20} REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies.

Outcomes

Primary outcomes for this study were postoperative mean peak pain scores, MME intake, and blood transfusion rates. Secondary outcomes included overall hospital LOS, ICU LOS, complication rates, and 30-day readmission rates.

Statistical Analysis

Appropriate study sample size was determined to provide 80% power at a two-sided *t*-test with a significance level of .05. An assumption of an effect size of an individual outcome was based on two available directly comparable studies.^{12,13} A group assignment ratio of 1:2 was chosen to reach power. All numerical variables were evaluated for the normality of distribution. Central tendency for numerical variables was expressed as mean $\pm$ standard deviation or median and first and third quartile, depending on the distribution. Student's *t*-test was used to compare normally distributed variables in ERAS and non-ERAS groups. The Chi-square test, set at a 95% confidence interval, was used for categorical data. Non-parametric data was analyzed with the Mann–Whitney *U* test. When more than four

parameters required comparison, the Holm-Bonferroni correction for multiple comparisons was employed.²¹ Descriptive statistics were used for parameters not included in primary or secondary outcomes and for exploratory analyses. All calculations were performed using Python 3.7 libraries StatsModels and SciPy.^{22,23} Significance was set at adjusted $P = .05$.

RESULTS

One hundred ninety-eight patients met our study criteria. One hundred thirty-two patients in the ERAS pathway were compared to 66 patients in the non-ERAS pathway. Characteristics of the study population are shown in Table I. There were no demographic differences among the two cohorts. Oncologic features were similar in both groups; this is shown in Table II.

Primary outcomes are shown in Table III, all are statistically significant ($P = .05$). Both postoperative pain scores and opioid use were lower for the ERAS group. Postoperative mean peak pain scores were significantly lower in the ERAS group up to postoperative day 2 when compared to the non-ERAS group. On each POD up to 5 days, ERAS patients required fewer opioids than non-ERAS patients. The differences in MME administration were significant (POD 0 adjusted $P = .010$, POD 1–5 adjusted $P = .000$). The mean pRBC transfusion rate was higher in the non-ERAS group, 3.1 vs. 2.1 units in the ERAS group. This also reached statistical significance (adjusted $P = .017$). Subgroup analysis of patients who used PCAs or had prior exposure to opioids revealed significant decreases in opioid and pRBC consumption (Table IV, online supplemental).

Secondary outcomes are shown in Table V. Mean hospital LOS did not differ between groups (adjusted $P = .878$). Postoperative mean ICU LOS was 58.08 ± 43.3 and 40.85 ± 30.5 hours in the non-ERAS and ERAS group respectively (adjusted $P = .630$). Surgical complication rates were similar between the two groups. The most common surgical complication in both groups was related to surgical wound healing. Thirty-day readmission rates were not statistically different either between groups (adjusted $P = 1.000$).

DISCUSSION

ERAS is a multimodal pathway that combines several interventions to improve patient comfort and hasten recovery. It was first tested in colorectal surgery in the late 1990s. Literature from other surgical disciplines shows ERAS patients have decreased hospital stays, pain scores, medical complications, and readmissions after discharge.^{24–29} Decreased costs are an additional benefit.^{30,31} As physicians shoulder increasing pressure to improve healthcare effectiveness, efficiency, and cost, these protocols are gaining popularity in HNC surgeries. However, implementation for HNC in the United States has been slow.^{12,13}

In this study, we initiated an ERAS pathway for patients who underwent HNC reconstruction surgery with tissue transfer surgery. A common criticism of these ERPs is that they are complicated and challenging to execute. The official protocol outlined by the ERAS society includes 17 interventions with 24 additional recommendations.³² Extensive ERP education was provided to clinical staff and patients both before and after surgery. We were able to ensure adherence using a simplified protocol that emphasized the use of opioids as a last resort, early mobilization, and early enteral feeding. Using visual aids, including

brightly colored wristbands and signs in patient rooms, allowed for easy identification of ERAS patients.

The intraoperative component of our protocol is unique for a variety of reasons. ERAS patients exclusively received TIVA because it achieves deep plane anesthesia with reduced risk of postoperative nausea and emesis. Immediate extubation after tissue transfer surgery decreases ICU LOS and reduces medical complications.^{33,34} Furthermore, a growing body of evidence shows volatile anesthetic usage, when compared to TIVA, is associated with greater mortality in patients with solid tumor cancers independent of ASA score, surgical severity, or presence of distant metastases.^{35,36} Our protocol is also the first to describe the use of methadone during HNC surgery. Intraoperative methadone decreases postoperative pain, opioid usage, and improves patient quality of life.³⁷

Expected pain is a major cause of presurgical stress and an independent predictive variable of postoperative pain in otolaryngology patients.³⁸ Improving pain control through the use of standardized treatment guidelines increases patient satisfaction.³⁹ A 2007 systematic review showed the prevalence of pain among HNC patients is 70%.⁴⁰ Pain intensity is highest on the day after surgery and decreases on subsequent days.⁴¹ We found the same was true in our patients, irrespective of ERAS or non-ERAS status. When compared to non-ERAS, our multimodal interventions resulted in significantly lower post-operative mean peak pain scores.

Analgesia selection matters. The economic burden of opioid misuse is estimated at \$78.5 billion annually.⁴² The prevalence of persistent opioid use after HNC surgery is as high as 41% of patients develop long-term opioid dependence after oral cavity resections.^{43,44} In our ERAS protocol, opioids were used as a last resource when all other methods of analgesia were exhausted. Regional anesthesia such as liposomal bupivacaine, acetaminophen, NSAIDs, gabapentinoids, and tramadol are safe and effective analgesic alternatives to opioids.⁴⁵ We show patients on ERAS required significantly fewer opioids immediately after HNC reconstruction. Preoperative opioid usage was also similar in both cohorts and therefore not a confounder in these results. Perioperative opioid intake is a known modifiable risk factor in the development of long-term opioid dependence.^{46,47} Our ERAS program reduced opioid usage during hospitalization, irrespective of prior opioid exposure or PCA usage, without compromising pain control.

Finally, we enforced a restrictive transfusion criteria during and after surgery by liberally using vasopressors known to improve flap flow. pRBCs were given on a unit-by-unit basis for Hg concentration less than 7 g/d with interval reevaluation. Standard practice has been to transfuse to a goal Hg greater than 10 g/dL with the expectation that liberal transfusion improves tissue oxygenation. Newer studies question this dogma. Blood transfusions are an independent risk factor for increased postoperative morbidity including wound infections, thrombosis, and even HNC recurrence.^{48–50} Of note, there appears to be a dose-related relationship in these findings. Patients who receive three or more units of red blood cells have increased risk of death after major reconstructive surgery for HNC.^{51,52} ERAS patients in our study received significantly fewer transfusions than those in the traditional pathway.

The changes in our intraoperative protocol did not increase complication rates or 30-day readmissions after discharge in our ERAS patients compared to traditional surgery.

Routine ICU admission and prolonged mechanical ventilation after HNC reconstruction surgery is an area of debate. New studies show avoiding or decreasing ICU care after surgery reduces hospital LOS without increasing complication rates.^{53,54} At our institution, ERAS patients are routinely taken off of mechanical ventilation after surgery is completed and transferred to the ICU “awake” for hourly Doppler and visual flap checks for at least the first 24 hours after surgery. From there, they move to an intermediate, non-ICU unit to receive care by nurses who specialize in otolaryngology. Yu et al. recommend immediate transfer after tissue transfer reconstruction to such a unit but this is not feasible in our hospital.⁵⁵ Average ICU LOS decreased from nearly 2 days to just over 1 day after initiation of ERAS. Reasons for prolonged ICU stays in the non-ERAS population are attributed to increased time on a mechanical ventilator, prolonged need for central line monitoring and delayed initiation of postoperative nutrition and mobilization. Shortened ICU stays were not associated with increased complication rates in the ERAS group. To our knowledge, this is the first study to demonstrate decreased ICU LOS as a benefit of using ERAS in HNC reconstruction surgery. Though we did not examine the difference in healthcare costs between groups, others have shown avoiding ICU care reduces costs of free flap surgery.⁵⁶

There are limitations to this study. We examined a heterogeneous patient population and applied the same ERAS protocol to all regardless of medical comorbidities, tumor type, or planned reconstructive surgery. It is well known that the morbidity of laryngeal malignancy is different from a cutaneous or paranasal one. Though the differences lacked statistical significance, we had an asymmetric distribution of laryngeal cancer and pedicled flaps patients in our ERAS and non-ERAS populations. The likelihood of tracheostomy, long-term enteral tube feeding, skin grafting, postoperative pain, and hospitalization rates varied in our HNC population due to differences in surgical morbidity. These factors influenced the complexity of care, opioid usage patterns, the likelihood of complications, the length of hospitalization, and the costs of care. This is one explanation for why the over-whelmingly positive outcomes seen in other specialties after initiation of ERAS have not been replicated in HNC reconstructive surgery. Multicenter trials are necessary to examine a homogeneous oncologic population, to allow for large group comparisons of the effects of ERAS on specific HNC and flap subtypes. Additional prospective studies are needed to analyze the impact of ERAS on post-discharge complications and cancer recurrence rates, especially when utilizing TIVA.

CONCLUSION

ERAS for head and neck reconstruction decreases postoperative pain and opioid utilization better than traditional regimens without increasing hospital length of stay, complications, or readmission rates. We are the first to utilize an intra-operative protocol that included TIVA, methadone, and restricted pRBC transfusion, with preoperative loading of non-opioid analgesics. We show for the first time ERAS specifically reduces red blood cell utilization, mean peak pain scores and the need for opioids after surgery in this population. These

clinical outcomes can be used to minimize morbidity, optimize resource utilization, mitigate costs, and improve patient satisfaction after HNC reconstructive surgery.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Summary of Enhanced Recovery After Surgery Pathway				
Preoperative Assessment: Patient listed as an "ERAS Patient" by scheduling ERAS education, verbal and written, provided to patient Preop assessment 2 weeks before surgery for baseline labs and studies Nutrition optimization Speech language therapist evaluation Pre-habilitation with physical and occupational therapist, encourage 30 minutes of exercise a day Smoking, alcohol, and drug cessation reinforced Begin oral pain regimen three days before surgery: • Gabapentin 300 mg every 8 hours daily • Celecoxib 200 mg every 12 hours • Tylenol 1000 mg every 8 hours daily Night before surgery, patient is reminded to have high carbohydrate drink 3 hours before to surgery	Day of Surgery: 3 hours before surgery, patient drinks high carbohydrate beverage No prolonged fasting. Clear liquids permissible up to 3 hours before surgery "ERAS Patient" armband will be worn by patient for duration of hospitalization Chronic pain patients take all home medications as scheduled Oral pain medication on day of surgery: • Gabapentin 300 mg • Celecoxib 200 mg • Tylenol 1000 mg • Aspirin 325 mg Obtain type and screen Follow perioperative antibiotic dosing recommendations	Intraoperative Management: Warm patient Regional block with liposomal bupivacaine injection to donor site Induction with IV lidocaine 0.5-1 mg/kg bolus, ketamine 0.5 mg/kg bolus, methadone 10 mg push, dexamethasone 4 mg, and magnesium sulfate Maintenance with propofol, dexmedetomidine, and ketamine. Avoid volatile anesthetics. Arterial line placement on case-by-case basis. Avoid central venous catheters Goal directed fluid restriction, aim to deliver < 5 L fluids Vasoactive agents used liberally to restrict need for blood transfusions Goal hemoglobin > 7g/dL Glucose goal between 110-180. Hourly checks. Emergence goal is a lucid patient in the operating room who does not require ventilator support	Immediate Postoperative Care: ICU for hourly flap and tracheostomy care. Signs on door and above pain patient say "ERAS Patient" Use standard post-operative ERAS order set Restart home medications Labs upon arrival to ICU (CBC, BMP, Mag, Phos, TSH). Daily chest-xray if ventilator dependent. No blood pressure parameters for flap viability Around the clock analgesia: • Acetaminophen 650 mg every 6 hours • Gabapentin 300 mg every 8 hours • Celecoxib 200 mg every 12 hours Additional analgesia as needed: • Tramadol 50 mg every 6 hours for moderate pain (3 - 6 / 10 pain scale) • Tramadol 100 mg every 6 hours as needed for severe pain (7 - 10 / 10 pain scale) • Morphine 2 mg IV every 3 hours for breakthrough pain Discontinue prophylactic antibiotics 24 hours after surgery Start gastrointestinal prophylaxis	Extended Postoperative Care: Evaluate and discontinue lines and drains on a daily basis Continue care in otolaryngology specific step-down unit Introduce aspirin 81 mg and enoxaparin 40 mg daily 24 hours after surgery Begin dietician guided enteral diet 24 hours after surgery and advance as tolerated. Swallow assessment with oral nutrition if appropriate Senna 8.6 mg every 12 hours Continue same ICU analgesia regimen Early mobilization with physical and occupational therapy Cast removal on postop day 5 for radial forearm and postop day 7 for fibula free flap donor sites Discharge planning starting postop day 5

Fig. 1. ERAS Protocol. Panel A: preoperative assessment. Panel B: day of surgery. Panel C: intraoperative management. Panel D: immediate postoperative care. Panel E: extended postoperative care. ERAS = enhanced recovery after surgery. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

Patient Demographics.

TABLE I.

	ERAS (n = 132)	Non-ERAS (n = 66)	P-value	Adjusted P-value
Mean age (years)	64.7 (SD 12.9)	60.7 (SD 13.4)	.03	.7
Male gender	52 (39%)	35 (53%)	.37	1.0
History of smoking	81 (61%)	31 (47%)	.37	1.0
History of alcohol use	71 (54%)	34 (52%)	.96	1.0
History of prior opioid use	56 (42%)	34 (52%)	.61	1.0
Mean BMI (kg/sq.m)	24.8 (SD 5.5)	26.0 (SD 6.9)	.16	1.0
Coronary artery disease	10 (8%)	9 (14%)	.32	1.0
Coronary kidney disease	12 (9%)	3 (5%)	.44	1.0
Diabetes	28 (21%)	8 (12%)	.27	1.0
Congestive heart failure	2 (2%)	3 (5%)	.44	1.0
History of H&N irradiation	48 (36%)	20 (31%)	.78	1.0
History of chemotherapy use	25 (19%)	20 (31%)	.21	1.0
Mean ASA score	2.8 (SD 0.5)	2.8 (SD 0.5)	.41	1.0
Mean length of surgery (min)	436.8 (SD 137.8)	466.1 (SD 121.9)	.18	1.0

Adjusted *P* .05 considered significant.

BMI = body mass index; ERAS = enhanced recovery after surgery; H&N = head and neck; SD = standard deviation.

TABLE II.**Oncologic Characteristics.**

	ERAS (n = 132)	Non-ERAS (n = 66)	P-value	Adjusted P-value
Primary lesion site				
Oropharynx	25 (19%)	15 (23%)	.73	1.0
Oral	74 (56%)	40 (61%)	.86	1.0
Cutaneous	12 (9%)	5 (8%)	.96	1.0
Lateral skull base	2 (2%)	2 (3%)	.86	1.0
Paranasal sinuses	4 (3%)	3 (5%)	.90	1.0
Larynx	14 (11%)	0 (0%)	.02	.7
Donor site				
Pedicled flaps	14 (10.6%)	1 (1.5%)	.065	1.0
Fibula	27 (20%)	16 (24%)	.74	1.0
Radial forearm	53 (40%)	39 (59%)	.16	1.0
ALT	35 (27%)	9 (14%)	.14	1.0
Latissimus dorsi	2 (2%)	0 (0%)	.81	1.0
T Stage				
T1	5 (4%)	T1	.26	1.0
T2	23 (17%)	T2	.45	1.0
T3	29 (22%)	T3	.90	1.0
T4	43 (33%)	16 (24%)	.47	1.0
N Stage				
N0	0.38 (50)	29 (44%)	.67	1.0
N1	0.08 (10)	6 (9%)	.94	1.0
N2	0.12 (16)	12 (18%)	.43	1.0
N3	0.14 (18)	9 (14%)	.84	1.0
NX	0.27 (36)	9 (14%)	.14	1.0
M stage				
M0	0.80 (106)	59 (89%)	.74	1.0
M1	0.05 (6)	0 (0%)	.20	1.0
MX	0.13 (17)	6 (9%)	.65	1.0

Adjusted P .05 considered significant.

ERAS = enhanced recovery after surgery.

TABLE III.

Primary Outcomes.

	ERAS (n = 132)	Non-ERAS (n = 66)	P-value	Adjusted P-value
Mean peak pain score				
POD 0	4.6 (S.D. 3.6)	6.5 (S.D. 3.5)	.0001	.0046**
POD 1	5.2 (S.D. 3.5)	7.3 (S.D. 2.3)	.0000	.0018**
POD 2	4.1 (S.D. 3.5)	6.6 (S.D. 2.8)	.0000	.0002**
POD 3	4.1 (S.D. 3.6)	6.1 (S.D. 3.2)	.0039	.1326
Mean opioid consumption (MME)				
POD 0	6.0 (S.D. 9.8)	10.3 (S.D. 10.8)	.0003	.0114**
POD 1	14.1 (S.D. 22.1)	34.2 (S.D. 23.2)	.0000	.0000**
POD 2	11.4 (S.D. 19.7)	37.6 (S.D. 31.7)	.0000	.0000**
POD 3	13.7 (S.D. 20.5)	37.9 (S.D. 42.3)	.0000	.0002**
POD 4	11.7 (S.D. 17.9)	36.2 (S.D. 39.2)	.0000	.0000**
POD 5	10.3 (S.D. 17.9)	35.4 (S.D. 45.6)	.0000	.0000**
Total opioid consumption (MME)	134.0 (S.D. 264.4)	361.9 (S.D. 467.7)	.0000	.0000**
Mean pRBC consumed	2.1 (S.D. 2.6)	3.1 (S.D. 2.3)	.0005	.0173**

Adjusted *P* .05 considered significant.

ERAS = enhanced recovery after surgery; MME = morphine milligram equivalent; POD = postoperative day; pRBC = packed red blood cells; SD = standard deviation.

TABLE IV.
Primary Outcomes in Patients with Prior Opioid Usage or Patient-Controlled Anesthesia.

	ERAS (n = 53)	Non-ERAS (n = 33)	P-value	Adjusted P-value
Mean peak pain score				
POD 0	5.4 (SD 3.5)	6.6 (SD 3.8)	.0141	.1287
POD 1	5.8 (SD 3.4)	7.7 (SD 2.4)	.0048	.0516
POD 2	4.7 (SD 3.6)	7.2 (SD 2.7)	.0012	.0181**
POD 3	5.2 (SD 3.7)	6.9 (SD 2.9)	.0543	.3235
Mean opioid consumption (MME)				
POD 0	7.2 (SD 12.3)	12.0 (SD 11.4)	.0035	.0451**
POD 1	18.5 (SD 28.9)	40.6 (SD 28.2)	.0000	.0001**
POD 2	17.9 (SD 26.5)	48.0 (SD 34.7)	.0000	.0001**
POD 3	21.5 (SD 27.0)	51.7 (SD 49.7)	.0012	.0181**
POD 4	18.1 (SD 23.7)	46.4 (SD 44.7)	.0007	.0104**
POD 5	17.1 (SD 24.6)	46.3 (SD 44.0)	.0001	.0025**
Total opioid consumption (MME)	213.5 (SD 383.0)	505.5 (SD 596.5)	.0000	.0001**
Mean pRBC consumed	2.3 (SD 2.4)	3.3 (SD 2.4)	.0005	.0044**

Adjusted *P* .05 considered significant.

ERAS = enhanced recovery after surgery; MME = morphine milligram equivalent; POD = postoperative day; pRBC = packed red blood cells; SD = standard deviation.

TABLE V.

Secondary Outcomes.

	ERAS (n = 132)	Non-ERAS (n = 66)	P-value	Adjusted P-value
Mean hospital LOS (hours)	229.09 (SD 147.03)	285.08 (SD 349.32)	.070	.878
Mean ICU LOS (hours)	40.85 (SD 30.51)	58.08 (SD 43.33)	.033	.630
Mean ventilation (hours)	9.3 (SD 29.2)	14.6 (SD 22.3)	.000	.001**
Mean central line time (days)	0.1 (SD 0.6)	1.7 (SD3.9)	.000	.000**
Time with urinary catheter (days)	1.8 (SD 2.0)	2.0 (SD 2.9)	.115	.959
Time to nutrition (hours)	30.4 (SD 23.4)	55.1 (SD56.1)	.000	.000**
Time to mobilization (hours)	55.6 (SD 43.9)	93.4 (SD 63.9)	.000	.003**
Complications				
Flap compromise	5 (4%)	2 (3%)	.900	1.000
Wound	44 (33%)	19 (29%)	.768	1.000
Cardiopulmonary	4 (3%)	1 (2%)	.802	1.000
Infectious	30 (23%)	15 (23%)	.900	1.000
Hematologic	12 (9%)	5 (8%)	.919	1.000
30-Day readmissions	32 (24%)	10 (15%)	.353	1.000

Adjusted *P* .05 considered significant.

ERAS = enhanced recovery after surgery; ICU = intensive care unit; LOS = length of stay; SD = standard deviation.