JPRAS Open 26 (2020) 91–100

Contents lists available at ScienceDirect

JPRAS Open

journal homepage: www.elsevier.com/locate/jpra

Microvascular reconstruction in head and neck cancer - basis for the development of an enhanced recovery protocol ☆

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ARTICLE INFO

Article history:
Received 10 September 2020
Accepted 30 September 2020
Available online 15 October 2020

Keywords:
Head and neck
microvascular reconstruction
free flap surgery
head and neck cancer
ERAS
enhanced recovery after surgery

ABSTRACT

Introduction: Microvascular reconstructions after head and neck cancer are among the most complicated procedures in plastic surgery. Postoperative complications are common, which often leads to prolonged hospital stay. Enhanced recovery after surgery (ERAS) is a peri- and postoperative care concept with the aim of achieving pain- and risk-free surgery. It has been previously established as superior to conventional care for a wide variety of procedures, including microsurgical procedures such as reconstructions of the breast. Several ERAS protocols for microvascular head and neck cancer reconstructions have been proposed, although most of these are based on extrapolated evidence from different surgical specialties. Results from the implementation of ERAS for these procedures are inconsistent.

☆ Accepted for presentation at the 31st annual EURAPS meeting, May 2020, Athens, Greece

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https://doi.org/10.1016/j.jpra.2020.09.008

Methods: The current study investigates our clinical experience of head and neck cancer reconstruction for the period of 2014-2016 with the aim of establishing a list of functional discharge criteria. By combining these with the current published knowledge on the subject, we developed an ERAS protocol.

Results: We performed 89 microvascular procedures in the study period, of which 58 were in the oral cavity/sinuses and 31 were laryngopharyngeal. Most cases were squamous cell carcinoma (89%). The average LOS was 20.3 days in both groups. Postoperative complications included infection (37%), 30-days re-operations (19%), and re-admissions (17%). Furthermore, we identified the following discharge criteria: adequate pain relief, ambulation, sufficient nutritional intake, normal infection-related blood parameter results and absence of fever, bowel function, and closure of tracheostomy.

Conclusion: Based on our retrospective analysis and identified discharge criteria, we present an approach to develop an ERAS protocol for microvascular reconstruction after head and neck cancer.

Introduction

Patients with advanced head and neck cancer have a poor prognosis and a 5-year survival rate as low as 35-37% for T3-T4 tumors[1,2]. The treatment is complex and often requires a multidisciplinary approach including surgery. The goal, besides removal of the cancer, is to restore function and appearance. If possible, both resection and immediate reconstruction should be performed in the same surgical procedure.[3]

Reconstructions using local flaps are often inadequate in patients with progressed T-stage disease. In addition to a large defect, the common use of postoperative radiotherapy necessitates reconstruction using a free flap in a joint venture operation that often includes several departments.[3,4]

Head and neck cancer patients are often malnourished with substantial weight loss within months prior to diagnosis and typically have a history of tobacco and alcohol abuse. Postoperative ICU treatment is common along with complications[5] such as infections, re-operations, delayed wound healing, or *refeeding syndrome*[6], which is reported in up to 35% of patients undergoing major surgery for head and neck cancer.[7]

Even with successful reconstruction, many patients suffer from long-term complications such as drooling, lack of adequate clenching, permanent gastric tube feeding, insufficient wound healing, and a high recurrence rate.

Enhanced recovery after surgery (ERAS) is a pre-, peri- and postoperative care concept with the aim of achieving pain and risk-free surgery.[8] It has been established to be superior to conventional care for a wide variety of procedures including microsurgical reconstructions of the breast. [9]

Previous reports of ERAS programs for head and neck cancer patients with microvascular reconstruction have delivered inconsistent results and published ERAS protocols are primarily based on extrapolated evidence from different procedures.[10-15] Extensive ERAS protocols can be challenging to introduce successfully, and it has been previously indicated that an ERAS protocol should be procedure specific[16] and based on relatively few core elements such as improved patient information, minimally invasive surgery, goal-directed fluid therapy, early ambulation, early oral intake and multimodal opioid-sparing analgesia.[17]

Additionally, it is important for departments to review the traditional care regimen and procedural results to establish a baseline and obtain knowledge about the challenges that typically arise during postoperative hospitalization. These experiences may be utilized to identify possible reasons for continued hospitalization and create functional criteria to be fulfilled ahead of discharge.[9,18]

The present retrospective study aimed to identify relevant clinical and logistic factors in the postoperative period after head and neck reconstructive surgery. We combine these with the well-established principles of enhanced recovery after surgery[8,19] to establish a number of discharge criteria to be used when introducing an enhanced recovery program for microvascular reconstruction after head and neck cancer.[16]

Materials and methods

The study was approved by the Danish Patient Safety Authority and the Danish Data Protection Agency. We retrospectively evaluated records of all consecutive patients for procedures of reconstruction with a free flap after head and neck cancer surgery in a 3-year period (2014-2016). All procedures were performed at Copenhagen University Hospital, Rigshospitalet – a tertiary, tax-funded, public health care facility with equal availability to all patients regardless of financial status.

Patients undergoing reconstruction due to osteoradionecrosis were not included.

Demographic data and data on reconstructive procedures such as adjuvant therapies, length of stay (LOS), surgical complications, medical complications, infections (defined as the need of additional IV antibiotic treatment besides the prophylaxis or newly administered after the discontinuation of the prophylaxis) and factors limiting the discharge of patients were collected. All patient regimens were thoroughly evaluated throughout the course from referral and until the time of follow-up.

Surgical procedures

All patients were subject to a multidisciplinary procedure, including plastic surgeons, ENT surgeons, and oral and maxillofacial surgeons in many cases.

All patients underwent reconstruction after head and neck cancer with a free fibular flap (FFF), a radial forearm flap (RFF), an anterolateral thigh flap (ALT) or a latissimus dorsi flap (LD) or a combination of two of those. Flap choice was based on an individual assessment at the MDT conference. Reconstructions of the oral cavity or sinuses (OS) and laryngopharyngeal (LP) reconstructions are presented separately. Scalp reconstructions were not included in this material.

Procedures were either de novo ablative procedures after newly discovered tumors or procedures for recurrent cancers preceded by other surgical interventions or radio- and/or chemotherapy.

Most patients receiving an FFF had a split-thickness skin graft (STSG) performed and used to cover the defect at the donor site.

All patients routinely received prophylactic antibiotic treatment with cefuroxime and metronidazole for 5-7 days postoperatively.

Depending on previous treatment and oncological indications, some patients received postoperative radiation therapy with or without adjuvant chemotherapy.

Statistical analysis

Statistical analysis was performed using “R” statistics. Student’s t-tests and Fisher’s exact test were used to determine significant differences for continuous and categorical outcomes, respectively.

Single variable linear models were created to graphically illustrate the factors in the postoperative regimen that limited the patients from hospital discharge.

Results

Demographical and peri- and postoperative data

Head and neck reconstructions were performed in 89 cancer patients (61 males and 28 females) during the 3-year period. Reconstruction after cancer in the oral cavity or sinuses (OS) was performed

Table 1
Demographic and disease-related data of OS and LP microvascular reconstructions.

	OS group (58)	LP group (31)	Total (89)
Sex			
- Male (%)	37 (64)	24 (77)	61(69)
- Female (%)	21 (36)	7(23)	28 (31)
Age, years (range)	62.3 (31-84)	64.4 (44-81)	62.9 (31-84)
BMI (range)	24.5 (14-34)	22.6 (13-34)	24.9 (13-34)
Tobacco use (%)			
- Active smokers	23 (40)	7 (23)	30 (34)
- Former smokers	13 (22)	22 (71)	35 (39)
- Nonsmokers	22 (38)	2 (6)	24 (27)
Comorbidities (%)			
- Diabetes	8 (14)	1 (3)	9 (10)
- Hypertension	20 (34)	11 (35)	31 (35)
- Pulmonary disease	9 (16)	3 (10)	12 (13)
- Ischemic heart disease	3 (5)	2 (6)	5 (6)
Primary cancer/procedure (%)	33 (57)	4 (13)	37 (42)
Recurrent disease (%)			
- Previous surgery	8 (14)	0	8 (9)
- Previous radiation	6 (10)	27 (87)	33 (37)
- Both	11 (19)	0	11 (12)

Data are presented as average (range) or numerical (% of column).

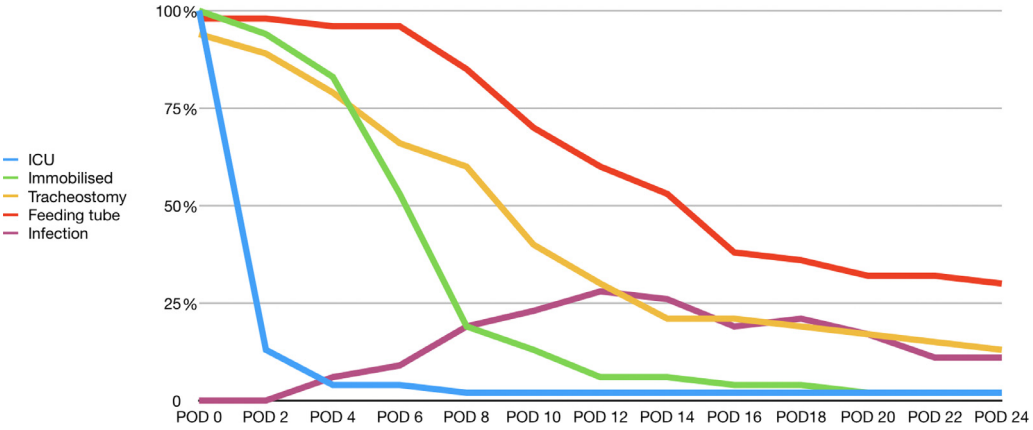

Figure 1. Graphical overview of factors responsible for keeping patients in the hospital for the oral cavity & sinus group. The graphs show the percentage of patients that remain to solve the current factor at a given time.

in 58 patients, while 31 patients underwent laryngopharyngeal (LP) reconstruction. The average age was 63 years (31-84) with an average body mass index of 24 kg/m^2 (13-34). Most patients had a history of tobacco use (62% OS and 94% LP). A detailed overview of patient demographics and procedure-related characteristics is shown in Tables 1 and 2.

The common clinical and logistical factors that needed resolution in the postoperative phase before patients were ready for discharge were ICU stay, mobilization, closure of tracheostomy, establishment of sufficient nutritional intake, and treatment of possible complications (most commonly infections). The proportion of the limiting factors for discharge is displayed graphically in Figures 1 and 2.

All patients were transferred to the ICU postoperatively and were sedated to tolerate endotracheal intubation throughout the first night after surgery. This was done to prevent compromise of the

Table 2
Procedure-related data of OS and LP microvascular reconstructions.

	OS group (58)	LP group (31)	Total (89)
Cancer location (%)			
- Oral cavity, lower*	45 (78)	0	45 (51)
- Oral cavity, upper**	10 (17)	0	10 (11)
- Sinus & nasal cavity	3 (5)	0	3 (3)
- Pharyngeal/Laryngeal	0	31 (100)	31 (35)
Tumor type (%)			
- Squamous cell carcinoma	48 (83)	31 (100)	79 (89)
- Osteosarcoma	2 (3)	0	2 (2)
- Adenoid cystic carcinoma	3 (5)	0	3 (3)
- Other	5 (9)	0	5 (6)
Operating time, avg. (min)	564 (346-838)	546 (376-797)	558(346-838)
Blood loss, avg. (ml)	1330 (170-2700)	662 (<100-1900)	1097 (<100-2700)
Blood transfusion (%)			
- SAG-M	26 (45)	6 (19)	28 (31)
- FFP	11 (13)	2 (6)	13 (15)
Flap type (%)			
- Free Fibula Flap	28 (48)	0	28 (31)
- Latissimus dorsi	15 (26)	0	15 (17)
- Anterolateral thigh	3 (5)	0	3 (3)
- Radial forearm	7 (12)	31 (100)	38 (43)
- Free fibula + LD/ALT	5 (9)	0	5 (6)
Foreign body (%)			
- Titanium plate (with FFF)	28 (48)	0	28 (31)
- Titanium plate (wrap-around)	14 (24)	0	14 (16)
- Titanium mesh	1 (2)	0	1 (1)

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

Table 3
Data regarding primary hospitalization after OS and LP microvascular reconstructions.

	OS group (58)	LP group (31)	Total (89)
Length of stay	20.3 (8-70)	20.3 (11-135)	20.3 (8-135)
ICU stay, avg. (h)	33.3 (10-212)	24.2 (17-89)	30.0 (10-212)
Nasogastric tube	58 (100)	31 (100)	89 (100)
- Duration	10 (17)	18 (58)	26 (1-126)
- After discharge	7 (12)	9 (29)	28 (31)
- Conversion to PEG			18 (20)
Tracheostomy	52 (90%)	2 (6)	
- Time to closure, days	12.4 (1-70)	123 (120-125)	16.7 (1-125)
- Provox gauge, NO	0	29 (94)	30
Time to ambulation, days	6.4 (1-19)	4.3 (2-8)	5.7 (1-19)

Data are presented as average (SD) or numerical (% of column).

airways due to postoperative swelling and to reduce the need for tracheostomies. The average duration of the ICU stay was 33 h in the OS group and 24 h in the LP group (Table 3).

Full ambulation was defined as patients being allowed to walk with or without walking aids. This was achieved on average on the seventh postoperative day for patients in the OS group (8th day for FFF and 5th day for LD/ALT) and on the 2nd or 3rd postoperative day for RFF patients. The cause for

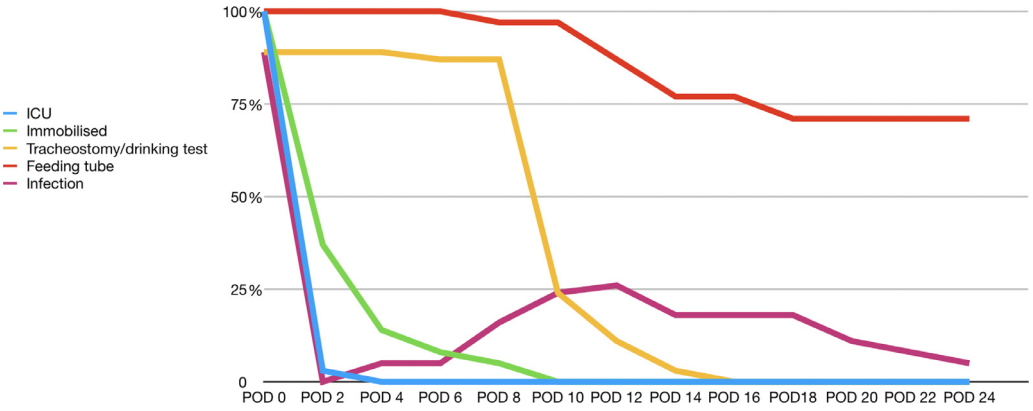

Figure 2. Graphical overview of factors responsible for keeping patients in the hospital for the laryngopharyngeal group. The graphs show the percentage of patients that remain to solve the current factor at a given time.

delayed ambulation for the FFF patients was due to monitoring of healing of the STSG at the donor site.

All but six patients (90%) in the OS group received tracheostomy. The tracheostomy was closed after an average of 12.4 days (1-770). Three patients (6%) were discharged to a different hospital with tracheostomy, and one was permanently dependent on it. In the LP group, 30 patients (97%) had placement of a speech prosthesis (Provox System in all) and 1 (3%) had a temporary tracheostomy due to hemi-laryngopharyngectomy, which was still necessary after primary discharge. An acceptable drinking test (without leakage) was achieved on the 10^{th} day on average (10-14) for LP patients.

All patients in both groups had a nasogastric tube for an average of 24 days (1-126/permanent). Prolonged nutritional assistance was required for 10 patients (21%) in the OS and 18 (56%) in the LP group. These patients were discharged with the nasogastric tube with thorough education of tube and nutritional management. Seven patients (8%) had a percutaneous endoscopic gastrostomy tube (PEG tube) prior to the procedure, three patients (3%) received it during primary hospitalization, and six (7%) after primary discharge due to prolonged nutritional issues. Of the 16 patients, seven were OS patients and nine were LP patients. Placement of a PEG tube was decided based on an individual assessment of the patients' prospect of being able to obtain a sufficient oral intake within the first weeks after primary discharge.

Average LOS was 20.3 days in both groups (range=8-70, median=17 for OS and range=11-135, median=15 for LP).

Complications

Infections were common in both groups as 33% of the OS group and 44% of the LP group required additional intravenous antibiotic treatment along with the prophylaxis prescribed at surgery. Additional antibiotic treatment was initiated based on clinical and biochemical suspicion of infection. The difference in incidence was not significant (p=0.26). A detailed overview of all complications is shown in Table 4.

Re-operations within the first 30 days were necessary in 15 patients (17%) for a total of 28 times, and the frequency of re-operations was equal for both groups (p>0.05). Re-admissions were more common in the LP group (26%) than in the OS group (10%) although not statistically significant (p=0.07).

Of the 89 patients, two patients experienced total flap loss and three showed a partial flap loss in need of surgical revision. One of these was after cardiac arrest and led to an additional RFF in order to cover the defect.

The 30-day mortality and hospital-mortality was 2% (n=1) in the OS group and 0% in the LP group.

Table 4
Data regarding complications after OS and LP microvascular reconstructions.

	OS group (58)	LP group (31)	Total (89)
Infection (%)	19 (33)	14 (45)	33 (37)
- Donor site	4 (7)	1 (3)	5 (6)
- Recipient site	8 (14)	9 (29)	17 (19)
- UTI	2 (3)	0	2 (2)
- Pulmonary	3 (5)	1 (3)	4 (4)
- Unknown	2 (3)	3 (10)	5 (6)
Re-operations 30 days, NO patients	13 (22)	4 (13)	17 (19)
- Hematoma*	2 (3)	1 (3)	3 (3)
- Flap loss*	2 (3)	0	2 (2)
- Tracheostomy problem*	3 (5)	1 (3)	4 (4)
- Flap revision*	3 (5)	1 (3)	4 (4)
- Donor-site complications*	4 (7)	0	4 (4)
- Abscess*	0	2 (6)	2 (2)
Re-admissions	6 (10)	9 (29)	15 (17)
- Infection	2 (3)	3 (10)	5 (6)
- Nutritional problem	1 (2)	4 (13)	5 (6)
- Wound revision	2 (3)	1 (3)	3 (3)
- Tracheostomy problem	1 (2)	1 (3)	2 (2)
Postoperative mortality	1 (2)	0	1 (1)

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

Table 5
List of our functional discharge criteria.

List of functional discharge criteria	
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 & normal biochemical infection parameters
Closure of tracheostomy	Closure or thorough education in self-management of tracheostoma
Bowel function	Stool and flatulence passing

Two patients suffered from cardiac arrest due to bleeding from the tracheostomy, one of them died and represents the abovementioned single death in the cohort.

Discussion

Based upon this retrospective review, we could identify factors responsible for keeping the patients hospitalized after head and neck reconstruction.

The main factors were delayed post-operative ambulation, infections (need for additional antibiotic treatment), use and closure of tracheostomy (and drinking test for LP patients) and tube dependency (insufficient nutritional intake). This provides valuable knowledge about the areas of intervention for enhanced patient recovery leading to the development of a list of functional discharge criteria for future implementation of an ERAS-protocol.

The list of developed criteria includes full ambulation, sufficient nutritional intake, bowel function, sufficient pain relief, normal infection-related blood results, absence of fever, and closure of tracheostomy (Table 5). The defined discharge criteria are largely comparable to those of previous studies.[10,11,18,20]

It has previously been advocated that ERAS programs should evolve around the implementation of five to six core elements (*improved patient information, goal-directed fluid therapy, early nutritional intake, early ambulation, minimally invasive surgery, and multimodal opioid-sparing analgesia*) and after

successful implementation, further development can progress.[17] In addition, procedure-specific recovery challenges may be apparent and adjusted for.

Procedure-specific *patient information* should be designed and be in concordance with the expected LOS after surgery. It is important to align expectations with the patient prior to surgery as it may be unsettling for many patients to be discharged after 10 days if they expect to stay in the hospital for 2-3 weeks.[9]

Prevention of surgical complications and minimizing surgical stress (*minimally invasive surgery*) is a key endpoint for ERAS and a central challenge to overcome in our study (Figures 1 & 2). It is sought to be achieved by shortening the duration of surgery[21] through the use of computer-assisted design and modeling in surgical planning (CAD/CAM)[22,23], optimizing a multimodal opioid-sparing regimen including high-dose glucocorticoid, and minimizing the use of temporary tracheostomies, which is a major limiting factor for discharge. Instead of routinely performing a tracheostomy for most patients, an individual approach should be taken, and by monitoring patients overnight at the ICU, unnecessary tracheostomies may be avoided, thereby preventing possible infections and other serious adverse events related to these.[24,25] To keep ICU stay as short as possible, patients should be assessed from the beginning of POD1 and be transferred back to the primary ward as soon as respiratory status is stable.

Postoperative infections were common in our study (33-44%) and were present in 25% of the patients on POD10. *Early ambulation* will hopefully help prevent some of these, especially pneumonia and urinary tract infections.[10,26] Additionally, it will prevent constipation by promotion of bowel movement and function and prevent thromboembolic complications.[27,28]

Major surgical procedures have been associated with urinary tract infections in head and neck cancer patients[29], and early catheter removal is associated with lower rates of urinary tract infections for patients undergoing other types of surgical procedures.[30] Catheter removal on POD1 is already a part of our postoperative care regimen.

Improved focus on *nutritional intake* in these patients may reduce the time of postoperative convalescence and prevent the development of refeeding syndrome, which although relatively common, is not often reported and may have been overlooked in previous studies.[7]

Opioid-spring multimodal analgesia has previously been shown to promote patient's performance status and reduced morphine-related constipation.[31] Introduction of COX-II inhibitors as a replacement for NSAIDs has previously shown promising results in ERAS-regimens for microvascular breast reconstruction and is associated with lower risk of post-operative hematoma.[20]

Our patients had an average postoperative LOS of almost 3 weeks (20.3 days for both groups), which is comparable to previous reports of similar patient cohorts.[10,11,14,32] By adhering to the suggested interventions, we expect the patients to meet the functional discharge criteria within 10-14 days.

Although the concept of enhanced recovery after surgery was established in the late 1990s, the application of ERAS in head and neck cancer reconstructions is relatively limited and only a few studies have been published.[10-12,14,15]

Several guidelines, not including clinical results, for ERAS for head and neck cancer patients have been proposed over the past decade. Most notably are the *consensus guidelines* published by the Enhanced Recovery After Surgery Society in 2017[13] although other programs with some similarities have been published.[10-12,14,15,33] As many of these protocols are extensive and require extensive resources, challenges may arise upon implementation. To establish the effects of a given ERAS program, it is necessary to verify the feasibility of these programs through clinical trials based upon the question "Why in hospital?".[15,34] The effectiveness of the individual interventions will have to be tested through controlled trials before postulating the effect on head and neck cancer patients.

In 2014, Yeung et al. published the results after the introduction of a clinical care pathway for patients undergoing major head and neck reconstruction and successfully reduced pulmonary complications, including pneumonia, by more than 50% and reduced the LOS from 21.6 days to 14.2 days.[10]

Coyle and colleagues recorded a LOS of 14.6 days after the implementation of an enhanced recovery program[11], and Bater et al. showed reduced LOS for patients needing reconstruction of bony defects from 14 to 10 days but did not observe a significant reduction for patients with soft-tissue

defects only.[12] The most recent study by Won et al. demonstrated a significant decrease in LOS from 59.7 days to 30.9 days.[15] Even though the LOS is long in the pre-ERAS as well as the ERAS group, the authors still present an absolute reduction in LOS of 29 days and a relative reduction of almost 50%. This show a significant effect of their ERAS protocol, which is very similar to other previously published.

Two studies did not demonstrate a reduction in LOS or other endpoints such as complication rate or number of readmissions[5,14] which was described as disappointing by the authors as their ERAS protocol were much alike the ones described in other studies and guidelines.[14]

Although many of the interventions used in the studies above are identical, such as improved patient information, improved nutritional intervention, goal-directed fluid-therapy, early ambulation, and discharge criteria/functional discharge goals, some level of heterogeneity still exists between the described ERAS protocols. Identical care practices, or thoroughly described interventions in reports have previously been suggested to facilitate the interpretation of results across centres.[13,34]

Despite the current study's limitation by its retrospective nature, it identified major and consistent challenges that patients face when undergoing microvascular reconstruction after head and neck cancer.

The heterogeneity of the patients and procedures makes the comparison with previous reports difficult. Among the published studies, there is a significant variability in the specificity of the reporting regarding descriptive data of the included patient cohorts and outcomes. The outcome is dependent on the included patients, which in our case represents all layers of society as our institution is free, tax-funded tertiary center. This underlines the previously suggested need for consensus in the reporting as it is necessary for appropriate knowledge-sharing between researchers.[13,34]

Conclusion

We have described the most common postoperative challenges for recovery in patients undergoing microvascular reconstruction for head and neck cancer and defined the following functional discharge criteria: full ambulation, sufficient nutritional intake, bowel function, sufficient pain relief, normal infection-related blood results, absence of fever, and closure of tracheostomy.

These findings serve as the basis for the future core of our ERAS program.

Declaration of Competing Interest

None

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jpra.2020.09.008.

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