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Comparisons of clinical and functional outcomes of different reconstructive methods for the hypopharyngeal defect

Song I. Park[1], Sung Yong Choi[1], Chung-Hwan Baek, Young-Ik Son, Han-Sin Jeong, Man Ki Chung*

Departments of Otorhinolaryngology-Head and Neck Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea

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ABSTRACT

Background: To compare clinical and functional outcomes of different reconstructive options for a hypopharyngeal defect after head and neck cancer surgery.
Methods: We retrospectively analyzed 127 cases who had undergone hypopharyngeal reconstruction, as either pedicled (25 cases), fasciocutaneous free flap (FCFF) (41 cases) or visceral flap (61 cases).
Results: Overall incidence of flap compromise was 10.2% (13 cases), and there were no statistically significant factors associated with flap compromise. Fistula or stenosis occurred in 36.2% (46 patients) and 23.6% (30 patients), respectively. Salvage surgery increased the risk of fistula formation (OR 2.93, 95% CI 1.32–6.52, $p < 0.01$), whereas FCFF showed a protective effect for stenosis, compared to pedicled flap (OR 0.09, 95% CI 0.01–0.47, $p < 0.01$).
Conclusion: Outcomes of hypopharynx reconstruction can be successful if different flap options are used appropriately according to the type of defect and previous treatment history of the patient.

Introduction

Reconstruction for hypopharynx defects with or without oropharyngeal and cervical esophageal defects, after cancer surgery or post-radiotherapy complication, is still challenging [1]. Hypopharynx reconstruction requires not only restoring the continuity of the track but also maintaining the functions of the hypopharynx as a digestive pathway [2]. Also, possible morbidities, such as a fistula or stricture formation after reconstruction, can prolong the in-hospital stay and rehabilitation process and can delay the appropriate timing of adjuvant therapy. Considering that reconstruction failure can worsen the short- and long-term prognosis of this specific group of cancer patients, careful planning and implementation of a reconstructive procedure is essential [3].

Depending on the types and extents of hypopharyngeal defects, the patient's condition, and the preference of the institution, various options are available, including pedicled flap (cutaneous, myocutaneous), fasciocutaneous flap, or visceral flaps. Each reconstruction method has its advantages and limitations [4]. Pedicled flaps from the supraclavicular, latissimus dorsi or pectoralis major muscle are still useful options for the defects in the head and neck, including the hypopharynx. Even in patients with significant morbidities, it can be performed quickly with high reliability and success rate [5,6]. A fasciocutaneous free flap (FCFF) for the hypopharyngeal defect can be obtained from the radial forearm or anterolateral thigh, and it shows many advantages over other reconstructive options, in terms of lower fistula and stricture rate than for a pedicled flap, and less post-surgical morbidities than for a visceral flap [7–10]. A visceral conduit is also quite useful for a circumferential hypopharyngeal defect, and a mostly free jejunal autograft is a better option than colon interposition [11,12].

Currently, there is not enough data comparing the outcomes between pedicled flaps, fasciocutaneous free flaps, and visceral flaps directly, and investigating the possible prognosticators to be used as a guideline for the optimal reconstructive approach. Also, in the era of chemoradiation therapy, the effects of the previous radiotherapy or the situation of salvage surgery on clinical decision making and post-operative complications have not been appropriately assessed [2,13]. The aim of this study is, by reviewing our similar series of patients, to compare clinical and functional outcomes between three different types of reconstruction options for the hypopharyngeal defect, in order to provide a useful and up-to-date assessment of the advantages and limitations of each flap. Specifically, the incidence and risk factors for flap compromise as well as flap complications (fistula/leakage and stenosis) were investigated to come up with a clinically relevant

* Corresponding author at: Department of Otorhinolaryngology-Head and Neck Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 06351, Republic of Korea.
E-mail address: chungmk@skku.edu (M.K. Chung).
[1] S.I. Park and S.Y. Choi contributed to the present manuscript as co-1st authors.

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algorithm for the choice of an optimal reconstructive method after hypopharyngectomy.

Material and methods

Patients

This study was approved by the Institutional Review Board of Samsung Medical Center (SMC IRB no. 2019-03-014). Inclusion criteria of the present study were patients who (1) were over 18 years old, (2) had undergone surgical resection and immediate reconstruction of the hypopharynx, and (3) had the proper integrity of medical records. From the head and neck cancer registry of our institution between January 1995 and January 2018, a total of 127 patients met the inclusion criteria, and their data were analyzed retrospectively. In addition to demographic data, patients' records were reviewed to find the reason for surgery, tumor location, treatment type, defect type, morbidity, and follow-up period. Diabetes mellitus (DM) was defined as having a fasting plasma glucose $\geq$126 mg/dL, the current use of oral hypoglycemic agents or the use of insulin during hospitalization. Hypertension was defined as an average systolic blood pressure $\geq$140 mmHg, diastolic blood pressure $\geq$90 mmHg or the current use of antihypertensive agents. Renal disease and liver disease was defined as having a history of the previous diagnosis given by a physician, based on appropriate medical evaluation. Hypoalbuminemia and anemia is defined as serum albumin level $<$ 3.0 g/dL and hemoglobin concentration $<$ 11 g/dL following the surgery, respectively

Outcome measurements

Outcomes of this study were measured as two endpoints: flap compromise and functional outcome. Flap compromise was defined as problems in blood circulation that required an entire or partial takedown operation, and functional outcomes were classified into three items: fistula/leakage, and stricture of reconstructed neopharynx. The presence of fistula/leakage and stricture was confirmed if there was any evidence on imaging studies (computed tomography or magnetic resonance image) or endoscopic examination (pharyngoscopy, esophagoscopy, or esophagography) with or without clinical symptoms.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 20; p values for each variable were calculated using the chi-square test, Fisher exact test, or logistic regression analysis. For the reconstruction type comparison about demographic and oncological characteristics, the chi-square test and Fisher exact test were used. Logistic regression analysis was performed to explore the risk factors and estimate the odds ratio (OR) for each outcome. Differences were considered statistically significant at $p < 0.05$.

Result

Patient characteristics

Detailed information is presented in Table 1. Mean age was 62.4 years old, and 89.8% was male. Most patients had undergone the hypopharyngeal surgery for cancer treatment (94.5%), radionecrosis management (3.9%), and postoperative complication management (1.6%) such as wound dehiscence. The hypopharynx was the most common location of the primary tumor (73.2%), followed by the larynx and the oropharynx. Patients were classified as stage I, II, III, and IV in 5 (4.2%), 16 (13.3%), 16 (13.3%), and 83 patients (69.2%), respectively. The purpose of the surgery was as salvage treatment in 53.5%, and as initial treatment in 46.5%. Types of the hypopharyngeal defect were classified as circumferential or non-circumferential, depending on the continuity of the hypopharyngeal tract; 69 patients (54.3%) had circumferential pharyngectomy, and 58 patients underwent non-circumferential pharyngectomy. Decisions on the reconstructive options were made based on several factors, such as defect types, patient's comorbidity, previous treatment history, and the availability of each reconstructive flap. Visceral flaps were used in 61 patients (48.0%), FCFF in 41 patients (32.3%), and pedicled flaps in 25 patients (19.7%). As a pedicled flap, a pectoralis major myocutaneous (PMMC) flap was most commonly used, followed by a latissimus dorsi myocutaneous (LD) flap. Anterolateral thigh and radial forearm were preferred donor sites as a fasciocutaneous flap (FCFF) for the hypopharyngeal reconstruction. In cooperation with the thoracic surgery team at our institution, a jejunal free graft was chosen frequently to restore most of the circumferential defect immediately. Visceral flaps were used in 61 patients (48.0%), FCFF in 41 patients (32.3%), and pedicled flaps in 25 patients (19.7%).

Clinical and functional outcomes

The correlation analysis between various clinical factors and the flap compromise, fistula, and stenosis following reconstruction are listed in Table 2. Overall, the flap compromise rate was 10.2% (13/127 cases): six cases in FCFF, five cases in a visceral flap, and two in the pedicled flap. When the flap compromise rate was analyzed according to the treatment types, there was no difference between the initial treatment group and the salvage treatment group (seven vs. six cases, respectively). Also, the numbers of flap compromise were similar between the different defect types (seven in circumferential vs. six cases in non-circumferential defects). The incidence of the flap compromise did not differ according to age, reconstruction methods, or the history of pre-reconstruction radiotherapy. For the salvage of a compromised visceral flap, a re-jejunal graft was most commonly chosen, followed by FCFF or pedicled flaps in our institution. For a compromised FCFF, a pedicled flap was preferred to restore the hypopharyngeal conduit. Fistula occurred in 36.2% (46/127 cases); 18 cases of visceral flaps, 13 cases of pedicled flaps, and 15 cases of FCFF. There was no difference in fistula rates according to defect types. However, the fistula rate was significantly higher in the salvage treatment group than in the initial treatment group ($p < 0.01$).

Moreover, patients who underwent radiotherapy showed a higher rate of fistula than did patients who did not undergo radiotherapy ($p = 0.01$). Of note, 63.0% (29/46 cases) of fistula/leakage developed within one month after the reconstruction, and in 19.6% (9/46 cases), it occurred even a year after surgery. Conservative treatment (no oral feeding with compressive dressing) was enough for the fistula management in 32.6% (15/46), and open surgical management (simple debridement, primary closure, re-flap reconstruction) was required in 67.4% (31/46). The rate of open surgical intervention tended to be higher in the salvage treatment group than in the initial treatment group (23/32, 71.9% vs. 8/14, 57.1%, respectively), though the difference was not statistically significant. The incidence of stenosis was 30 out of 127 cases (23.6%); this occurred in 19 cases (63.3%) with visceral flap, two cases (6.7%) of FCFF, and nine cases (30.0%) with the pedicled flap. More than half of the stenosis cases occurred in the visceral flap, which was mainly used for circumferential defects because of its advantages in tubular defects. Conservative management such as endoscopic balloon dilatation or transoral bougination were successfully performed for all of them.

Next, univariable and multivariable analysis was used to identify the possible risk factors affecting both the flap outcomes and the functional outcomes (Table 3). We found that salvage treatment was associated with an increased risk of fistula in the univariable analysis (OR 2.85; 95% CI 1.32–6.14; $p < 0.01$), which was also evident in multivariate analysis. Radiotherapy also showed an increased risk of fistula in univariable analysis (OR 2.72; 95% CI 1.28–5.78; $p < 0.01$). Interestingly, the risk of stenosis was significantly lower in the FCFF group than in the pedicled flap group by multivariable analysis (OR

Table 1
Study patients.

		Overall (N = 127)	Pedicled flap (n = 25)	FCFF (n = 41)	Visceral flap (n = 61)	P*
Age, mean ± SD, years		62.41 ± 9.68	63.84 ± 10.79	61.02 ± 8.78	62.75 ± 9.84	0.48
Gender, n						
Male:Female		114:13 (89.8%:10.2%)	24:1 (96.0%:4.0%)	38:3 (92.7%:7.3%)	52:9 (85.2%:14.8%)	0.24
Reason for surgery, n (%)						
Cancer treatment		120 (94.5)	22 (88.0)	41 (1 0 0)	57 (93.4)	
Radionecrosis		5 (3.9)	2 (8.0)	0 (0.0)	3 (4.9)	0.21
Postoperative complication		2 (1.6)	1 (4.0)	0 (0.0)	1 (1.7)	
Tumor location, n (%)						
Hypopharynx		93 (73.2)	20 (80.0)	24 (58.5)	49 (80.3)	0.17
Larynx		13 (10.2)	2 (8.0)	5 (12.2)	6 (9.8)	
Oropharynx		10 (7.9)	1 (4.0)	7 (17.1)	2 (3.3)	
Others		11 (8.7)	2 (8.0)	5 (12.2)	4 (6.6)	
Treatment type, n (%)						
Initial		59 (46.5)	8 (32.0)	25 (61.0)	26 (42.6)	
Salvage		68 (53.5)	17 (68.0)	16 (39.0)	35 (57.4)	0.05
Type of hypopharyngeal defect, n (%)						
Circumferential		69 (54.3)	1 (4.0)	7 (17.1)	61 (1 0 0)	< 0.01
Non circumferential		58 (45.7)	24 (96.0)	34 (82.9)	0 (0.0)	
Morbidity, n						
DM		20	3	5	12	0.58
HTN		30	4	8	18	0.36
Renal disease		5	2	0	3	0.16
Liver disease		6	1	1	4	0.85
Smoking	None	53 (41.7)	6 (24.0)	17 (41.5)	30 (49.2)	0.028
	Former	51 (40.2)	14 (56.0)	12 (29.3)	25 (41.0)	
	Current smoker	23 (18.1)	5 (20.0)	12 (29.3)	6 (9.8)	
Anemia		29	7	5	17	0.14
Hypoalbuminemia		9	2	3	4	1.00
Follow-up, median, days (range)		501 (17–5421)	465(28–2823)	612 (19–5421)	489 (17–4941)	0.94

* Chi-square test, Abbreviations; DM, diabetes mellitus, HTN, hypertension, Fasciocutaneous Free Flap, FCFF.

Table 2
Correlation analysis between clinical factors and clinical/functional outcomes of hypopharyngeal reconstruction.

	Flap compromise			Fistula			Stenosis		
	No	Yes	P*	No	Yes	P*	No	Yes	P*
Age									
≤Median	58/114	4/13	0.24	39/81	23/46	0.85	49/97	13/30	0.53
> Median	56/114	9/13		42/81	23/46		48/97	17/30	
Treatment type									
Initial	52/114	7/13	0.77	45/81	14/46	< 0.01	45/97	14/30	> 0.99
Salvage	62/114	6/13		36/81	32/46		52/97	16/30	
Defect type									
Non-circumferential	52/114	6/13	> 0.99	33/81	25/46	0.19	48/97	10/30	0.14
Circumferential	62/114	7/13		48/81	21/46		49/97	20/30	
Reconstruction method									
Pedicled flap	23/114	2/13	0.59	12/81	13/46	0.14	16/97	9/30	< 0.01
FCFF	35/114	6/13		26/81	15/46		39/97	2/30	
Visceral flap	56/114	5/13		43/81	18/46		42/97	19/30	
Radiotherapy									
No	57/114	7/13	> 0.99	48/81	16/46	0.01	50/97	14/30	0.68
Yes	57/114	6/13		33/81	30/46		47/97	16/30	

Abbreviations; Fasciocutaneous Free Flap, FCFF.
* Chi-square test.

0.09; 95% CI 0.02–0.47; $p < 0.01$).

Based on our institutional experiences, a suggested algorithm of appropriate reconstructive methods is depicted in Fig. 1. In both initial and salvage treatments with a non-circumferential defect, FCFF is the preferred reconstruction method because it has a lower stenosis rate than does a pedicled flap. For a circumferential defect, either the FCFF or the visceral flap is a good option. However, close monitoring for stenosis must be done primarily with a visceral flap.

Discussion

Clinical decisions for reconstructive methods for a hypopharyngeal defect should be made based on the characteristics of the defect, the patient's morbidity, and the institutional resources. In this retrospective study, we tried to compare the outcomes of the most commonly preferred flaps—the pedicled flap, a fasciocutaneous flap (FCFF), and visceral flap—in terms of flap compromise and fistula and stenosis incidence. The flap compromise rate was comparable between each reconstructive method, regardless of treatment type, defect type, or radiotherapy history.

The overall flap compromise rate in our study was 10.2%, which is higher than in other literature, where it ranged from 2.98 to 9.65%, probably because we included not only total failures but also cases with partial failure or flap compromise [12,14,15]. Even though the FCFF group showed higher rates of flap failure/compromise (six cases, 14.6%) than did other groups (the visceral group with five cases, 8.2%;

Table 3
Prognosticator analysis for clinical and functional outcomes of hypopharyngeal reconstruction.

	Flap compromise						Fistula						Stenosis					
	Univariable			Multivariable			Univariable			Multivariable			Univariable			Multivariable		
	OR	95% CI	P*	OR	95% CI	P*	OR	95% CI	P*	OR	95% CI	P*	OR	95% CI	P*	OR	95% CI	P*
Age																		
≤ Median	Ref			Ref			Ref			Ref			Ref			Ref		
> Median	2.33	0.67–8.00	0.17	2.41	0.69–8.44	0.17	0.92	0.45–1.91	0.84	0.85	0.40–1.84	0.69	2.55	1.10–5.89	0.02	1.26	0.52–3.03	0.61
Treatment type																		
Initial	Ref			Ref			Ref			Ref			Ref			Ref		
Salvage	0.71	0.22–2.27	0.57	0.83	0.25–2.78	0.76	2.85	1.32–6.14	< 0.01	2.99	1.34–6.70	< 0.01	0.98	0.43–2.24	0.97	0.69	0.28–1.69	0.42
Defect type																		
Non circumferential	Ref			Ref			Ref			Ref			Ref			Ref		
Circumferential	0.97	0.31–3.09	0.97	2.16	0.33–14.28	0.42	0.57	0.27–1.19	0.14	1.25	0.25–6.32	0.79	1.95	0.83–4.61	0.12	1.43	0.10–19.49	0.79
Reconstruction method																		
Pedicled flap	Ref			Ref			Ref			Ref			Ref			Ref		
Fasciocutaneous free flap	1.97	0.36–10.62	0.43	1.83	0.31–10.70	0.50	0.53	0.19–1.46	0.22	0.68	0.23–2.00	0.48	0.09	0.02–0.47	< 0.01	0.08	0.01–0.44	< 0.01
Visceral flap	1.02	0.18–5.67	0.97	0.51	0.05–5.83	0.59	0.38	0.14–1.00	0.05	0.33	0.05–2.08	0.24	0.80	0.30–2.14	0.66	0.55	0.04–8.09	0.67
Radiotherapy																		
No	Ref						Ref						Ref					
Yes	0.85	0.27–2.70	0.79				2.72	1.28–5.78	< 0.01				1.21	0.53–2.76	0.64			

pedicled flap group with two cases, 8.0%), there was no statistically significant difference between these groups. Management of flap compromise in these patients required surgical debridement and secondary repair with other flaps or conservative management.

The related risk factors of flap compromise were the history of renal comorbidity (OR 6.73; 95% CI 1.01–44.68; $p = 0.048$) and hypoalbuminemia (OR 9.69; 95% CI 2.21–42.57; $p = 0.003$), as was consistent with previous studies (data not shown). Hideo Yasunaga *et al.* reported that flap failure rate was increased 3.67 times in renal failure patients. They explain it as impaired wound healing and decreased cell-mediated immunity caused by decreased renal function [16]. Also, hypoalbuminemia has been consistently indicated as an adverse prognostic factor for oncological outcomes, as concurs with our results [14,17]. However, neither treatment type, reconstruction method, nor defect type influenced flap failure rate in this study.

For fistula/leakage, the results in various studies ranged from 8.2% to 23.0% [12,18,19]. However, within the same study, there was a difference in the incidence of a fistula between groups that had previously received radiation therapy and those who did not. Lam reported that an anastomotic fistula occurred in 36% of the patients who received radiotherapy, whereas only 14% of the patients who did not receive radiotherapy developed a fistula [18]. McCombe and Jones reported that fistula incidence increased from 4 to 39% when radiotherapy was performed [20]. Also, a tube type of reconstruction increased the risk of fistula [21]. This finding is in close resemblance to the results of our study, with a fistula rate as high as 36.2% (46 patients). In our study, almost half of the patients had previously received radiation therapy and were of the circumferential defect type. These correlations also appeared in our study, with a 2.99-fold higher risk of developing fistula in the salvage operation group than in the initial group. However, unlike the study of Chao, that the PMMC flap had a higher fistula rate than did the free fasciocutaneous flap group, this study did not show any association between types of reconstruction and fistula [22]. More than half of these fistulas (31 patients, 67.4%) needed surgical management, such as primary closure, reconstruction, or pharyngostoma. Fifteen patients (33%) were treated with conservative management.

In our center, barium esophagography or endoscopy was routinely performed on postoperative 7–10 days and at three months to assess stenosis. Only when clinically warranted, patients underwent a modified barium swallow study or endoscopic examination to evaluate for dysphagia. The overall stenosis rate was 23.6% in this study. More than half of the stenosis cases happened in the visceral flap group (19 patients, 63.3%). This finding is different from the result of other studies that showed higher stricture rates in the radial forearm free-flap reconstruction group than in the free jejunal free graft group in circumferential defects [15]. When we consider the fact that there is a higher risk of stricture in circumferential pharyngeal defects, it can be understood that our results differ from those of other studies, because a visceral flap is mostly used for reconstruction of circumferential defects in our study [7]. In our institution, distal jejunoesophageal anastomosis was performed in an end-to-end manner using (1) hand-sewn sutures or (2) mechanical stapler. In hand-sewn suture cases, double layer of interrupted sutures was applied to the mucosa and submucosal layers of the jejunum and esophagus, followed by simple sutures between the jejunal serosa and the esophageal muscular and adventitial layers. In the mechanical stapler cases, the jejunoesophageal anastomosis was completed by 25 or 28-mm end-to-end anastomosis (EEA) circular mechanical stapler (Covidien, Mansfield, MA, USA). Moreover, then, the distal jejunal stump was closed by double layer suturing using a linear stapler and absorbable sutures. On the contrary, proximal anastomosis with pharynx was always performed in an extended end-to-end fashion by double layer hand suturing.

The stricture was identified in 8/26 patients in the mechanical stapler group: 1 at the pharyngojejunal anastomosis and seven at the jejunoesophageal anastomosis. This finding was comparable with the

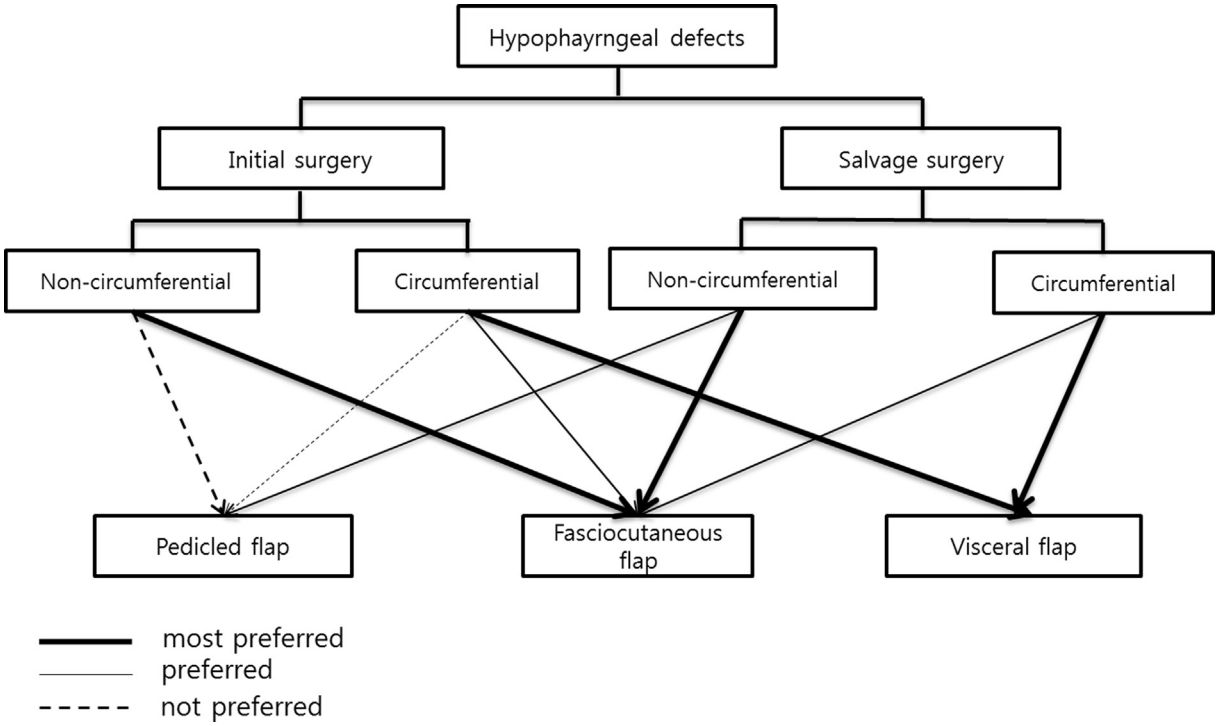

Fig. 1. Proposed algorithm for optimal reconstructive methods of the hypopharyngeal defects.

hand-sewn suture group, where the pharyngoesophageal stricture was seen in 7/25 patients with 1 case at the pharyngojejunal anastomosis site and 6 cases at the jejunoesophageal anastomosis. There was no statistically significant difference between the rate of fistula and rate of stricture between two groups.

One interesting point is that FCFF protects against stenosis more than does a pedicled flap. This result was also found in Chao's study comparing PMMC with free fasciocutaneous flap. In that study, postoperative stricture was found only in the PMMC group, even though there was no statistical significance [22]. We usually performed endoscopic balloon dilatation or intraoral bougination as a first-line treatment for stenosis, while surgical revision was rarely considered. As a result, endoscopic balloon dilatation (11 patients, 37%) and intraoral bougination (four patients, 13%) were two treatment options most often used in our study. Most institutions or surgeons adhere to only one or a few methods when they do reconstruction. Therefore, most papers compare the advantages and disadvantages of only one or two reconstruction methods.

However, there are several limitations to our study. The type of defect limited our institution's reconstruction method. For example, because a visceral flap, such as a jejunal free flap, was mostly used for tube-type reconstruction, it could not be easily compared with other methods for a circumferential defect. Also, only the first reconstruction surgery after resection of the hypopharynx was included in this study. Therefore, the reconstruction methods and outcomes used after flap failure were not discussed in this report.

To our knowledge, our study was the first to classify hypopharynx reconstruction methods as a visceral flap, FCFF, and pedicled flap, and to compare these methods based on a single institution's data. Because different reconstruction methods are relatively well used in our center, we could discuss the advantages and disadvantages of each type of flap, and the situation in which each flap is used, and suggest appropriate reconstruction methods depending on the situation.

Conclusions

The outcome of reconstruction with visceral flap, fasciocutaneous free flap, or pedicled flap was equally successful if used appropriately according to the defect type, previous medical history, and comorbidities. Identifying relevant risk factors and paying attention to associated outcomes can reduce the complication rates after reconstruction in head and neck surgery.

Declaration of Competing Interest

The authors declared that there is no conflict of interest.

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