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ORIGINAL ARTICLE – HEAD AND NECK ONCOLOGY

Enhanced Recovery After Surgery (ERAS) in Head and Neck Oncologic Surgery: A Case-Matched Analysis of Perioperative and Pain Outcomes

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ABSTRACT

Background. Enhanced recovery after surgery (ERAS) pathways are well established in certain surgical specialties because findings have shown significant improvements in outcomes. Convincing literature in head and neck cancer (HNC) surgery is lacking. This study aimed to assess the effect of an ERAS pathway on National Surgical Quality Improvement Program (NSQIP)-based occurrences and pain-related outcomes in HNC surgery.

Methods. The study matched 200 patients undergoing head and neck oncologic surgery on an ERAS pathway between 1 March 2016 and 31 March 2019 with control subjects (1:1 ratio) during the same period. Demographic and perioperative data collected from the NSQIP database were extracted. Pain scores and medication usage were electronically extracted from our electronic medical record system and compared. Risk factors for high opioid usage also were assessed.

Results. Both groups were statistically similar in baseline characteristics. The ERAS group had fewer planned intensive care unit (ICU) admissions (4% vs. 14%; $p < 0.001$), a shorter mean hospital stay (7.2 ± 2.3 vs. 8.7 ± 4.2 days; $p < 0.001$), and fewer overall complications (18.6% vs. 27.0%; $p = 0.045$). Morphine milligram equivalent requirements over 72 h were significantly reduced during 72 h in the ERAS group (138.8 ± 181.5 vs. 207.9 ± 205.5; $p < 0.001$). In the multivariate analysis, the risk factors for high opioid analgesic usage included preoperative opioid usage, age younger than 65 years, race, patient-controlled analgesia use, and ICU admission.

Conclusion. The study findings showed that ERAS in HNC surgery can result in improved outcomes and resource use, and that these results are sustainable. The outcomes described in this report can be further used to optimize ERAS pathways.

Enhanced recovery after surgery (ERAS) protocols are widespread in fields such as colorectal surgery,[1] hepatobiliary surgery,[2] and thoracic surgery.[3] The concept of enhanced recovery, conceived more than 20 years ago, focuses on optimizing and standardizing perioperative aspects of care in a bid to improve patient outcomes.[4] This is achieved through principles such as patient education, goal-directed fluid therapy (GDFT), multimodal analgesia (MMA), and early mobilization, among others.[5]

Over time, the cited studies and others have shown impressive outcomes after implementation of ERAS such as reduced complication rates and shorter hospital length of

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stay (LOS). Furthermore, ERAS pathways have been shown to reduce opioid usage, which is especially relevant in light of the recent opioid crisis in America.[6]

Head and neck oncologic surgeries with free-tissue transfer reconstruction are considered high-acuity cases with the potential for significant morbidity.[7] As such, these surgeries are ideally suited for perioperative standardization with an ERAS protocol and offer the potential for considerable improvement in outcomes.

Dort et al.[8] published a consensus review and recommendations from the International ERAS Society for head and neck surgery, discussing the evidence for various pre-, intra-, and postoperative interventions.[8] Since then, several other series have been published, but this area remains plagued by small sample sizes, variations in intervention, and limited outcome measurements.[9–11] The largest head and neck study before the current study, with 144 patients on an ERAS pathway, also failed to show any difference in complication rate or LOS.[12]

At the University of Texas MD Anderson Cancer Center (UTMDACC), the Head and Neck Surgery and Plastics Reconstructive Surgery Departments collaborated to develop a head and neck/reconstructive surgery ERAS (HNRS-ERAS) pathway, adhering to the aforementioned principles. Since June 2017, all head and neck oncologic surgeries with free-flap reconstruction have been enrolled on the pathway. We analyzed a case-matched cohort of 400 patients, comparing perioperative outcomes derived from the Head and Neck-Reconstructive Surgery (HNRS) National Surgical Quality Improvement Program (NSQIP) database. This platform was built on traditional NSQIP, including procedure- and disease-specific metrics with 100% capture of head and neck ablative surgeries requiring free-tissue transfer reconstruction.[7] The secondary outcomes included pain scores, opioid usage, and risk factors for high opioid usage postoperatively. To our knowledge, this is the largest and most comprehensive outcome analysis to date on ERAS in the field of head and neck oncologic surgery.

METHODS

This study was approved by the Institutional Review Board (PA17-1001) and conducted according to the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) initiative. A control group of 200 patients who underwent head and neck oncologic surgery with major-flap reconstruction between March 2016 and April 2017 was used. Electronic medical records (EMR) were not available for patients before this date, limiting the size of the control group. These cases then were matched 1:1 based on age, surgery type, and flap type to patients on the HNRS-ERAS pathway between June 2017 and March 2019. These factors were selected because they had previously been shown in unpublished data to affect outcomes such as LOS. Only patients undergoing surgery for oncologic reasons were included in the study. Patients undergoing surgery for infection or osteoradionecrosis were excluded.

HNRS-ERAS Pathway

The key components of the HNRS-ERAS pathway are preoperative patient education by a dedicated clinic nurse, pre-medication before anesthesia, GDFT, avoidance of intensive care unit (ICU) admission where medically suitable, postoperative MMA, early mobilization, and early removal of urinary catheter. Specifically, the preoperative medications administered just before surgery were celecoxib 400 mg, tramadol extended release 300 mg, and gabapentin 300 mg, whereas the postoperative MMA regimen was a scheduled combination of the celecoxib 200 mg every 12 h, gabapentin 100 mg three times daily, and tramadol 50 mg every 6 h. A detailed overview of the HNRS-ERAS pathway is included in the Supplemental Material.

Data Collection

Patient demographics, comorbidities, and objective outcomes including complication rate, LOS, unplanned return to the operating room (URTOR), and readmission rates were derived from captured data in the Head and Neck-Reconstructive Surgery NSQIP (HNRS-NSQIP) database of UTMDACC. As a surrogate composite index of comorbidities, the Modified Frailty Index (MFI-5) score was calculated for each patient. Our specialized HNRS-NSQIP database is derived from the American College of Surgeons (ACS) NSQIP methods. The outcomes, collected by a NSQIP-trained surgical clinical reviewer, are specific and comprehensive for major head and neck oncologic surgery.[7]

We also electronically retrieved outcomes related to pain and medication usage from the institutional EMR. Preoperative opioid usage, pain management team visits, pain scores in the postanesthesia care unit (PACU) on postoperative day (POD) 1, POD3, and day of discharge were obtained.

The pain scores were recorded in the EMR during the patient's hospital stay by nursing staff using an 11-point numeric rating scale (NRS) ranging from 0 (no pain) to 10 (most severe pain). The 24-h mean pain score then was calculated for the respective days.

We also tracked patient-controlled analgesia (PCA) usage and morphine milligram equivalent (MME) dose

within 72 h postoperatively, including all opioid analgesics administered via intravenous, transdermal, and oral routes. Patient-controlled analgesia was not routinely provided to all patients but prescribed based on needs and pain scores postoperatively. High opioid analgesic usage was defined as an MME of 180 mg or more during 72 h because the Federal Drug Administration (FDA) defines a patient as opioid-tolerant if the oral morphine intake is at least 60 mg/day.[13]

Discharge analgesic prescriptions also were recorded, with mild opioid prescriptions and strong opioid prescriptions differentiated for the purposes of analysis. Strong opioids include schedule 1 and 2 drugs as defined by the World Health Organization (WHO) analgesic ladder[14] and the United States Drug Enforcement Administration (DEA),[15] whereas weak opioids include tramadol and codeine, which are schedule 3 and 4 drugs.[15] Time spent in the PACU, planned ICU admissions from the operating room, and data on compliance with HNRS-ERAS interventions also were collected.

Statistical Analysis

To correct for potential confounders, each patient in the control group was matched (1:1 ratio) to a patient in the ERAS group using exact matching based on age (within a 5-year age range), surgery type (cutaneous or mucosal), and flap type (soft tissue, osseous, or multiple).

Descriptive statistics such as means, standard deviations, medians, and ranges were used as appropriate. Pearson's Chi square and Fisher's exact tests were used to examine associations between treatment groups and categorical variables, and the Wilcoxon rank-sum test was used for continuous variables. To analyze risk factors for high opioid usage postoperatively, uni- and multivariable logistic regression using a backward selection method was applied to fit the most parsimonious multi-variable model. Imputation of missing data was not performed. A p value lower than 0.05 was considered statistically significant. The analyses were performed using IBM SPSS v24 (IBM Corp, Armonk, NY, USA).

RESULTS

Demographics

The study identified enrolled 200 patients in the control group and 602 patients in the ERAS group. After matching, the demographics and outcomes of 400 patients (200 matched pairs) were analyzed. Both groups were similar in terms of all baseline characteristics, with no statistically significant difference in functional status, comorbidities, MFI-5 index, prior treatment (radiotherapy or surgery), wound class, or American Society of Anesthesiologists (ASA) classification (Table 1). The incidence of hypertension was higher in the control group (55%) than in the ERAS group (47%), but this difference did not reach statistical significance ($p = 0.089$).

Perioperative Outcomes

The comparison of outcomes (Table 2), showed that the ERAS group had fewer postoperative planned ICU admissions (4% vs. 14%; $p < 0.001$), a shorter mean LOS (7.2 ± 2.3 vs. 8.7 ± 4.2 days; $p < 0.001$), a shorter time in the operating room (9.08 ± 2.32 vs. 9.41 ± 2.30 h; $p = 0.023$), and less intravenous fluid administered intraoperatively (2240 ± 800 vs. 3288 ± 1168 ml; $p \leq 0.001$). The rate of URTOR, discharge destination, and readmission within 30 days did not differ between the groups.

The groups differed significantly in terms of overall complications, with 37 patients (18.6%) in the ERAS group experiencing at least one complication versus 54 patients (27%) in the control group ($p = 0.045$). This difference likely was attributable to a higher rate of medical complications (e.g., respiratory complications) (9.0% vs. 4.5%; $p = 0.073$) and neurologic complications (9.0% vs. 1.0%; $p < 0.001$) in the control group. The groups did not differ in rate of overall wound complications ($p = 0.281$) or individual wound/flap complications.

Pain-Related Outcomes

Both groups had similar rates of preoperative opioid analgesic use ($p = 1.000$) and preoperative referrals to the pain management clinic ($p = 0.487$) (Table 3). However, the ERAS group was noted to require a shorter time in the PACU (117 ± 51 vs. 141 ± 51 min; $p < 0.001$), with a significantly lower first pain score in the PACU (2.5 ± 3.2 vs. 3.5 ± 3.4; $p = 0.003$). The mean pain score on POD1 ($p = 0.892$), POD3 ($p = 0.236$), and day of discharge ($p = 0.273$) did not differ between the groups, but showed an overall decreasing trend from POD1 to day of discharge in both groups (Fig. 1). During 72 h, the ERAS group showed a significant reduction in postoperative PCA use (31.0% vs. 74.5%; $p < 0.001$) and MME requirements (138.8 ± 181.5 vs. 207.9 ± 205.5; $p < 0.001$). Furthermore, fewer patients in the ERAS group received a strong opioid analgesic discharge prescription (64.5% vs. 81.5%; $p < 0.001$). Compliance with the administration of at least two pre-medications was 87%, and compliance with the administration of at least two postoperative scheduled medications was 92.5%.

The study also assessed risk factors for high opioid analgesic requirements (MME ≥ 180 mg during 72 h)

TABLE 1 Demographics

	Total *n* (%)	ERAS group *n* (%)	Control group *n* (%)	*p* value
No. of patients	400	200	200	
Mean age (years)	62.4 ± 13.1	62.4 ± 13.1	62.4 ± 13.0	0.979
Gender				
Male	283 (70.8)	142 (71.0)	141 (70.5)	0.912
Female	117 (29.3)	58 (29.0)	59 (29.5)	
Mean BMI (kg/m^2)	26.5 ± 5.5	26.4 ± 5.4	26.6 ± 5.5	0.744
Race				
White	354 (88.5)	172 (86.0)	182 (91.0)	0.292
African American	15 (3.8)	9 (4.5)	6 (3.0)	
Others	31 (7.8)	19 (9.5)	12 (6.0)	
Smoker	73 (18.3)	42 (21.0)	31 (15.5)	0.154
Alcohol use	33 (8.3)	20 (10.0)	13 (6.5)	0.203
Functional status				
Independent	398 (99.5)	198 (99.0)	200 (100.0)	0.499[a]
Partially dependent	2 (0.5)	2 (1.0)	0 (0)	
Modified Frailty Index-5				
0	181 (45.4)	96 (48.0)	85 (42.5)	0.617[a]
1	164 (41.0)	80 (40.0)	84 (42.0)	
2	52 (13.0)	23 (11.5)	29 (14.5)	
3	3 (0.8)	1 (0.5)	2 (1.0)	
Comorbidities				
Hypertension	205 (51.2)	94 (47.0)	111 (55.5)	0.089
Diabetes	49 (12.3)	24 (12.0)	25 (12.5)	0.245
CHF	4 (1.0)	2 (1.0)	2 (1.0)	1.000[a]
COPD	17 (4.3)	7 (3.5)	10 (5.0)	0.457
CAD	43 (10.8)	21 (10.5)	22 (11.0)	0.872
Steroid use for chronic condition	30 (7.5)	14 (7.0)	16 (8.0)	0.704
Weight loss > 10% in 6 months	20 (5.0)	8 (4.0)	12 (6.0)	0.359
Nutritional intake status				
Full per oral	383 (95.8)	190 (95.0)	193 (96.5)	0.732[a]
Partially tube-dependent	2 (0.5)	1 (0.5)	1 (0.5)	
Fully tube-dependent	15 (3.8)	9 (4.5)	6 (3.0)	
Mean preoperative albumin (g/dL)	4.2 ± 0.4	4.2 + 0.4	4.1 + 0.4	0.292
Prior radiotherapy	166 (41.5)	82 (41.0)	84 (42.0)	0.839
Prior head and neck surgery	165 (41.3)	81 (40.5)	84 (42.0)	0.761
Recurrent disease	173 (43.3)	93 (46.5)	80 (40.0)	0.190
Wound class				
Clean	91 (23.0)	40 (20.4)	51 (25.6)	0.392[a]
Clean-contaminated	297 (75.2)	153 (78.1)	144 (72.4)	
Contaminated	7 (1.8)	3 (1.5)	4 (2.0)	
ASA classification				
2	25 (6.3)	12 (6.0)	13 (6.5)	0.762
3	367 (91.8)	183 (91.5)	184 (92.0)	
4	8 (2.0)	5 (2.5)	3 (1.5)	
Type of surgery				
Cutaneous	104 (26.0)	52 (26.0)	52 (26.0)	1.000
Upper aerodigestive tract	296 (74.0)	148 (74.0)	148 (74.0)	

TABLE 1 continued

	Total *n* (%)	ERAS group *n* (%)	Control group *n* (%)	*p* value
Flap type				
Soft tissue	290 (72.5)	145 (72.5)	145 (72.5)	1.000
Osseous	86 (21.5)	43 (21.5)	43 (21.5)	
Multiple	24 (6.0)	12 (6.0)	12 (6.0)	

ERAS enhanced recovery after surgery, *BMI* body mass index, *CHF* congestive heart failure, *COPD* chronic obstructive pulmonary disease, *CAD* coronary artery disease, *ASA* American Soceity of Anestheioogy

[a]Fisher's exact test

TABLE 2 Perioperative outcomes in the eras and control groups

	Total *n* (%)	ERAS group *n* (%)	Control group *n* (%)	*p* value
No. of patients	400	200	200	
Mean operating room time (h)	9.24 ± 2.32	9.08 ± 2.32	9.41 ± 2.30	**0.023**
Intraoperative total intravenous fluid (ml)	2765 ± 1129	2240 ± 800	3288 ± 1168	< **0.001**
ICU admission postoperatively	36 (9.0)	8 (4.0)	28 (14.0)	< **0.001**
Mean hospital stay (days)	7.9 ± 3.4	7.2 ± 2.3	8.7 ± 4.2	< **0.001**
Overall complications (per patient)	91 (22.8)	37 (18.6)	54 (27.0)	**0.045**
Cardiac complications (cardiopulmonary resuscitation, myocardial infarction, supraventricular tachycardia)	3 (0.8)	2 (1.0)	1 (0.5)	0.623
Respiratory complications (pneumonia, re-intubation, intubation > 48 h, pulmonary embolism)	27 (6.8)	9 (4.5)	18 (9.0)	0.073
Neurologic complications (cerebrovascular accident, coma > 24 h, altered mental status)	20 (5.0)	2 (1.0)	18 (9.0)	< **0.001**
Urinary tract infection	4 (1.0)	1 (0.5)	3 (1.5)	0.623[a]
Overall medical complications (per patient)	44 (11.0)	12 (6.0)	32 (16.0)	**0.001**
Transfusion within 72 h	110 (27.5)	45 (22.5)	65 (32.5)	**0.025**
Wound				
Hematoma	20 (5.0)	7 (3.5)	13 (6.5)	0.169
Seroma	8 (2.0)	3 (1.5)	5 (2.5)	0.475[a]
Thrombosis	8 (2.0)	4 (2.0)	4 (2.0)	1[a]
Partial loss	2 (0.5)	2 (1.0)	0 (0)	0.499[a]
Total loss	3 (0.8)	1 (0.5)	2 (1.0)	1[a]
Fistula	10 (2.5)	4 (2.0)	6 (3.0)	0.751[a]
Recipient-site infection or disruption	38 (9.5)	19 (9.5)	19 (9.5)	1
Donor-site infection or disruption	5 (1.3)	1 (0.5)	4 (2.0)	0.372[a]
Overall wound complications (per patient)	66 (16.5)	29 (14.5)	37 (18.5)	0.281
Return to operating room	62 (15.5)	30 (15.0)	32 (16.0)	0.782
Discharge destination (other than home)	38 (9.5)	14 (7.0)	24 (12.1)	0.085
Feeding tube at 30 days	230 (57.5)	114 (57.0)	116 (58.0)	0.840
Readmission within 30 days	32 (8.0)	18 (9.0)	14 (7.0)	0.461

ERAS enhanced recovery after surgery, *ICU* intensive care unit

[a]Fisher's exact test

Bolded numbers indicate statistical significance

TABLE 3 Pain-related outcomes in the ERAS and control groups

	Total *n* (%)	ERAS group *n* (%)	Control group *n* (%)	*p* value
No. of patients	400	200	200	
Preoperative opioid analgesic use	180 (45.0)	90 (45.0)	90 (45.0)	1
Preoperative pain service consultation	61 (15.3)	28 (14.0)	33 (16.5)	0.487
Postoperative care unit duration (min)	129 ± 52	117 ± 51	141 ± 51	< **0.001**
Mean pain score				
Postoperative care unit		2.5 ± 3.2	3.5 ± 3.4	**0.003**
Postoperative day 1	6.3 ± 2.6	6.3 ± 2.6	6.4 ± 2.6	0.892
Postoperative day 3	5.3 ± 2.7	5.1 ± 2.8	5.5 ± 2.5	0.236
Day of discharge	2.7 ± 2.8	3.4 ± 2.8	3.7 ± 2.9	0.273
Postoperative patient-controlled analgesia use	211 (52.8)	62 (31.0)	149 (74.5)	< **0.001**
Postoperative patient-controlled analgesia duration, (days)	2.7 ± 1.3	2.7 ± 1.3	2.6 ± 1.3	0.643
MME 72 h	173.3 ± 196.7	138.8 ± 181.5	207.9 ± 205.5	< **0.001**
Discharge prescriptions				
Strong opioid analgesic	292 (73.0)	129 (64.5)	163 (81.5)	< **0.001**
Weak opioid analgesic	114 (28.5)	77 (38.5)	37 (18.5)	< **0.001**
Others	160 (40.0)	94 (47.0)	66 (33.0)	**0.004**

ERAS enhanced recovery after surgery, *MME* morphine milligram equivalent

Bolded numbers indicate statistical significance

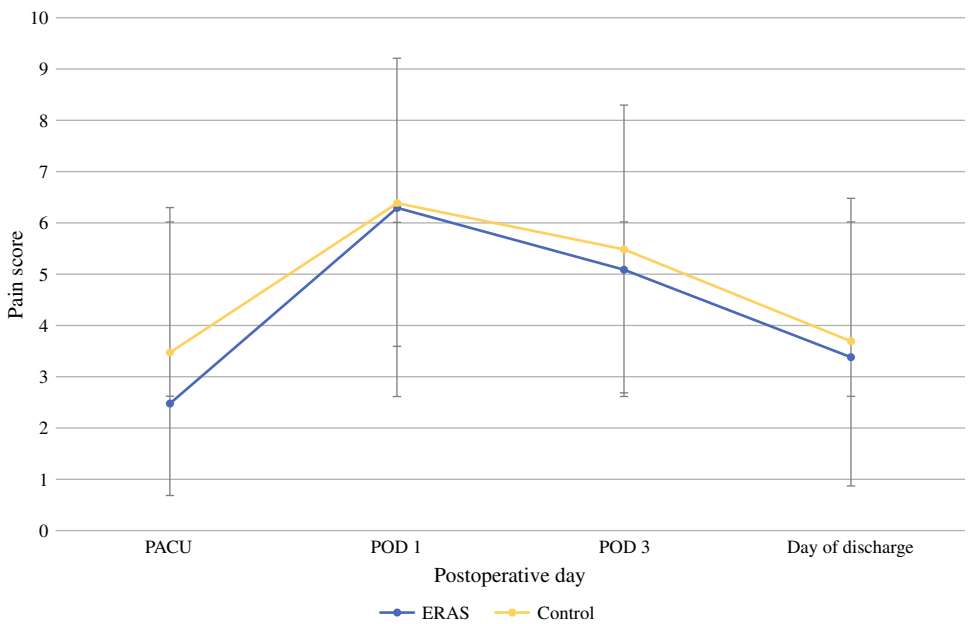

FIG. 1 Pain scores from postanesthesia care unit (PACU) to discharge

across the whole cohort (Table 4). After adjustment for significant factors, the multivariate analysis showed that age older than 65 years continued to decrease the risk for high opioid analgesic usage (odds ratio $[OR]_{adjusted}$, 0.33; 95% confidence interval [CI], 0.20–0.57). The risk factors for high opioid analgesic usage were African American race ($OR_{adjusted}$, 3.68; 95% CI, 1.12–12.10), prior radiotherapy ($OR_{adjusted}$, 1.76; 95% CI, 1.05–2.94), preoperative opioid analgesic use ($OR_{adjusted}$, 3.00; 95% CI, 1.77–5.08), ICU admission ($OR_{adjusted}$, 2.94; 95% CI, 1.28–6.72), and PCA use postoperatively ($OR_{adjusted}$, 3.58; 95% CI, 1.97–6.52). Preoperative pain service consultation was not analyzed in the multivariate analysis despite the strong association observed in the univariate analysis (OR, 15.27; 95% CI, 7.82–29.82) because this is a subset of the patients with preoperative opioid analgesic use.

TABLE 4 Uni- and multivariate analysis: risk factors for high postoperative opioid requirements[a]

	Unvariate analysis		Multivariate analysis	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
ERAS	0.45 (0.29–0.70)	< **0.001**	0.64 (0.36–1.33)	0.126
Age> 65 years	0.26 (0.16–0.42)	< **0.001**	0.33 (0.20–0.57)	< **0.001**
Female	1.24 (0.77–1.98)	0.374		
Race				0.091
White	1.00	–	1.00	
African American	3.12 (1.10–8.83)	**0.032**	3.68 (1.12–12.10)	**0.032**
Others	1.50 (0.69–3.25)	0.304	1.53 (0.61–3.79)	0.363
Alcohol use	0.94 (0.42–2.08)	0.870		
Prior radiotherapy	1.89 (1.22–2.93)	0.005	1.76 (1.05–2.94)	**0.032**
Recurrent disease	1.54 (1.00–2.38)	0.053		
Preoperative opioid analgesic use	4.13 (2.59–6.59)	< **0.001**	3.00 (1.77–5.08)	< **0.001**
Preoperative pain service consultation	15.27 (7.82–29.82)	< **0.001**		
Surgery type: upper aerodigestive tract	2.72 (1.52–4.89)	0.001		
Flap type				
Soft tissue	1.00			
Osteocutaneous	1.22 (0.72–2.07)	0.461		
Combination/multiple	2.82 (1.21–6.54)	0.016		
ICU admission	2.79 (1.40–5.59)	0.004	2.94 (1.28–6.72)	**0.011**
Patient-controlled analgesia use postoperatively	5.87 (3.49–9.88)	< 0.001	3.58 (1.97–6.52)	< **0.001**

OR odds ratio, *CI* confidence interval, *ERAS* enhanced recovery after surgery, *ICU* intensive care unit

Bolded numbers indicate statistical significance

[a]Multivariate model adjusted for: ERAS status, age > 65, race, prior radiotherapy, preoperative opioid analgesic use, ICUt admission, and patient-controlled analgesia use postoperatively

DISCUSSION

In multiple specialties, ERAS programs have been implemented globally, showing significant improvements in patient outcomes.[1–3] Head and neck oncologic surgery is another area that could potentially benefit from evidence-based standardization of patient care because these patients are prone to complications and prolonged hospital stays.[7] A systematic review in 2015 identified 13 articles that covered a range of perioperative measures aimed at improving clinical outcomes.[16] However, most of these studies were confined to small cohorts of fewer than 100 patients and were focused on individual process changes rather than a structured ERAS program aimed at multiple aspects of perioperative care.

In recent years, several other head and neck cohorts have demonstrated varied results with formal ERAS programs. Bater et al.[10] showed a significantly shorter LOS (10 vs. 14 days) but no difference in complication rates or readmission rates in their cohort of 100 ERAS patients compared with historical controls. Jandali et al.[17] also showed a reduction in LOS (7.83 vs. 9.71 days), a reduction in MME requirements postoperatively, and fewer patients requiring postdischarge narcotic prescriptions/refill within 30 days postoperatively. However, the largest head and neck ERAS cohort before this series, with 144 patients on an ERAS protocol, failed to show any reduction in postoperative complications, leading the authors to conclude that any benefit associated with ERAS in head and neck surgery with free-tissue transfer flap reconstruction is likely to be modest[12].

Our data showed that ERAS has resulted in a significantly shorter mean LOS (7.2 vs. 8.7 days) and a reduction in overall complications ($p = 0.045$). The lower overall complication rate likely was attributable to the reduction in medical complications ($p < 0.001$) rather than fewer wound complications ($p = 0.281$). In particular, ERAS resulted in lower rates of respiratory complications such as pneumonia and neurologic complications such as altered mental state.

Our findings may be related directly or indirectly to a reduction in ICU admissions (4% vs. 14%; $p < 0.001$). Findings have shown that non-ICU admission after head and neck surgery with free-flap reconstruction is feasible and can result in a shorter LOS with comparable morbidity and mortality[18,19]. Other factors that may contribute to the

lower incidence of medical complications in the ERAS group include a shorter LOS, implemented measures of early mobilization by POD1, and GDFT.

In our practice of GDFT, we reduced the mean total intraoperative intravenous fluid administration by 1 L pre- and post-ERAS ($p < 0.001$). We were able to achieve this by titrating intravenous fluid input against arterial line stroke volume assessments, urine output, noninvasive hemodynamic monitoring, and use of vasopressors to optimize blood pressure.

Multiple studies have shown that GDFT reduces mortality, the major complication rate, and LOS.[20,21] Consistent with stable wound complication rates, the rate of URTOR did not differ significantly between the groups. Because our ERAS interventions were not specifically designed to reduce wound complications, this finding is not unexpected. Prior series reviewing ERAS implementation in head and neck oncologic surgeries have not found a difference in complication rates.[10, 12] This may be related to the smaller cohort sizes and the definition of complications as assessed by retrospective data collection in other series.

Because we extracted data from a HNRS-NSQIP database with data collection by specialized clinical personnel trained in documenting outcomes based on stringent NSQIP criteria, our data are less subject to biased reporting. Furthermore, compliance with ERAS measures may have been an issue in those studies, resulting in a perceived lack of improvement. A large adherence study in colorectal surgery has shown that low adherence to ERAS protocols can affect the LOS, complication rate, and functional recovery of patients.[22]

A key component of our ERAS protocol is the emphasis on preemptive analgesia with premedication before surgery and MMA in the postoperative period. Multiple studies of head and neck surgery have shown that MMA,[17,23,24] celecoxib,[25] and gabapentin[26] are safe and result in decreased opioid analgesic requirements postoperatively. Consistent with the literature, our ERAS group reported a reduction in PACU pain score ($p = 0.003$), decreased use of PCA ($p < 0.001$), and decreased MME usage in 72 h ($p < 0.001$). Furthermore, we report a decrease in the proportion of patients discharged with strong opioid analgesics (64.5% vs. 81.5%), with a preference for the prescription of weak opioid analgesics (38.5% vs. 18.5%) and other classes of analgesia (47.0% vs. 33.0%) instead. The ERAS group had a reduction in pain scores on POD1, POD3, and the day of discharge, but this did not reach statistical significance, similar to the findings by Du et al.[23] Regarding the safety of celecoxib, our study did not find any increase in the hematoma rate for the patients in the ERAS group, consistent with findings in the literature[25].

We also analyzed factors associated with high usage of opioid analgesics (MME > 180 mg) during the first 72 h postoperatively. Other studies have shown that the use of opioid analgesics preoperatively and chronic pain are significantly associated with higher pain scores postoperatively.[23,27,28] Our study also found that preoperative opioid analgesic use and pain management service consultations, a surrogate for chronic or uncontrolled pain, was associated with high opioid analgesic use postoperatively.

In the multivariate analysis, the patients older than 65 years were less likely to have high opioid requirements, as corroborated by Du et al.,[23] who also found that increasing age was associated with lower MME usage. The multivariate analysis also found race to be a significant factor associated with higher opioid analgesic requirements postoperatively. This finding has been shown for head and neck surgery specifically,[23] as well as for general populations, and may be a reflection of underlying biologic, social, cultural, and psychological factors.[29]

We also found that prior radiotherapy (RT) was associated with high opioid usage, a finding not reported in other studies. Although a higher proportion of patients with prior RT were taking opioids preoperatively ($p = 0.039$), RT as a factor influencing postoperative high opioid requirements remained significant in the multivariate analysis ($OR_{adjusted}$, 1.76; 95% CI, 1.05–2.94). Patients with previous RT may have radiation-induced cervical dystonia, resulting in muscle spasms and pain,[30] which could be exacerbated by surgery. Interestingly, neither surgery type (upper aerodigestive tract or cutaneous) nor flap type (soft tissue vs. osseocutaneous vs. multiple flaps) were found to be associated with higher opioid usage in our multivariate analysis. Our study is among the largest analyzing patient factors related to high opioid analgesic usage after major head and neck surgery, thus uncovering significant associations.

Finally, we found that ICU admission and PCA usage were independently associated with high opioid analgesic usage postoperatively. Some centers have encouraged PCA use based on studies showing decreased pain scores and lower rescue analgesia requirements for patients receiving PCA.[31,32] However, although PCA use has not been compared head-to-head with MMA in the head and neck literature, studies in other disciplines have suggested that MMA rather than PCA can lead to shorter LOS, lower cost, and faster functional recovery with similar pain scores and patient subjective satisfaction scores.[33,34] However, temporal causality cannot be established in our finding of high opioid analgesic use by patients provided with PCA. It is unknown whether PCA results in high usage or whether anticipated high usage triggered the provision of PCA. At UTMDACC, the provision of PCA is not routine, and we

have attempted to decrease PCA use with emphasis on MMA where clinically appropriate. For patients with chronic pain or high opioid analgesic requirements preoperatively, we involve the inpatient pain management team as early as POD0 to assist with titration of pain medications.

We present the largest matched head and neck ERAS cohort to date. The baseline demographics were statistically similar between the groups, indicating good matching. Jandali et al.[17] reported that a significantly greater number of patients in their control group were using opioid analgesics preoperatively, which may have affected their results from comparison of discharge medications. Our groups were comparable in terms of preoperative opioid analgesic consumption and pain management team consultations. Furthermore, our ERAS group comprised patients matched during a relatively long period of 2 years, compared with a single cohort matched during several months. This indicates durable implementation and sustainability of the HNRS-ERAS program over years, with good results that endure. Compliance with ERAS pre- and postoperative medication orders from a feasibility study conducted at our institution from January to March 2018 was 84.6% for both[35] (C. M. Lewis, unpublished data). This increased slightly to 87% and 92.5%, respectively, during the period of our study, indicating that ERAS measures can be sustainable.

One potential limitation of our study was that it investigated a single-institution experience from a high-volume specialized center, which may affect the generalizability of the results to other centers. We faced some initial challenges implementing the ERAS program due to the coordination required between multiple stakeholders. Also, resources may differ between institutions. However, this emphasizes that ERAS programs are meant to be individualized to a particular center and can result in improved outcomes if evidence-based medicine and standardization are used where possible. Also, although prescription of strong opioid analgesics at discharge decreased significantly in the ERAS group, 64.5% still received a discharge prescription for these medications. Given the low pain scores on the day of discharge, it may be feasible to decrease the prescription of strong opioid analgesics further, with more reliance on weak opioid analgesics and other classes of analgesia. Additionally, after discharge, opioid analgesic usage was not tracked in our outcomes and it is unknown whether our patients were prescribed opioid medication at outpatient follow-up visits and whether they experienced the development of dependence.

Finally, the standardization of care with ERAS can potentially assist with episode-based payments, which in turn may cut health care costs and improve patient satisfaction.[36,37] Currently, a significant emphasis is focused on value-based health care. Reducing complications and ICU admissions can drive major reductions in health care costs with improvement in outcomes.[38] We have shown successful implementation of an ERAS program with excellent, durable results. Based on lowered LOS and ICU admissions, decreased resource use was realized and translated into reduced cost of care. Further analysis of reductions in cost and improvements in patient satisfaction should be studied in the head and neck population.

CONCLUSION

To date, ERAS pathways in head and neck oncologic surgery still are not well established[39] compared with other specialties such as colorectal surgery, in which the benefits of such pathways are well elucidated. Our study provided the strongest evidence to date that ERAS pathways in head and neck oncologic surgery can improve outcomes and decrease the need for opioid analgesics. We also identified additional factors associated with high opioid analgesic usage in the immediate postoperative period, with potential implications for long-term opioid dependence. The evolving evidence provides additional information on how to optimize care for patients undergoing head and neck cancer surgery, and we strive to further enhance our ERAS program.

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