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Original Article

Enhanced recovery after microvascular reconstruction in head and neck cancer – A prospective study

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ABSTRACT

Objectives: Patients undergoing microvascular reconstruction after head and neck cancer typically have several comorbidities, and the procedures are often followed by complications and prolonged hospitalization. Consequently, the application of *enhanced recovery after surgery* (ERAS) for these patients undergoing microvascular reconstruction has gained attention in recent years. ERAS is a peri- and postoperative care concept that has repeatedly shown beneficial results for a wide variety of surgical procedures, including microvascular reconstruction. This study presents the results after the introduction of our ERAS protocol for head and neck cancer reconstruction.

Methods: We prospectively treated 30 consecutive patients according to our ERAS protocol from June 2019 to December 2020 and

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compared the results of the treated patients with those of patients treated with our *traditional recovery after surgery* (TRAS) protocol. We are based on our ERAS protocol on the following core elements of recovery: *improved patient information, goal-directed fluid therapy, minimally invasive surgery, opioid-sparing multimodal analgesia, early ambulation,* and *pre-defined functional discharge criteria.*

Results: The baseline characteristics of the groups were comparable. The ERAS group had a significantly shorter length of stay (13.1 vs. 20.3 days, $p < 0.001$), significantly shorter time to ambulation (3.0 days vs. 6.4 days, $p < 0.001$), shorter time to removal of nasogastric tube (13.3 days vs. 22.7 days, $p = 0.05$), and fewer tracheostomies performed (10% vs. 90%, $p < 0.001$). There were no differences in complications, flap survival, or 30-day re-admissions between the two groups.

Conclusion: The introduction of ERAS in patients with head and neck cancer undergoing microvascular reconstruction seems safe and results in improved recovery.

Level of evidence: 3

Introduction

Patients with advanced-stage head and neck cancer that require microvascular reconstruction after ablative surgery have a poor prognosis and high perioperative complication rate.[1,2]

The treatment involves a multidisciplinary approach, including physicians from several specialties, and postoperative care is highly dependent on close cooperation with the nursing staff.

Surgical procedures are often long as dissection of the tumor may be difficult, and reconstruction is complex. Furthermore, patients frequently suffer from several comorbidities, including years of smoking, atherosclerosis, and prior radiation, which in turn affect the quality of the vessels used for anastomosis and the wound healing process.[3]

Enhanced recovery after surgery (ERAS) is a peri- and postoperative care concept that has proven to be superior for a wide range of surgical procedures, including microvascular reconstructive procedures after breast cancer.[4] Although the application of ERAS for head and neck reconstruction has gained interest in recent years, the results vary greatly because of overly complicated ERAS programs that are not realistically implementable[5] due to the complexity and heterogeneity of the procedures and because some reports include patients with and without free flap reconstruction.[6]

We have previously published our work on the process of developing an enhanced recovery protocol (ERP) for head and neck cancer reconstructions,[7] which was based on well-established core elements of enhanced recovery.[8]

The current prospective cohort study presents the results after the implementation of our ERP for microvascular reconstruction after head and neck cancer. Additionally, it discusses options for further development and progress in the treatment of this challenging patient population.

Materials and methods

The collection of baseline data for the current study was approved by the Danish Patient Safety Authority. All data handling was approved by the Danish Data Protection Agency, and the study was registered at www.clinicaltrials.gov (NCT04308525). Informed consent was obtained by all patients

included. Initiation of the study was approved at our institution, Copenhagen University Hospital, Rigshospitalet.

From June 2019 to December 2020, we prospectively included data for all patients who underwent free flap reconstruction after head and neck cancer (ERAS group). All patients were treated at Copenhagen University Hospital, Rigshospitalet, which is a tax-funded, public, and tertiary healthcare facility. The results of the ERAS group were compared to the historical results of patients treated with *traditional recovery after surgery* (TRAS) – a cohort of consecutive patients from the period 2014–2016 treated at our institution.[7]

Demographic data and data on comorbidities were documented preoperatively. All data regarding the surgical procedures, daily progress in postoperative recovery, re-operations, complications, and 30-day readmissions were recorded. Postoperative length of hospital stay (LOS) was the primary endpoint, with complications and readmissions as secondary outcomes. Infections were defined as treatment with additional antibiotics after postoperative prophylaxis.

Surgical procedures

The procedures were performed as joint-venture operations between the department of plastic surgery and the department of head and neck surgery. The department of oral and maxillofacial surgery contributed to procedures involving osseous resection of the maxilla or mandible.

All patients undergoing ablative surgery for tumors originating from the oral cavity or facial sinuses were included. The flaps included *the myocutaneous latissimus dorsi flap* (LD), *osteocutaneous free fibula flap* (FFF), and *anterolateral thigh flap* (ALT). Patients undergoing laryngectomy and those who underwent reconstruction due to ORN were not included in this study.

All patients received prophylactic antibiotic treatment with metronidazole and cefuroxime for 5 days after surgery and acetylsalicylic acid as microvascular thromboprophylaxis (150 mg/24 h) for 14 days postoperatively. Innohep was administered (4500 IE/24 h) until full ambulation.

Enhanced Recovery Protocol

Our ERAS protocol includes interventions related to the following six core elements of enhanced recovery: improved patient information, goal-directed fluid therapy, minimally invasive surgery, multimodal opioid-sparing analgesia, early ambulation, and pre-defined discharge criteria.[7]

Patient information was revised, and the landmarks were emphasized during the postoperative treatment regimen, such as expected LOS, time at the intensive treatment unit (ITU), time to ambulation, and oral feeding. Patients were initially informed about the surgery at the time of the indication. Elaborated information regarding the course of the postoperative treatment and answers to questions that the patients had thought of in the meantime were provided by a member of the surgical team at a visit to the department 1–3 days prior to surgery. *Goal-directed fluid therapy* aims to reduce fluid overload and blood transfusions[9] with the aim of a positive fluid balance of 500–1000 ml on crystalloids, a difference that has traditionally been much larger. It was not individualized for different flap types but followed standards for ERAS protocols of fluid therapy.[10] *Minimally invasive surgery*, in its traditional sense, was not possible because there are no endoscopic alternatives to open surgery for these patients. We aimed to shorten the operating time by introducing a CAD/CAM system[11] and discontinuing the routine performance of tracheostomies[12] in favor of individual assessment of the need for tracheostomy. Before CAD/CAM introduction, we hand-bent all reconstructive plates during the surgical procedure and visually performed osteotomies; however, after the introduction of this system, the surgical team was provided with pre-bent reconstructive plates and prefabricated cutting guides to secure precise osteotomies. We previously performed tracheotomy on almost all patients before the oncologic surgical procedure, while after ERAS implementation, we assessed all patients at the end of surgery and performed tracheotomy only if it was unavoidable due to compromised airways. In this way, we aimed to reduce the number of surgical procedures performed on the patients and, in turn, reduce the number of tracheostomy-related complications. Our *multimodal opioid-sparing* analgesic (MOSA) strategy included 400 mg of COX-II inhibitor preoperatively (Celecoxib, STADA Nordic,

Table 1
Demographic data of the ERAS and TRAS groups

	ERAS group (30)	TRAS group (58)	p
Sex			
- Male (%)	20 (67)	37 (64)	0.8
- Female (%)	10(33)	21 (36)	0.8
Age, years (range)	64.5 (43–85)	62.3 (31–84)	0.4
Body mass index (range)	24.6 (18–33)	24.5 (14–34)	1
Tobacco use (%)			
- Active smokers	17 (57)	23 (40)	0.17
- Former smokers	7 (23)	13 (22)	1
- Non-smokers	6 (20)	22 (38)	0.10
Comorbidities (%)			
- Diabetes	1(3)	8 (14)	0.74
- Hypertension	11 (37)	20 (34)	1
- Pulmonary disease	7 (23)	9 (16)	0.4
- Ischemic heart disease	3 (10)	3(5)	0.4
Primary cancer/procedure (%)	19 (63)	33 (57)	0.7
- T4	18 (95)	31 (94)	1
- T3	0	1 (3)	1
- T2	1 (5)	1 (3)	1
Recurrent disease (%)	11 (37)	25 (43)	0.7
- Previous surgery	0	8 (32)	0.08
- Previous radiation	4 (36)	6 (24)	0.5
- Both	7 (64)	11 (44)	0.5

Herlev, Denmark) followed by 200 mg/12 h, gabapentin (300 mg/8 h), dexamethasone (12–16 mg preoperatively + 12 mg/24 h for three days), and paracetamol (1 g/6 h). Opioids were administered only on request. *Early ambulation* is encouraged from POD1 and possible in FFF patients by applying a self-adhering pressure bandage (COBAN-II, 3M, Minneapolis, USA) to the FFF donor site. Our *functional discharge criteria* were based on our previous experience in ERAS for autologous breast reconstruction[4] and adjusted for head and neck cancer patients (Table 1).[7] Discharge criteria were monitored daily and included full ambulation, adequate nutritional intake, sufficient pain relief, bowel function, non-suspicion of infection, and closure of tracheostomy (if any).

Statistical analysis

Statistical analyses were performed using "R" Core Team (2020), R: Language and Environment for Statistical Computing, R Foundation for Statistical Computing, Vienna, Austria. T-test was used for continuous outcomes and Fischer's exact test for dichotomous outcomes. All results from the prospective study were compared with the baseline results.

Results

The 30 patients in the ERAS group were compared to 58 consecutive patients in the TRAS group. The patients in the ERAS and TRAS groups were comparable in terms of age (64.5 vs. 62.1 years) and body mass index (24.6 vs. 24.5 kg/m^2).

Primary tumors were the cause of surgery in 63% of the ERAS patients and 57% of the TRAS patients. Comorbidities, such as active smoking (57% ERAS and 40% TRAS), hypertension (37% ERAS and 34% TRAS), and pulmonary disease (23% ERAS 16% TRAS), were common. A detailed overview of the demographic data is presented in Table 2.

Most patients in both groups were treated for advanced squamous cell carcinomas (>80%), and reconstruction was performed with either an ALT, FFF, or LD flap.

The procedures were significantly shorter in the ERAS group (446 min vs. 564 min, $p < 0.0001$). The reduction in surgical time was significant for all types of flaps as the duration for FFF procedures

Table 2
Procedure-related data of ERAS and TRAS reconstructions

	ERAS group (30)	TRAS group (58)	p
Cancer location (%)			
- Oral cavity, lower*	23 (77)	45 (78)	1
- Oral cavity, upper**	3 (10)	10 (17)	0.53
- Sinus & nasal cavity	4 (13)	3 (5)	0.22
Tumour type (%)			
- Squamous cell carcinoma	26 (87)	48 (83)	0.76
- Osteosarcoma	1 (3)	2 (3)	1
- Adenoid cystic carcinoma	0	3 (5)	0.55
- Other	3 (10)	5 (9)	1
Operating time, avg. (min)	446 (311–582)	564 (346–838)	**<0.001**
Flap ischemia time, avg. (min)	68 (24–180)	86 (24–240)	0.09
Blood loss, avg. (ml)	945 (350–2600)	1330 (170–2700)	**0.01**
Blood transfusion (%)			
- SAG-M	4 (13)	26 (45)	**0.004**
- FFP	7 (23)	11 (13)	0.78
Flap type (%)			
- Free fibula flap	8 (27)	28 (48)	0.07
- Latissimus dorsi	7 (23)	15 (26)	1
- Anterolateral thigh	15 (50)	3 (5)	**<0.0001**
- Radial forearm	0	7 (12)	0.09
- Free fibula + LD/ALT	0	5 (9)	0.16
Foreign body (%)			
- Titanium plate (with FFF)	8 (27)	28 (48)	0.07
- Titanium plate (+ soft tissue)	13 (43)	14 (24)	0.09
- Titanium mesh	1 (3)	1 (2)	1

Note: Data presented as average (SD) or numerical (% of column)
* Includes area around mandible, floor of mouth, tongue root, and gingiva
** Upper part of the oral cavity includes soft and hard palate, maxilla, and fauces

Table 3
Postoperative data for ERAS and TRAS patients

	ERAS-group (30)	TRAS group (58)	p
Length of stay, avg. (days)	13.1 (4–33)	20.3 (8–70)	**<0.001**
ITU stay, avg. (hrs.)	31.9 (0–160)	33.3 (10–212)	0.85
Nasogastric tube (%)	27 (90)	56 (96)	0.33
- Duration (days)	13.3 (1–30)	22.7 (1–126)	**0.05**
- Persistent after discharge (%)	4 (13)	10 (17)	0.76
- Conversion to PEG	2 (7)	7 (12)	0.71
Patients with tracheostomy (%)	3 (10)	52 (90)	**<0.00001**
- Time to closure, days	8 (6–11)	14.6 (1–120)	0.053
Time to ambulation, avg. (days)	3.0 (1–11)	6.4 (1–19)	**<0.0001**

Note: Data presented as average (SD) or numerical (% of column)

decreased from 566 min to 470 min ($p = 0.001$), ALT decreased from 564 min to 423 min ($p < 0.001$), and LD decreased from 564 min to 468 min ($p = 0.03$). Data regarding the reconstructive procedures are presented in Table 3.

The average LOS in the ERAS group was 13.1 days, which was significantly shorter than that in the TRAS group (20.3 days ($p < 0.001$). For the subgroups of different flap types, the average LOS was reduced from 21.5 to 14.3 ($p = 0.03$) for FFF and from 15.3 to 11.0 for ALT flaps ($p = 0.04$). LOS for LD flaps declined from 21.4 to 16.1 days but did not reach statistical significance ($p = 0.2$). Table 4 summarizes the data regarding postoperative hospitalization. Factors limiting patients from discharge are shown in Fig. 1. All but two ERAS patients (93%) were discharged directly to their homes. One patient fulfilled all discharge criteria by POD16 but was transferred to the department of otolaryngology for 13 days of treatment for lymphedema and psychological vulnerability following a long ITU stay. The other patient was completely self-reliant on POD10 but was transferred to the Department

Table 4
– Data regarding complications after OS- and LP-microvascular reconstructions

	ERAS group (30)	TRAS group (58)	P
Infection (%)	11 (37)	19 (33)	0.8
- Donor-site	0	4 (7)	0.29
- Recipient-site	4 (13)	8 (14)	1
- Urinary tract infection	1 (3)	2 (3)	1
- Pulmonary	1 (3)	3 (5)	1
- Unknown	5 (17)	2 (3)	**0.04**
Re-operations 30 days, no patients (%)	5 (17)	13 (22)	0.59
- Hematoma*	3 (10)	2 (3)	0.33
- Flap loss*	1 (3)	2 (3)	1
- Tracheostomy problem*	0	3 (5)	0.55
- Flap revision*	5 (17)	3 (5)	0.12
- Donor-site complications*	1(3)	4 (7)	0.66
Re-admissions	3 (10)	6 (10)	1
- Infection	2 (7)	2 (3)	0.6
- Nutritional problem	0	1 (2)	1
- Wound revision	1 (3)	2 (3)	1
- Tracheostomy problem	0	1 (2)	1
Cardiopulmonary complication			
- Pulmonary embolus	1 (3)	0	1
- Cardiac arrest	1 (3)	2 (3)	1
Post-op mortality	0	1 (2)	1

Note: Data presented as average (SD) or numerical (% of column)
*Displays number of procedures performed rather than the number of patients

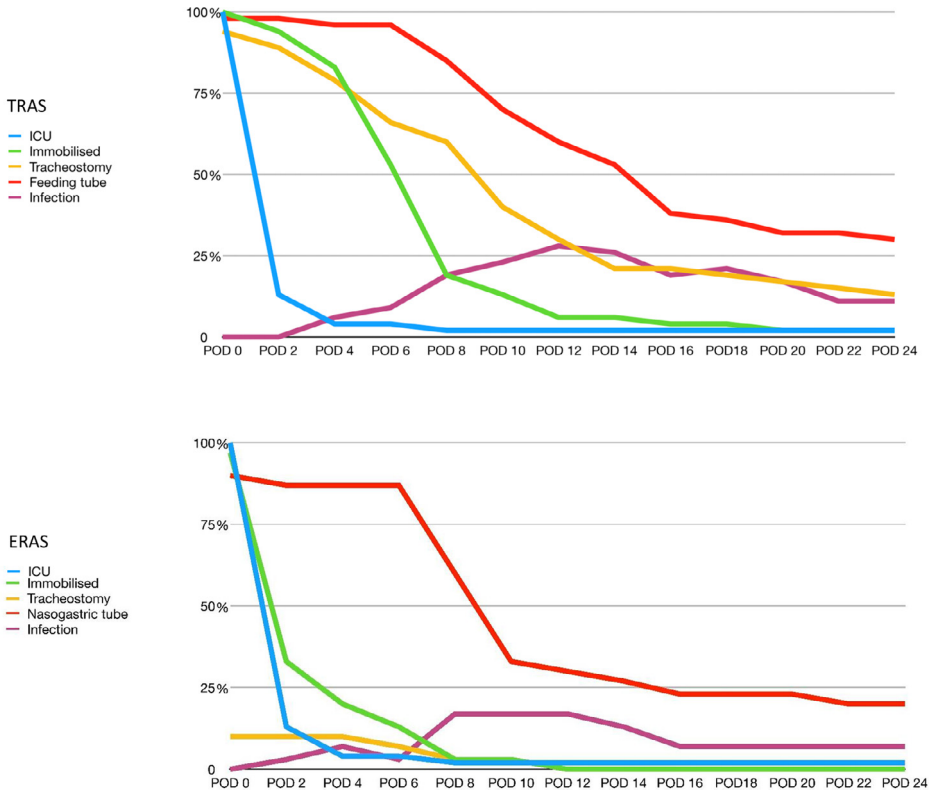

Fig. 1. Graphical overview illustrating factors keeping the patients hospitalized at a given time during their course of treatment for the TRAS and ERAS groups.

Table 5
Causes for prolonged LOS in ERAS patients

	ERAS group n = 7 (23%)
Elevated biochemical infection parameters	1 (3)
Nutritional problem	3 (10)
- Unavailability of occupational therapist	2 (7)
- Lack of compliance	1 (3)
Psychological vulnerability	1 (3)
Flap failure	1 (3)
Cardiac arrest	1 (3)

Table 6
List of functional discharge criteria included in our ERAS protocol.

Full ambulation	Walking unrestricted
Sufficient nutrition	Intake of calculated daily nutritional calorie requirement
Sufficient pain relief	No need for analgesia in excess of the per oral opioid-sparing regimen
No suspected infection	Normothermia and normal biochemical infection parameters
Closure of tracheostomy	Closure or thorough education in self-management of tracheostoma
Bowel function	Stool and flatulence passing

of Cardiology for 6 days of stabilization of cardiac issues most likely related to years of untreated or controlled systematic lupus erythematosus.

Postoperative ITU stay was similar with an average of 31.9 h in the ERAS group and 33.3 h in the TRAS group ($p = 1$). In the ERAS group, 90% of the patients had a nasogastric feeding tube placed perioperatively compared to 100% in the TRAS group. Time to removal of the nasogastric tube and sufficient oral nutritional intake were shorter in the ERAS group (13.3 vs. 22.7 days, $p = 0.05$). A significant reduction in the number of patients receiving a tracheostomy was found in three patients in the ERAS group (10%) compared to 52 (90%) in the TRAS group. The average time to ambulation was reduced from 6.4 days in average to 3.0 days in the ERAS group ($p < 0.05$). Specifically, the time to ambulation was reduced from 7.9 days to 4.4 days ($p = 0.01$) for the FFF subgroup.

Specific factors keeping the patients hospitalized at a given time in the ERAS and TRAS groups are visualized in Fig. 1.

No difference in perioperative complications such as infections, re-operations, or re-admissions was observed between the groups (Table 5).

Of the 30 patients included in the ERAS program, seven had a prolonged LOS of more than 14 days. None of these were due to complications associated with the ERAS protocol. The causes of the delayed discharge are displayed in Table 6. One patient with prolonged LOS due to nutritional problems was discharged with a nasogastric tube, and one had a PEG tube placed. Re-admission rates within the first 30 days were the same in both groups (10%).

Discussion

We successfully implemented an ERAS protocol for microvascular reconstruction after head and neck cancer. Our postoperative LOS was reduced from 20.3 to 13.1 days without increasing the risk of infections, surgical complications, or re-admission rate.

In recent years, the concept of ERAS and the application of ERPs for head and neck reconstruction have attracted increasing interest. Our ERAS program is based on core elements of recovery and aims to present an easily implementable care regimen.

This study contributes valuable data to the field where different ERPs have been published without subsequent feasibility studies.[14,15] A common factor in these protocols is extensive lists of recommendations and interventions to implement even though the recommendations often originate from other specialties and procedures, and therefore need to be tested in a relevant setting. The issue with these

extensive guidelines has been pointed out by several authors as it necessitates the creation and adaption of a novel protocol for many institutions.[2,5,16]

The strengths of the current study lie in the well-controlled prospective cohort with an extensive evaluation of postoperative parameters. The knowledge obtained were specifically designed to analyze challenges in the recovery period rather than just numerical data. The prospectively included procedures and the retrospective controls were consecutive during their time frames and performed within the same institution for comparable set-ups. The study's main weakness is the relatively small sample size. This is naturally limited by the relatively low number of patients presented at our institution during the study period, although it is representable of the average during the past 20 years. This results in some variation regarding flap type but tumor grading, and location remained the same. The study was not performed as a randomized controlled trial (RCT) but as a case-control study. Although RCTs are the gold standard for the highest level of evidence, they are not always suitable for a study of multiple interventions without the possibility of proper blinding. Controlled cohort studies followed by the assessment of the individual interventions by RCTs have been proposed to be a better option.[13] To further validate the results of our ERAS protocol, a multicenter study including institutions with similar settings could facilitate a larger number of included patients and even out demographic differences in this heterogenous patient population.

A significant reduction in LOS has previously been reported after the application of ERP for head and neck cancer reconstruction. Kiong et al. performed on of the largest studies to date on 200 ERAS patients and found a reduction in LOS from 8.7 to 7.2 days, with 93% of the patients being discharged to home. In addition, they found a reduction in overall complications, which was mostly attributable to a large reduction in postoperative medical complications.[16] In contrast, more than 50% of the patients in this ERAS population were dependent on tube feeding at 30 days postoperatively, despite 95% relying on full oral feeding before surgery. Low et al. investigated the compliance of their ERAS program and found compliance to the protocol in more than 80% of the cases and a postoperative LOS of 8.3 days.[17] Bater et al. showed a reduction in LOS from 14 to 10 days for patients undergoing reconstruction after head and neck cancer resection including osseous parts, but also discharged 86% of the patients before the establishment of sustained oral intake and 87% before decannulation of tracheostomy.[18] Coyle et al. showed a reduction in LOS from 18 to 14.6 days after ERAS implementation and established adequate and partially oral nutritional intake, adequate mobilization, acceptable social circumstances, wound care in place, and ability to communicate as discharge aims, but did not establish formal criteria.[19] None of the authors reported a difference in complication rates or readmissions. Yeung et al. reduced the LOS from 21.6 to 14.2 days while also decreasing pulmonary complications, including pneumonia, by more than 50%. They also included a set of discharge goals, including decannulation of tracheostomy, sufficient fluid diet, mobilization, and oral administration of pain management.

Won et al. drastically reduced LOS by 50% from 59.7 to 30.9 days, time at ITU by 87% from 9.5 to 1.2 days, time to ambulation by 72% from 23.8 to 6.7 days, and time to oral feeding by 33% from 23.4 to 15.7 days.[20] It is noteworthy that these results of the ERAS group in the study by Won are similar to many published results of TRAS. However, their ERP utilizes the same areas of intervention as generally seen in ERAS and shows that they may accelerate recovery in a healthcare system that traditionally has a much longer LOS than expected in European or American institutions.

Other studies have failed to establish a reduction of LOS after ERAS implementation as Imai et al. had a postoperative LOS of 29 days in their control group and 26 days in their ERAS group.[21] Likewise, McMahon et al. found no reduction in LOS or positive effect perioperative complications, which was described as disappointing and perplexing.[2] A recent study by Clark et al. did not find a statistically significant reduction in LOS as their ERAS group was discharged after 9.6 days and their control group after 11.9 days, which are both relatively short compared to the other reports.[22] They did report a decrease in opioid usage, pain scores, and blood-product utilization, and the first point being especially relevant considering the ongoing surge in opioid usage in America.[23,24]

Our study found no significant decrease in flap loss (3%), surgical complications (17%), or readmissions (10%) in the ERAS group; however, the complication rates were comparable to those reported in the literature.

The proportion of patients using different types of flaps changed between the TRAS and ERAS cohorts in our study. A significant increase in the number of ALT flaps was observed, while the proportion of FFF decreased. The goal remains autologous osseous reconstruction for all patients undergoing mandibulectomy/maxillectomy, but the patient population involved is heterogeneous, and the proportion of different reconstructive procedures will fluctuate over time in an institution like ours. Nonetheless, the introduction of our ERAS protocol seemed to impact all the subgroups, as we reduced LOS, although not significantly for the LD flaps. Furthermore, it should be noted that, although the proportion of ALT flaps increased from 5% to 50%, the converse reduction in RFF flaps from 12% to 0 should be considered as the use of an RFF for oral cavity, and sinonasal reconstructions have been purposely abandoned and replaced by ALT flaps in our department.

Tracheostomy reduction has been a central part of our ERAS program, and the reduction in the number of patients who underwent tracheostomy was significantly lower (10% vs. 90%, $p < 0.001$). Minimizing invasive procedures is a core element of ERAS, and tracheostomies have previously been associated with complications and even fatalities.[7,25] Coyle et al. demonstrated the safety of replacing tracheostomies with overnight admission to the ITU, which resulted in fewer respiratory complications and shorter ITU stays (3.7 vs. 1.4 days).[12] The results of our study are in line with these findings regarding time in the ITU, and we found no change in the average duration of ITU stay compared to our TRAS cohort (31.9 vs 33.3 h, $p = 0.9$). Furthermore, we managed to reduce the duration of the surgeries by an average of almost 2 h, which may contribute to the prevention of complications.[26]

Early ambulation of the patients is another marked advance compared to our TRAS cohort, as the time to ambulation was significantly reduced from 6.4 to 3.0 days. A central part of this was the introduction of self-adhering pressure bandages for the protection of a split-thickness skin graft that was used to cover the donor site defect in FFF patients. This allowed them to ambulate directly after returning from the ITU, compared to previously, when they would have to wait for seven days to secure a graft.[7]

A MOSA strategy is pivotal for ERAS programs as the multi-focus strategy prevents the need for high-dosage of a single type of analgesics.[27] The introduction of MOSA secured that opioids were only administered on request. Some patients were dependent on high doses of opioids preoperatively as a result of tumor-related severe pain, and a phasing out plan for opioids was performed in these cases. The specific effects and reduction in opioid consumption among our patients are currently being investigated.

Our *functional discharge criteria* were monitored daily by nursing staff. In addition to assessing the daily progress of each individual patient, the data gathered helped us to identify systematic challenges that patients face across the ERAS population. Discharge criteria have become routinely incorporated in ERAS protocols and are a useful tool for monitoring the daily progress of patients.[5,16,19]

We noted a change in flap choice as the ALT flap was most commonly used, in 50% of the cases, while only 5% of the TRAS patients were used. We primarily attributed this to a change of preference in the surgical team, which was led by the same team of consultants through both periods, as the distribution of primary/secondary cancers, cancer types, location, and need for placement of a titanium foreign body to support osseous structures were similar in both groups (Tables 1 and 2).

After successful implementation of the core elements of an ERP, it is important to assess the possibilities of further improving the treatment. The ability to consume sufficient nutrition orally during the postoperative period was a major limiting factor for discharge in our patients. Problems with wound healing, re-operations, and complications related to the recipient site after free flap reconstruction can delay the time to oral nutritional intake, and some patients may be dependent on tube feeding permanently after surgery. Early identification of patients at risk of nasogastric tube dependency could prevent prolonged hospitalization and allow discharge with a nasogastric tube or a permanent PEG tube. Discharge with a nasogastric tube or establishment of a PEG tube could allow discharge of more than 80% of the patients by POD7, as this is the only remaining challenge (Fig. 1). Discharging patients with a tube is a strategy that can also be extrapolated from the published series with the shortest LOS, performed by Kiong et al. This requires a focused outpatient regimen for return to oral feeding which is important for convalescence and quality of life.[28] Additionally, introducing a focused prehabilitation regimen that includes five days of preoperative immunonutrition, lung-physiotherapy,

and a five-day activity program, may further reduce pulmonary complications and improve postoperative mobility in patients undergoing major head and neck surgery.[29]

Conclusion

By introducing a pragmatic and evidence-based ERAS protocol, we safely reduced LOS in patients undergoing microvascular reconstruction after head and neck cancer from 20.3 to 13.1 days and described strategies for further improvement.

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Ethical approval

The study was institutionally approved at Copenhagen University Hospital, Rigshospitalet.
The retrospective data extraction was approved by the Danish Patient Safety Authority.
Data handling was approved by the Danish Data Protection Agency.

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Presented at

Parts of the manuscript is accepted for presentation at the 31st EURAPS meeting in Athens, Greece, May 2021 and have been accepted for presentation at the 11th Congress for the World Society of Reconstructive Microsurgery, June, 2022.

Conflict of Interest

Nothing to disclose

References

1. Montero PH, Patel SG. Cancer of the oral cavity. *Surg Oncol Clin N Am*. Jul 2015;24(3):491–508. doi:10.1016/j.soc.2015.03.006.
2. McMahon J, Handley TPB, Bobinskas A, et al. Postoperative complications after head and neck operations that require free tissue transfer - prevalent, morbid, and costly. *Br J Oral Maxillofac Surg*. Oct 2017;55(8):809–814. doi:10.1016/j.bjoms.2017.07.015.
3. Krupski WC. The peripheral vascular consequences of smoking. *Ann Vasc Surg*. May 1991;5(3):291-304. doi:10.1007/BF02329389
4. Bonde CT, Khorasani H, Elberg J, Kehlet H. Perioperative Optimization of Autologous Breast Reconstruction. *Plast Reconstr Surg*. Feb 2016;137(2):411–414. doi:10.1097/01.prs.0000475749.40838.85.
5. Hojvig JH, Kehlet H, Bonde CT. Enhanced Recovery After Head and Neck Cancer Reconstruction With a Free Flap-What Is Next? *J Oral Maxillofac Surg*. Jan 2020;78(1):10–11. doi:10.1016/j.joms.2019.07.021.
6. 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*. May 2020;130(5):1227-1232. doi:10.1002/lary.28191
7. Hojvig JH, Pedersen NJ, Charabi BW, et al. Microvascular reconstruction in head and neck cancer - basis for the development of an enhanced recovery protocol. *JPRAS Open*. Dec 2020;26:91–100. doi:10.1016/j.jpra.2020.09.008.
8. Kehlet H. Enhanced postoperative recovery: good from afar, but far from good? *Anaesthesia*. Jan 2020;75(1):e54–e61 Suppl. doi:10.1111/anae.14860.
9. Lahtinen SL, Liisanantti JH, Poukkanen MM, Laurila PA. Goal-directed fluid management in free flap surgery for cancer of the head and neck. *Minerva Anestesiol*. Jan 2017;83(1):59–68. doi:10.23736/S0375-9393.16.11451-8.
10. Makaryus R, Miller TE, Gan TJ. Current concepts of fluid management in enhanced recovery pathways. *Br J Anaesth*. Feb 2018;120(2):376–383. doi:10.1016/j.bja.2017.10.011.
11. Wang YY, Zhang HQ, Fan S, et al. Mandibular reconstruction with the vascularized fibula flap: comparison of virtual planning surgery and conventional surgery. *Int J Oral Maxillofac Surg*. Nov 2016;45(11):1400–1405. doi:10.1016/j.ijom.2016.06.015.
12. Coyle MJ, Tyrrell R, Godden A, et al. Replacing tracheostomy with overnight intubation to manage the airway in head and neck oncology patients: towards an improved recovery. *Br J Oral Maxillofac Surg*. Sep 2013;51(6):493–496. doi:10.1016/j.bjoms.2013.01.005.

13. Joshi GP, Alexander JC, Kehlet H. Large pragmatic randomised controlled trials in peri-operative decision making: are they really the gold standard? *Anaesthesia*. Jul 2018;73(7):799–803. doi:10.1111/anae.14238.
14. Bianchini C, Pelucchi S, Pastore A, Feo CV, Ciorba A. Enhanced recovery after surgery (ERAS) strategies: possible advantages also for head and neck surgery patients? *Eur Arch Otorhinolaryngol*. Mar 2014;271(3):439–443. doi:10.1007/s00405-013-2502-4.
15. 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*. Mar 1 2017;143(3):292–303. doi:10.1001/jamaoto.2016.2981.
16. Kiong KL, Vu CN, Yao C, et al. Enhanced Recovery After Surgery (ERAS) in Head and Neck Oncologic Surgery: A Case-Matched Analysis of Perioperative and Pain Outcomes. *Ann Surg Oncol*. 2021;28(2):867–876 Feb. doi:10.1245/s10434-020-09174-2.
17. Low GMI, Kiong KL, Amaku R, et al. Feasibility of an Enhanced Recovery After Surgery (ERAS) pathway for major head and neck oncologic surgery. *Am J Otolaryngol*. 2020;41(6):102679 Nov - Dec. doi:10.1016/j.amjoto.2020.102679.
18. Bater M, King W, Teare J, D'Souza J. Enhanced recovery in patients having free tissue transfer for head and neck cancer: does it make a difference? *Br J Oral Maxillofac Surg*. 2017;55(10):1024–1029 Dec. doi:10.1016/j.bjoms.2017.10.012.
19. Coyle MJ, Main B, Hughes C, et al. Enhanced recovery after surgery (ERAS) for head and neck oncology patients. *Clin Otolaryngol*. 2016;41(2):118–126 Apr. doi:10.1111/coa.12482.
20. Won HR, An JY, Lee JJ, et al. The effectiveness of an enhanced recovery after surgery protocol in head and neck cancer surgery with free-flap reconstruction. *Ann Surg Treat Res*. Nov 2019;97(5):239–244. doi:10.4174/astr.2019.97.5.239.
21. Imai T, Kurosawa K, Yamaguchi K, et al. Enhanced Recovery After Surgery program with dexamethasone administration for major head and neck surgery with free tissue transfer reconstruction: initial institutional experience. *Acta Otolaryngol*. Jul 2018;138(7):664–669. doi:10.1080/00016489.2018.1429651.
22. Clark BS, Swanson M, Widjaja W, et al. ERAS for Head and Neck Tissue Transfer Reduces Opioid Usage, Peak Pain Scores, and Blood Utilization. *Laryngoscope*. 2020 Jun 9. doi:10.1002/lary.28768.
23. Pang J, Tringale KR, Tapia VJ, et al. Chronic Opioid Use Following Surgery for Oral Cavity Cancer. *JAMA Otolaryngol Head Neck Surg*. 2017;143(12):1187–1194 Dec 1. doi:10.1001/jamaoto.2017.0582.
24. Stone AB, Wick EC, Wu CL, Grant MC. The US Opioid Crisis: A Role for Enhanced Recovery After Surgery. *Anesth Analg*. 2017;125(5):1803–1805 Nov. doi:10.1213/ANE.0000000000002236.
25. Halfpenny W, McGurk M. Analysis of tracheostomy-associated morbidity after operations for head and neck cancer. *Br J Oral Maxillofac Surg*. 2000;38(5):509–512 Oct. doi:10.1054/bjom.2000.0310.
26. Karakida K, Aoki T, Ota Y, et al. Analysis of risk factors for surgical-site infections in 276 oral cancer surgeries with microvascular free-flap reconstructions at a single university hospital. *J Infect Chemother*. Oct 2010;16(5):334–339. doi:10.1007/s10156-010-0108-y.
27. Bonde C, Khorasani H, Hoejvig J, Kehlet H. Cyclooxygenase-2 inhibitors and free flap complications after autologous breast reconstruction: A retrospective cohort study. *J Plast Reconstr Aesthet Surg*. 2017;70(11):1543–1546 Nov. doi:10.1016/j.bjps.2017.06.007.
28. Pattamatta M, Fransen LFC, Dolmans-Zwartjes ACP, et al. Effect of direct oral feeding following minimally invasive esophagectomy on costs and quality of life. *J Med Econ*. 2021;24(1):54–60 Jan-Dec. doi:10.1080/13696998.2020.1859843.
29. Moore J, Scoggins CR, Philips P, et al. Implementation of Prehabilitation for Major Abdominal Surgery and Head and Neck Surgery: a Simplified Seven-Day Protocol. *J Gastrointest Surg*. 2020 Jul 23. doi:10.1007/s11605-020-04740-1.