European Archives of Oto-Rhino-Laryngology (2019) 276:2577–2584
https://doi.org/10.1007/s00405-019-05526-1

HEAD AND NECK

Total laryngopharyngectomy with circumferential reconstruction: Helsinki institutional study

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Received: 16 April 2019 / Accepted: 18 June 2019 / Published online: 25 June 2019

Abstract

Purpose Surgical complications after total laryngopharyngectomy (TLP) are common, reconstruction is challenging, and patients often lose their ability to swallow and speak. To evaluate these aspects, we analysed outcome after TLP.

Methods We reviewed all patients who underwent TLP and subsequent circumferential pharyngeal reconstruction through 2004–2017 at the Helsinki University Hospital.

Results For the 26 eligible patients, TLP was the primary treatment for 11 and salvage surgery for 15, followed by reconstruction with free flaps in 22 patients and pedicled flaps in 4. An early (≤ 30 days) pharyngocutaneous fistula developed in seven patients (27%; median time 13 days; range 6–26), and a late (> 30 days) fistula in five patients (19%; median time 370 days; range 46–785). In addition, ten patients (39%) developed an oesophageal stricture. Four patients (15%) resumed full oral feeding. A speech prosthesis was inserted for 15 patients (58%) and most of them could produce intelligible speech. We found acceptable survival figures for patients undergoing TLP both as a primary treatment and as salvage procedure: the overall survival at 1 year was 82% and 67%, and at 5 years 33% and 27%, respectively. Disease-specific survival at 1 year was 90% and 70%, and that at 5 years was 45% and 43%, respectively.

Conclusions Despite fair survival, TLP carries a high risk for postoperative complications with limited functional outcome, thus necessitating cautious patient selection and surgical experience.

Keywords Larynx cancer · Hypopharynx cancer · Free flaps · Fistula · Stricture · Survival

Introduction

Total laryngopharyngectomy (TLP) is indicated as a primary or salvage treatment for some hypopharyngeal and advanced laryngeal cancers [1]. Primary wound healing is of utmost importance to permit timely administration of possible adjuvant therapy [1, 2]. Despite complex surgery and adjuvant therapy, patients tend to have unfavorable prognosis with estimated 5-year disease-specific survival (DSS) between 25 and 56% [3, 4].

Patients often have nutritionally compromised general state or/and have undergone radiotherapy (RT) or chemoradiotherapy (CRT) portending a higher risk of complications [5, 6, 7]. The most common complications after TLP are pharyngocutaneous fistula and stricture formation [2, 8]. The reconstruction method after TLP remains controversial [9]. Pedicled musculocutaneous flaps and free visceral or fasciocutaneous flaps have been used for the reconstruction of the circumferential hypopharyngeal defects and creation of the neoconduit for digestive continuity [1, 5, 10]. Currently, free flaps are preferred, although none of them outperforms. They provide better surgical and functional outcome with less complications than pedicled flaps [11], which should be reserved for revision procedures or for neck skin resurfacing [12]. Anterolateral thigh (ALT) flap, radial forearm flap, and jejunum flap have become most commonly used reconstructive options with comparable results [1, 9].

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In the current study, we aimed to retrospectively assess the reconstructive methods, surgical complications, survival, and functional outcome of patients who underwent TLP with subsequent circumferential pharyngeal reconstruction at our institution.

Materials and methods

We reviewed all patients who underwent TLP and subsequent circumferential (360°) hypopharyngeal reconstruction from January 1, 2004 until December 31, 2017 at the Departments of Otorhinolaryngology—Head and Neck Surgery and Plastic Surgery, Helsinki University Hospital, Helsinki, Finland. The treatment for all patients had been evaluated by the institutional multidisciplinary head and neck tumor board. Contraindications for TLP are distant metastasis, patient denial, and poor general health not allowing major surgery such as TLP. All patients were classified as M0 by performing a PET-CT or CT of thorax and upper abdomen. At our institution, otorhinolaryngologists are responsible for tumor resection and neck dissection, and plastic surgeons harvest the flap and perform vessel anastomosis. The selection of the flap was made by the plastic surgeon in charge of the reconstruction. Both teams participate in designing and creating the neopharynx. According to our protocol, prophylactic antibiotic and proton pump inhibitor treatment is routinely used when performing TLP.

Hospital records were reviewed for patient and tumor characteristics, treatment, any early and late complications, survival, and functional outcome. We follow an institutional follow-up algorithm for all head and neck cancer patients up to 5 years. Physiotherapists, speech therapists, and dieticians are actively involved in the treatment and rehabilitation. Pharyngocutaneous fistulas were divided into two groups based on the time point of its development after surgery: early fistulas within the first 30 days and late fistulas after 30 days after reconstruction [13]. Data on functional results concerning speech and swallowing were obtained from the follow-up records. Assessment of verbal communication was done 6 months after tracheoesophageal puncture (TEP) and voice prosthesis placement, and was grouped as: understandable, understandable with difficulties, and not understandable. Swallowing was evaluated 6 months after the reconstructive surgery or at last follow-up if the patient died within the first 6 months and was grouped as: full oral intake, partly percutaneous gastrostomy (PEG)-dependent, and totally PEG-dependent.

This was a single-institution retrospective study approved by the Helsinki University Hospital Review Board (Sect. 3; HUS/66/2018). No ethical issues were raised.

Statistical analysis

IBM SPSS v23 (USA) software was used for the statistical analysis. Obtained data were demonstrated as mean and/or median values. Kaplan–Meier method was used to express overall, disease-specific survival and loco-regional tumor control rates. Non-parametric Mann–Whitney *U* test was used to compare variables among different groups (primary, residual or recurrent tumors; type of the flap; operative surgeons; status of the fistula or stricture; status of speech and swallowing), but Spearman's rank correlation coefficient was calculated to determine correlation among variables. Univariate regression analysis was done to predict fistula and stricture relation based on the following variables: previous surgery, pre- and postoperative RT or CRT, operation time, length of stay in the intensive-care unit (ICU), neck resurfacing, age-adjusted Charlson Comorbidity Index (CCI), TEP, and smoking. Cox regression analysis was done to analyze related variables such as tumor resection margins, extranodal extension, perineural or lymphovascular infiltration, growth through laryngeal cartilage, pN class, grade and CCI for prediction of survival and recurrence. The multivariate regression analysis could not be performed due to the small number of patients and many variables. All evaluates were two-tailed and value of $P < 0.05$ was considered statistically significant.

Results

General aspects

During the study period, 27 patients underwent TLP and circumferential pharyngeal reconstruction. One patient with locally advanced papillary thyroid carcinoma was excluded from the analysis due to lack of follow-up data. Thus, 26 patients with squamous cell carcinoma (SCC) formed the study cohort. Patient characteristics, treatment, and outcome data are shown in Table 1. There were 19 males and 7 females. Median age was 60.5 years (range 47–79). Eight patients had concomitant cardiovascular or respiratory diseases, while two patients had been treated previously for other malignancies. Age-adjusted CCI ranged from 2 to 10.

Localization of the primary tumor was as follows: the hypopharynx ($n = 16$), the larynx ($n = 9$), and the oropharynx ($n = 1$; recurrence after previous surgery). TLP with reconstruction was performed as a primary treatment for 11 and as salvage surgery for 15 patients. Of these 15 patients, residual tumor within 3 months after the primary treatment was diagnosed in eight patients, while seven

Table 1 Patient characteristics, treatment, and outcome data

No.	Age	Sex	Tumor status	Tumor site	Flap	ST, min	ICU days	PCF occurrence, treatment	Oesophageal stricture	Nutrition	TEP, speech analysis	Follow-up status, length of fu
1	53	M	Primary	L	ALT	n/a	n/a	–	Stricture	PEG	–	DOD, fu-57 mo
2	61	F	Recurrent	L	ALT	n/a	7	–	–	PEG	–	NED, fu-106 mo
3	55	M	Residual	H	ALT	n/a	9	106th day, conservative	–	PEG	–	DOD, fu-4 mo
4	60	M	Recurrent	L	ALT	317	8	–	Stricture	Per os	84th day, U-d	NED, fu-82 mo
5	60	M	Residual	H	f-LD	513	5	–	–	PEG	71st day, U	DOD, fu-16 mo
6	78	M	Primary	L	p-LD	512	0	–	–	Both	–	DOD, fu-4 mo
7	47	M	Residual	H	p-LD	456	3	–	Stricture	Both	68th day, U	NED, fu-90 mo
8	59	F	Recurrent	L	ALT	643	15	–	Stricture	Per os	79th day, U	NED, fu-65 mo
9	63	M	Primary	H	ALT	529	4	–	Stricture	Both	232nd day, U	AWD, fu-64 mo
10	62	F	Primary	L	f-LD	271	6	9th day, revision	–	PEG	–	DOC, fu-2 mo
11	71	M	Recurrent	L	IMA	584	10	13th day, revision	–	PEG	–	DOC, fu-51 mo
12	68	M	Recurrent	L	ALT	751	7	–	–	Per os	308th day, U	DOD, fu-16 mo
13	54	M	Residual	H	f-LD	392	5	575th day, revision	Stricture	Both	95th day	DOC, fu-22 mo
14	53	M	Primary	H	ALT + pLD	426	4	9th day, revision	Stricture	PEG	359th day	DOC,fu-26 mo
15	58	M	Residual	H	ALT	590	5	–	–	PEG	P, U-d	DOD, fu-13 mo
16	74	M	Recurrent	H	ALT + PM	403	4	–	Stricture	PEG	126th day	DOD, fu-7 mo
17	67	M	Residual	H	ALT	496	5	6th day, conservative	–	PEG	–	DOD, fu-4 mo
18	59	F	Recurrent	L	ALT + PM	702	5	43rd day, conservative	–	PEG	43rd day	DOD, fu-17 mo
19	69	M	Primary	H	ALT	567	5	785th, revision		PEG	221st day, U	NED, fu-40 mo
20	57	M	Primary	H	ALT	614	5	–	Stricture	PEG	–	AWD, fu-41 mo
21	64	M	Residual	H	ALT + PM	534	5	–	–	PEG	–	DOC, fu-5 mo
22	64	F	Primary	H	J + PM	423	3	–	–	PEG	172nd day, U	AWD, fu-22 mo
23	57	M	Primary	H	RFF	561	25	9th day, revision	–	Per os	195th day, U	NED, fu-20 mo
24	67	F	Primary	H	pLD	600	0	26th day, revision	Stricture	PEG	–	NED, fu-16 mo
25	58	M	Primary	O	ALT	569	4	370th day, revision	–	PEG	136th day, –	NED, fu-15 mo
26	79	F	Residual	H	ALT	491	21	7th day, revision	–	PEG	–	DOC, fu-0 mo

M male, *F* female, *L* larynx, *H* hypopharynx, *O* oropharynx, *ALT* anterolateral thigh, *f-LD* free latissimus dorsi, *pLD* pedicle latissimus dorsi, *IMA* internal mammary artery, *PM* pectoralis major, *J* jejunum, *ST* surgery time, *n/a* not available, *ICU* intensive-care unit, *PCF* pharyngocutaneous fistula (days after TLP), *PEG* percutaneous endoscopic gastrostomy, *Peros* nutrition, *both* PEG and Per os nutrition, *TEP* tracheoesophageal puncture (days after TLP), *U-d* understandable but difficult, *U* understandable, *P* primary, *fu* follow-up, *DOD* died of disease, *NED* no evidence of disease, *AWD* alive with disease, *DOC* died of other causes, *mo* months

experienced a recurrence exceeding a follow-up period of 3 months. The previous treatment for patients with residual and recurrent tumors included: CRT with curative intent ($n=7$), total laryngectomy and reconstruction with pedicled internal mammary artery flap and postoperative CRT ($n=1$), RT with curative intent ($n=4$), total laryngectomy and partial pharyngectomy, and reconstruction with pectoralis major pedicled flap and postoperative RT ($n=1$), and laser surgery with postoperative RT ($n=2$).

Median follow-up time for the whole cohort was 18.5 months (range 0–106) and 41 months for the surviving patients (range 15–106).

Treatment aspects

The number of individual plastic surgeons who performed reconstructive surgery and their complication rate are shown in Table 2. Mean total operation time was 526 min (range 271–751) for free flaps, and 538 min (range 456–600) for pedicled flaps. Plastic surgeon who performed only three TLP reconstructions had longer operation time ($U=3000$; $p=0.016$) compared to the plastic surgeon who did ten of them.

Free flaps were used for 22 patients (85%). ALT was the most commonly used free flap ($n=17$; 77%). Other flaps included free latissimus dorsi flap ($n=3$), radial forearm flap ($n=1$), and jejunum flap ($n=1$). Pedicled flaps were used for four cases including latissimus dorsi flap ($n=3$) and internal mammary artery flap ($n=1$). In addition, a pedicled flap was utilized for neck skin resurfacing for five patients (19%) in conjunction with free flaps. Neck dissection was performed for 22 patients (85%), and it was unilateral in 15 and bilateral in seven patients.

Median hospitalization time was 20.5 days (range 13–74), including median ICU admission rate of 5 days (mean 6.8 days; range 0–25). One patient with a pedicled latissimus dorsi musculocutaneous flap reconstruction was treated in the ward only.

Four patients received CRT and six patients received RT after TLP with a mean dose of 65 Gy (range 60–70).

Histopathological aspects

Metastatic regional lymph nodes were found in 15 patients (68%) with extranodal extension in seven patients (47%). Resection margins were positive in 8 cases (31%), close (≤ 5 mm) in 13 cases (50%), and free (>5 mm) in 5 cases (19%).

Tumor invasion through laryngeal cartilages was found in 13 patients, lymphovascular invasion in three patients and perineural invasion in 10 patients.

Early complications within the first 30 days after TLP

One pedicled internal mammary artery flap was lost due to necrosis and was replaced with a radial forearm flap. None of the free flaps was lost.

Necrotic tissue in the tracheostoma was observed in three patients (12%): one without further consequences (patient no. 15), one with late oesophageal stricture (no. 16), and one with early pharyngocutaneous fistula (no. 17). They were all treated conservatively.

Early pharyngocutaneous fistula developed in seven patients (27%, median time 13 days; range 6–26). Five of them had a free-flap reconstruction (23%) and two had a pedicled flap (50%). Of the 17 patients with ALT flaps, a fistula developed in 3 (18%). Revision surgery was performed for six patients in a median time of 5 days (range 2–15) after the occurrence of the fistula. The risk for a fistula showed no correlation with any other variable, and no difference in fistula rate between primary and salvage TLP. One patient developed mediastinitis (patient no. 10).

Table 2 Operative details and complications per plastic surgeon

	Operations, *n*	mST (min)	Flap loss, *n*	Early fistula, *n*	Late fistula, *n*	Stricture, *n*	Stoma necrosis, *n*
Plastic surgeon							
PS 1	10	469	0	2	1	5	1
PS 2	6	559	0	1	1	2	1
PS 3	4	625	0	2	1	1	1
PS 4	3	n/a	1	0	1	2	0
PS 5	1	567	0	0	1	1	0
PS 6	1	561	0	1	0	0	0
PS 7	1	491	0	1	0	0	0

PS plastic surgeon, *n* number, *mST* mean surgery time, *min* minutes, *n/a* not available

Late complications after 30 days following TLP

A late pharyngocutaneous fistula developed in five patients (19%, median time 370 days; range 46–785). All of them had had a free-flap reconstruction and postoperative RT (patient no. 3, 13, 18, 19, 25).

Oesophageal stricture occurred in ten patients (38%); for two patients with a pedicled flap (50%) and for eight patients with a free flap (36%), of which seven patients (47%) had an ALT reconstruction. No correlation was observed between fistula formation and stricture. A strong correlation was found between stricture formation and survival time ($r_s = 0.5$; $p = 0.008$) indicating that the risk of developing a stricture continues during follow-up.

Recurrence and survival rate

One patient died in the ICU on the 21st day after surgery due to progression of cardiovascular insufficiency. Hence, the perioperative mortality rate in our study was 4%.

Thirteen patients experienced a recurrence in a median time of 6 months (mean 15.5 months; range 2–57), five patients in the primary TLP group, and 8 in the salvage surgery group. The distribution of the recurrences was as follows: local ($n = 2$), local and regional ($n = 1$), distant ($n = 6$), local and distant ($n = 2$), and local, regional, and distant ($n = 2$). Palliative treatment was offered for 12 of them, of whom nine died of disease and three were alive with disease at the end of follow-up (64, 41, and 22 months). One patient received additional surgery with curative intent for local recurrence and has remained disease free during the 60-month follow-up after recurrence. Median time from recurrence till death was 64 days (range 15–462). Six patients died due to other causes.

Estimated loco-regional control (LRC) rates in primary and salvage patient groups for 1 year were: 90% and 78%, for 3 years: 75% and 46%, and for 5 years: 25% and 47%, respectively (Fig. 1). A correlation was seen between local recurrence and presence of metastatic lymph nodes ($r_s = 0.409$; $p = 0.042$). Estimated 1-year overall survival (OS) in primary and salvage patient groups were 82% and 67%, 3-year OS 66% and 33%, and 5-year OS 33% and 27%, respectively (Fig. 2). Estimated 1-year DSS in primary and salvage patient groups were 90% and 70%, 3-year DSS 90% and 43%, and 5-year DSS 45% and 43%, respectively

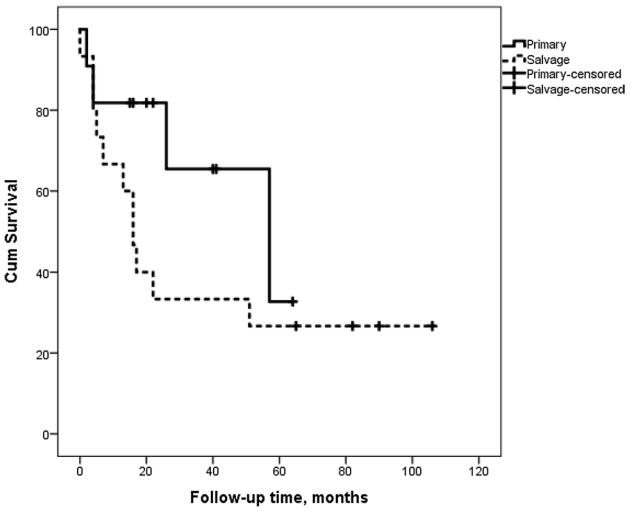

Fig. 2 Overall survival after primary and salvage total laryngopharyngectomy

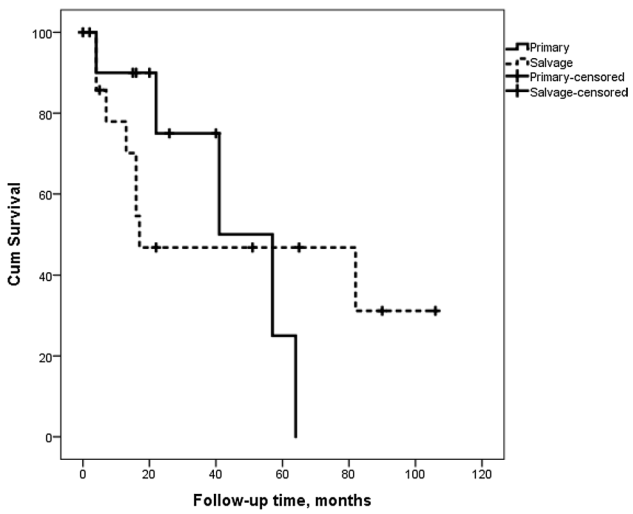

Fig. 1 Loco-regional control after primary and salvage total laryngopharyngectomy

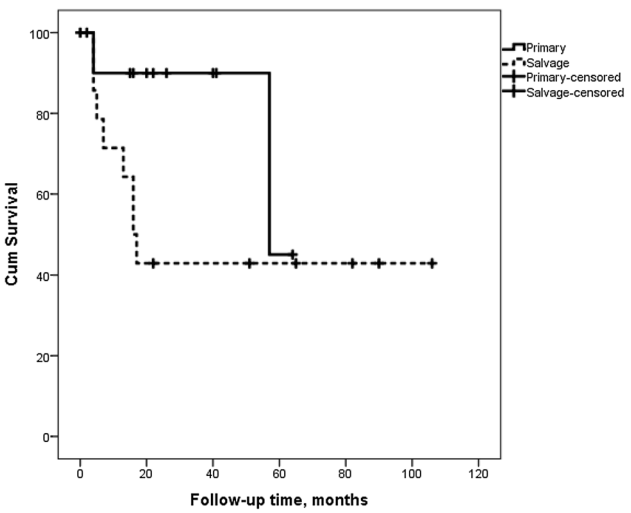

Fig. 3 Disease-specific survival after primary and salvage total laryngopharyngectomy

(Fig. 3). Cox regression analysis showed that CCI (HR 6.950, $p=0.001$) and age (HR 1.087; $p=0.022$) related to poorer OS.

Speech and swallowing

Fifteen patients received a speech prosthesis. Primary TEP and speech prosthesis placement were performed in one patient, while, in 14, it was done secondarily, with a median of 126 days postoperatively (range 43–359). Speech evaluation was available for 10 of them at 6 months after TEP. Intelligible speech was achieved in eight patients (80%), while speech in two patients was understandable with difficulties. Two patients had TEP-related fistula (patient no. 13 and no. 25).

Six months after TLP and reconstruction, four patients had resumed full oral feeding (15%), four patients (15%) were able to swallow, but needed gastrostomy as support, and 18 patients were totally PEG-dependent (69%).

Discussion

We present a series of 26 consecutive patients who underwent primary or salvage TLP and circumferential pharyngeal reconstruction. The 5-year DSS in primary and salvage TLP patient groups were 45% and 43%, respectively, which can be regarded as acceptable or even good in this patient group. Similar results were demonstrated in a study by Clark et al. in which 5-year DSS figures after primary and salvage TLP were 45% and 40%, respectively [14]. Chen et al. reported even higher 5-year DSS (54%) after salvage laryngopharyngectomy [2]. The perioperative mortality rate in our study was 4%. It fits well within the range of 0–8% reported in the current literature, where the highest mortality figures have been reported in patients undergoing visceral flap harvest from the abdomen for circumferential pharyngeal reconstruction [10, 15, 16].

Pharyngocutaneous fistula is the most common complication during early postoperative period, which often prolongs the length of hospital care. We found early fistulas in 27% of all patients, coinciding with the previous studies showing saliva leakage in up to 25% of patients after circumferential pharyngeal reconstructions [17, 18–20]. Chepeha et al. recently published a multicenter study on patients undergoing salvage TLP and reconstruction with free flaps and found a fistula rate of 39% [7]. In our study, fistula rate for salvage TLP was 20%. Parmar et al. reported that the highest fistula rate was after ALT flaps, in which saliva leakage occurred in 50% of patients, even though salivary bypass tube (SBPT) was kept for 2 weeks [8]. In our series, the fistula rate after ALT flap was 18%, and we did not use SBPT. Piazza et al. recently argued that the use of SBPT for 45 days may have an impact on the decreased fistula rate from 26 to 7% ($p<0.001$) [21]. Our study shows that fistulas may appear within days or years after TLP, similarly presented in another study where late fistulas occurred in 15% of the cases between 30 days and 4 years postoperatively [13]. We found late fistulas in 19% of the patients, and all had history of RT. Few articles discuss possible risk factors for late fistulas: these include reflux that delays wound healing [22] and leakage at the site of the anastomosis in the neopharynx [13, 23].. We found no difference in the frequency of fistulas between patients with or without a history of RT. On the contrary, Tsou et al. reported in a series of 160 patients that, after preoperative RT, the fistula rate for primary TLP is 21% and for salvage TLP 58% [24]. Perez-Smith et al. emphasized that the risk of complications increases with less experience [10]. This was obvious also in the present study, since surgeons performing fewer TLPs had more fistulas.

Voice prosthesis was placed for 15 (58%) patients, and usually at a second stage. Of the ten patients with data available, eight were able to produce intelligible speech. The most common reason for omitting voice prosthesis was early recurrence of the disease. Over 90% success rates in achieving fluent understandable speech for secondary TEP and voice prosthesis insertion after TLP have been reported [1, 25]. Lewin et al. reported fluent speech in 90% of their patients with ALT flaps and a primary voice prosthesis placement [26]. Their series showed no difference in complication rates between primary or secondary stage procedures, but suggest to avoid TEP in patients with extended resection to the oropharynx or lower esophagus, with severe cardiopulmonary diseases, or for patients unable to take care of the prosthesis [26]. Less satisfactory results have been presented among patients with jejunum flaps: understandable speech outcome varies between 22 and 78% [10, 17, 25]. Taken together, it seems that, in most patients, TEP and voice prosthesis placement is a feasible method for voice restoration after pharyngeal reconstructions with fasciocutaneous flaps.

In our study, oesophageal stricture rate was 38% for all patients, and 47% for patients who underwent reconstruction with ALT flaps, which is more than in other studies (13–40%) [2, 6, 12, 13, 20, 27]. Stricture rates after jejunum flap reconstruction vary between 2 and 31% [10, 17, 27]. Some authors state that previous fistualization and postoperative RT are main predisposing factors for strictures [6, 18, 27], and Murray et al. reported stricture formation in only 14% of patients without the previous saliva leakage [28]. We did not detect any correlation between RT or previous fistula and the risk of stricture formation, although, due to the small size of our cohort, we are unable to draw definitive conclusions. The mean follow-up time in our study was 31 months, which might partly explain the high rate of strictures. Others have reported stricture rate of 13% during a mean follow-up time of 16 months [20] and 30% during a

follow-up of 19 months [12], and thus, more strictures may develop in follow-up.

In our series, only four (15%) patients achieved total independency from PEG at 6 months postoperatively. The previous studies have reported PEG-independency to vary between 16 and 91% after ALT flap reconstructions [1, 2, 18, 25–28], while after jejunal flap in 62–95% of patients [10, 17, 27], although evaluation of oral intake was evaluated later in follow-up in a mean time of 12–82 months after surgery [1, 2, 17, 26, 27]. In addition, in some studies, patients with recurrence or flap loss have been excluded from the analysis [18, 25]. In addition to the earlier point of evaluation, the relatively high complication rate in the present study assumedly decreases success of oral intake.

The mean length of ICU care was 6.8 days. The lack of a step-down unit in our institution may partly influence this, since, after ICU, treatment continues in a regular ward. Longer stay in the ICU may increase complications. Yu et al. reported significantly shorter stay of 1.9 ± 2.2 days with less complications [18]. Murray et al. concluded in their review that patients might spend unnecessary long time in the ICU, which could be associated with local policies and practices among health care units [29].

Conclusion

We demonstrated acceptable survival figures for 26 patients who underwent TLP with subsequent circumferential pharyngeal reconstruction as a primary or salvage procedure. The frequency of pharyngocutaneous fistulas and oesophageal strictures was, however, high contributing to the poor functional outcome. Only few patients resumed full oral intake, but most patients with a voice prosthesis could produce intelligible speech. TLP can be considered justifiable for patients where all other options for curative treatment are spent to maintain quality of life. Due to the limited number of TLPs, the procedure requires to be centralized among institutions to experienced surgeons while keeping training of younger followers in mind.

Acknowledgements This study was supported by the Helsinki University Hospital Research Funds.

Funding This study was supported by the Helsinki University Hospital Research Fund.

Compliance with ethical standards

Conflict of interest None of the authors have a personal conflict of interest to declare.

Ethical approval This article does not contain any studies with human or animal participants performed by any of the authors. This research involved only patient charts. For this type of study, formal consent is not required.

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