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Ten-year Experience of Reconstructive Techniques After Resection of Hypopharyngeal Squamous Cell Carcinoma (SCC): Changing Trend from Gastric Pull up to Free Flaps

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Abstract

Background: Hypo-pharyngeal squamous cell carcinoma (H-SCC) is a rare type of head and neck malignancy often necessitating extensive surgical resection and subsequent reconstruction.
Objectives: This study presented a 10-year retrospective analysis of reconstructive surgeries following the resection of H-SCC.
Methods: A cross-sectional study was conducted on H-SCC patients who underwent reconstructive surgery after either laryngopharyngoesophagectomy (13 cases, 42%) or pharyngolaryngectomy (18 cases, 58%). Various reconstructive techniques were employed, including gastric pull up (12 cases, 39%), pectoralis major myo-cutaneous flap (PMMCF) (11 cases, 35%), and free flaps such as jejunum (2 cases, 6%), ileocecal (2 cases, 6%), or antero-lateral thigh (ALT) (4 cases, 13%).
Results: The study included 31 patients with a mean age of 56.26 ± 3.98 years, predominantly male (64%). Smoking habit was observed in 22 (71%) patients. The total complication rate was 48% including 2 (6%) cases of flap loss, 2 (6%) cases of cervical anastomosis leak, 1 (3%) case of hematoma, 2 (6%) cases of neck wound infection, 5 (16%) cases of pneumonia, and 3 (10%) cases of pleural effusion, with a mortality rate of 16%. GPU and PMMCF had total number of post operative complications of 12 and 6, respectively. ALT flap, jejunal flap and ileocecal flap had 3, 2 and 1 total complications, respectively. Severe stenosis at cervical anastomosis was found in 4 (13%) patients after GPU and not other techniques.
Conclusions: Advances in microvascular anatomy knowledge have led to the evolution of reconstructive techniques. The study suggests that in upcoming years, the free flap techniques hold promise as a preferred method for hypo-pharyngeal reconstruction.

Keywords: Squamous Cell Carcinoma, Hypopharynx, Reconstruction, Laryngopharyngoesophagectomy

1. Background

Hypo-pharyngeal squamous cell carcinoma (H-SCC) is a rare form of head and neck malignancy, comprising 2.4% of newly diagnosed malignancies and 5% of all head and neck cancers (1, 2). The primary sites affected are the piriform sinus (70%), retro-cricoid region (15% - 20%), and the posterior wall (10 - 15%) (3). Typically, H-SCC presents in advanced stages with symptoms such as neck mass, hoarseness, referral earache, and dysphagia. Additionally, tumor invasion into the larynx can lead to vocal cord paralysis or rupture, compromising the airway, or causing a mass effect (3-5). The current standard treatment involves initial surgery followed by adjuvant radiotherapy or definitive chemo-radiation. Surgical intervention may be necessary for residual disease or tumor recurrence. Treatment plans may be modified based on factors including tumor stage, underlying health conditions, and physical performance. Unfortunately, the prognosis for H-SCC is generally unfavorable due to its tendency to be locally advanced and to cause early distant metastases. Given the historically high morbidity and mortality rates associated with surgical approaches, there exists a

dilemma regarding the standard treatment. The proximity of the tumor to the larynx dictates the extent of resection, often requiring laryngectomy, pharyngectomy, and modified dissection of cervical lymph nodes in most cases (6, 7). However, in instances where achieving a negative margin necessitates extensive annular resection of the hypopharynx, a complete laryngopharyngectomy becomes imperative, resulting in the removal of 5-6 cm from the lower part of the cervical esophagus (8).

In the past, the standard treatment for hypopharyngeal cancers was total laryngectomy with total or partial pharyngectomy. However, since the introduction of chemo-radiation in the 1990s, the approach has shifted towards organ preservation strategies (1, 2). Various reconstructive methods are currently available. Gastric pull up (GPU) and myocutaneous flap techniques are commonly employed for resection area reconstruction. Anterolateral thigh (ALT) and radial forearm free flap (RFFF) techniques are other commonly used reconstructive methods. Recently, the ileocecal free flap has been introduced as a reconstructive technique. It has been suggested that this method closely mimics natural anatomy and texture (4, 9-12).

Regardless of the chosen treatment, both the disease itself and its management, whether surgical or through definitive chemo-radiotherapy, entail significant morbidity and mortality. Hence, it is imperative to prioritize the patient's quality of life while designing treatment plans. Additionally, reconstructive procedures are primarily carried out in a limited number of specialized centers within each country, and the collective experience in this field is relatively scarce (13-15).

2. Objectives

This study presented our 10-year experience with reconstructive surgeries following H-SCC resection.

3. Methods

This research conducted a retrospective cross-sectional study on patients who visited the Cancer Institute, Tehran University of Medical Sciences, Iran between January 2012 and January 2022. The study included consecutive patients with confirmed biopsy results of Hypo-pharyngeal Squamous Cell Carcinoma (H-SCC) who underwent reconstructive surgery following laryngopharyngoesophagectomy or pharyngolaryngectomy. The study protocol was approved by the ethics committee of Tehran University of Medical Sciences.

Before the surgery, all patients underwent various evaluations, including nasopharyngeal endoscopy and tumor biopsy, magnetic resonance imaging of the brain, face, and cervical soft tissues, thoraco-abdomino-pelvic computed tomography scan, and cervical lymph node ultrasonography scan. After the oncologic resection, three types of reconstructive surgery were performed: Gastric pull up (GPU), pectoralis major myo-cutaneous flap (PMMCF), and free flap using either ileocecal, jejunum or antero-lateral thigh. The choice of reconstructive technique was based on factors such as the patient's surgical history, performance status, known risk factors for atherosclerosis (e.g., diabetes mellitus, ischemic heart disease, cigarette smoking), and the size of the pectoralis major muscle.

Data retrieved from medical records included information on age, gender, underlying diseases, primary tumor site, histologic grade, tumor stage according to TNM classification, history of neoadjuvant treatment, cervical dissection, and postoperative complications. Categorical variables were presented as numbers and relative frequencies, while continuous variables were expressed as mean ± standard deviation. Statistical analyses were performed using the two-sided method with Statistical Package of Social Science software (SPSS version 22; SPSS, Inc., Chicago, IL).

4. Results

The study included 20 (64%) male patients and 11 (36%) female patients. The average age at the time of surgery was 56.2 ± 3.9 years, ranging from 39 to 77. Among the patients, 22 (71%) were smokers, with 19 (61%) currently active, and 3 (10%) having quit. Nine (29%) patients had never smoked. Additionally, nine (29%) patients had opium addiction at the time of surgery. The most common underlying diseases were ischemic heart disease and diabetes mellitus, each presented in 4 (13%) patients. Two (6%) patients had a history of hypertension, and 1 (3%) patient had controlled hyperthyroidism. One (3%) patient tested positive for hepatitis C virus infection ((Table1).

All patients were preoperatively staged based on cTNM classification, and there were no cases of metastasis at the time of surgery. The histologic grade of the tumor was well differentiated in 19 (61%) cases, moderately differentiated in 8 (26%) cases, and poorly differentiated in 4 (13%) cases (Table 1).

Nine (29%) patients underwent surgery as their primary treatment, while 22 (71%) patients had received previous neoadjuvant treatment. Thirteen (42%) patients underwent laryngopharyngoesophagectomy, and 18 (58%) patients underwent pharyngolaryngectomy.

Table 1. Characteristics of Study Population

Subtype	Frequency (%)
Gender	
Male	20 (64)
Female	11 (36)
Smoking status	
Current smoker	19 (61)
Quit smoking	3 (10)
Never smoked	9 (29)
Underlying disease	
IHD	4 (13)
DM	4 (13)
HTN	2 (6)
Hyperthyroidism	1 (3)
HCV positive	1 (3)
TNM classification	
T2N1	1 (3)
T3N0	15 (48)
T3N1	9 (29)
T4N0	5 (16)
T4N1	1 (3)
Histology grade	
Well differentiated	19 (61)
Moderate differentiated	8 (26)
Poor differentiated	4 (13)
Resection type	
laryngopharyngoesophagectomy	13 (42)
pharyngolaryngectomy	18 (58)
Reconstruction technique	
GPU	11 (35)
PMMCF	12 (39)
Jejunal flap	2 (6)
ALTflap	4 (13)
ileocecal flap	2 (6)

Abbreviations: IHD, was ischemic heart disease; DM, diabetes mellitus; HTN, hypertension; HCV, hepatitis C virus; GPU, Gastric pull up; PMMCF, Pectoralis major myo-cutaneous flap; ALT, Antro-lateral thigh.

Reconstruction techniques included Gastric pull up (GPU) in 11 (35%) patients and pectoralis major myo-cutaneous flap (PMMCF) in 12 (39%) patients. Free flap reconstruction was performed using jejunal flap, anterolateral thigh (ALT) flap, and ileocecal flap in 2 (6%), 4 (13%), and 2 (6%) patients, respectively ((Table1).

The in-hospital mortality rate was 16% (n = 5). The primary cause of death was multi-organ failure, occurring in 2 (6%) patients. Other causes of death included sepsis, acute respiratory distress syndrome, and sudden cardiac arrest, each accounting for one (3%) patient. The mean hospital stay for deceased patients was 32 days, while the mean hospital stay for the entire study population was 22 days (Table 2).

In-hospital complications occurred in 15 (48.3%) cases, including 2 (6%) cases of flap loss, 2 (6%) cases of cervical anastomosis leak, 1 (3%) case of hematoma, 2 (6%) cases of neck wound infection, 5 (16%) cases of pneumonia, and 3 (10%) cases of pleural effusion. There were no cases of abdominal wound dehiscence or infection. Among PMMCF reconstructions, flap loss occurred in 2 (18%) cases, which was repaired using contralateral pectoral major muscle. Cervical anastomosis leak was managed conservatively by restricting oral feeding and initiating total parenteral nutrition. Patients who developed hematoma, wound infection, pleural effusion, and pneumonia did not require further intervention. Severe stenosis at cervical

Table 2. Post-operative Complications

Post-operative Complication	Frequency (%)
In hospital mortality	5 (16)
Flap loss	2 (6)
Cervical anastomosis leak	2 (6)
Hematoma	1 (3)
Neck wound infection	2 (6)
Pneumonia	5 (16)
Pleural effusion	3 (10)
Severe stenosis of cervical anastomosis	4 (13)

Table 3. Post-operative Complications in each Reconstruction Technique

Post-operative Complication	GPU	PMMCF	Jejunal Flap	ALT Flap	Ileocecal Flap
In hospital mortality	3	1	0	1	0
Flap loss	0	2	0	0	0
Cervical anastomosis leak	1	1	0	0	0
Hematoma	0	1	0	0	0
Neck wound infection	1	0	1	0	0
Pneumonia	2	0	0	2	1
Pleural effusion	1	1	1	0	0
Severe stenosis of cervical anastomosis	4	0	0	0	0

Abbreviations: GPU, Gastric pull up; PMMCF, Pectoralis major myocutaneous flap; ALT, Antro-lateral thigh.

anastomosis was found in 4 (13%) patients, occurring at least 3 months postoperatively (Table 3).

Patients were followed in the outpatient clinic at our center, but unfortunately, we lost track of patients after 6 months postoperatively. Complete oral intake was achieved in 22 (85%) patients, while 4 (15%) patients remained partially or completely dependent on jejunostomy tube feeding. There is no recorded data on speech rehabilitation. Severe stenosis of cervical anastomosis occurred in 4 (15%) patients. Three (11.5%) patients underwent adjuvant chemo-radiation.

5. Discussion

In this study, we have shared our 10-year experience in performing surgical resection and reconstructive surgery for H-SCC. The Cancer Institute, affiliated with Tehran University of Medical Sciences, serves as a specialized cancer center for complex cases nationwide, providing an exceptional scientific platform for investigating treatment outcomes.

Leterza et al. introduced the Gastric Pull Up (GPU) technique for reconstructing gastrointestinal continuity after esophageal resection. Their extensive study on 167 patients with primary hypo-pharyngeal and cervical esophageal cancer demonstrated that GPU was linked to lower recurrence rates and higher survival rates compared to previously employed methods (16). Another study by Cahow and Sasaki evaluated the outcomes of GPU technique in this patient group and reported a postoperative mortality rate of 5%, with a total post-operative complication rate of 32%. Most patients resumed oral feeding within six days post-surgery and were discharged after an average of 16 days. The study observed two temporary salivary fistulas and four cases of anastomotic stenosis, none of which were permanent. The mean overall survival was 12 months, ranging from 1 to 100 months post-surgery. They concluded that GPU reconstruction was a safe and effective technique associated with low mortality and favorable long-term functional results for patients with primary tumors in the hypo-pharyngeal, laryngeal, and cervical esophageal regions (17). Ho et al. conducted a retrospective evaluation of treatment outcomes for hypo-pharyngeal cancer in 109 patients. The authors found no significant difference in local recurrence rates between patients who underwent laryngo-pharyngectectomy alongside esophagectomy and those who had laryngopharyngectomy alone. However, complications like bleeding, cardiac arrhythmias, and

pulmonary issues were more prevalent following esophagectomy. The tumor was locally controlled in 86% of the study population, with most cases of local recurrence occurring at the upper edge of the resection (18).

Based on our experience, similar complications prompted us to transition towards utilizing local flaps for reconstruction.

Rezaii et al. demonstrated that the incidence of salivary fistula was higher with the PMMCF technique compared to the GPU technique. However, there was no significant difference in the frequency of anastomotic stenosis or swallowing dysfunction between the two methods (14). In our study, we observed that the rate of complications per number of cases performed is higher in GPU than other techniques, and the occurrence of complications per number of cases performed was lower in the free flap method. It's important to note that due to our limited sample size, we cannot make a definitive recommendation about the superiority of any of these techniques.

In recent years, significant progress has been made in the treatment of head and neck tumors, both in surgical approaches and chemo-radiation techniques (19, 20). Surgical treatment of head and neck malignancies often necessitates radical tumor resection for oncological clearance, which can lead to significant functional impairments in swallowing, speech, and breathing. Free tissue transfer reconstruction offers a reliable solution for these tissue defects (21-25). Even in cases where the patient's prognosis may appear grim, this approach can provide a satisfactory quality of life (26).

Previously, myocutaneous flaps like the pectoralis major and latissimus dorsi flap were commonly used for head and neck reconstruction. However, the curvature of rotation and the substantial volume of these flaps were limiting factors (25). The pectoralis major myocutaneous flap (PMMCF) is considered a fundamental technique for flap-based reconstruction in the head and neck region. While the operating time for this reconstruction method is shorter compared to free flap reconstruction, its complications are relatively high (26). Additionally, its suboptimal functional and aesthetic outcomes diminish its efficacy (27).

With the growing understanding of donor site anatomy and advancements in microvascular surgery techniques, free flap reconstruction has become a reliable and effective approach for cases involving substantial tissue loss (28, 29). Ideal reconstruction aims to achieve a delicate balance between aesthetics, function, and the coverage of vital structures. Initially, free flaps were developed to address these needs, yet they often fell short of achieving a harmonious balance (30). While pioneers in free flap design initially had concerns about tissue transfer viability and necrosis, increasing experience and technological advances have resulted in over 95% flap survival rates in recent studies (31, 32).

The primary objectives in reconstructing extensive head and neck lesions after radical resection are prompt coverage of mucosal or cutaneous defects, restoration of bony support, and reconfiguration of specific structures such as the cervical esophagus (33). Extensive evidence supports the effectiveness of free tissue transfer as a one-stage reconstruction method for major head and neck lesions, achieving success rates of 98 - 99% in specialized centers. This approach also offers enhanced functional outcomes (34). Free tissue transfer offers several advantages over other methods, including improved blood-tissue flow crucial for wound healing and tissue survival, unrestricted positioning of the flap, capacity for utilizing large amounts of composite tissue, and potential for functional reconstruction (both sensory and motor) (33).

Bianchi et al. conducted a study on 352 patients who underwent a total of 376 reconstructive surgeries with free flaps in the head and neck region. The average age was 55.6 years, with the majority (63.1%) being male. Twenty-four patients received two types of flaps. Of the study population, 46% had a history of smoking, 41.8% had underlying diseases (most commonly diabetes mellitus and hypertension), and 18.2% had a history of neoadjuvant radiation therapy. The most frequently used free flaps were the radial forearm free flap (RFFM) at 31.4%, followed by the fibula flap at 26.9%. The overall complication rate was 47%. Complete flap necrosis occurred in 15 (4%) patients, and partial flap failure occurred in 8 (2.1%) cases (35).

Haugheri studied 236 patients using flaps from the radial forearm and fibula. Post-operative complications were associated with severe underlying disease, age over 55 years, and receiving more than seven liters of intravascular crystalloid transfusions during surgery. The average hospital stay was 11 days. Reconstruction-related complications, including salivary fistulas, wound dehiscence, and hematoma or seroma formation, occurred in 29% of patients (27). Pesko et al. reported a mortality rate of 13% and a morbidity rate of 50% after reconstructive surgery for head and neck malignancies. These reconstructions included 50 cases with GPU, 10 cases with ileocecal free flap, and 5 cases with jejunal free flap (36).

Today, employing the intestinal tract as a free flap is a popular technique for reconstructing the esophagus,

throat, and vocal cords following oncologic resection of head and neck tumors. However, this method of reconstructing tissue defects after the resection of cervical tumors is technically demanding. These flaps are highly sensitive to ischemia and reperfusion injury after micro-anastomosis due to the presence of intestinal microbial flora and the high metabolic activity in the intestinal tract. Therefore, preventing ischemia and subsequent damage to the intestinal tract is of utmost importance (37-39).

Reconstructive methods are chosen based on individual patient conditions. Over the years in our center, there has been a shift from more radical methods like GPU to pedicled flaps and now free flaps. We've noticed that localized reconstructive methods have allowed for larger resections, ensuring complete tumor removal and reducing the risk of local recurrence. Previously, some defects were deemed non-resectable because of reconstruction limitations. Localized methods also provide flexibility in shaping flaps according to the defect's size and shape, while minimizing surgical manipulation in other body cavities. For instance, in the Anterolateral Thigh (ALT) free flap method compared to GPU, manipulation of the mediastinum and thorax is avoided. Consequently, in case of potential leakage, concerns about mediastinitis are eliminated. We've observed that patients faced complications like bleeding, mediastinitis, and pneumonia following GPU application, leading to fatalities. In contrast, newer techniques have resulted in more localized post-operative complications. Recently, we've been employing the ileocecal transfer method more frequently at our center, which has shown noticeable outcomes.

Sartoris et al. reported successful reconstruction of the pharynx and cervical esophagus using the ileocolic free flap in six patients, with recovery taking place within eighteen to thirty-eight days post-surgery. They suggested that this flap could be a successful option with minimal complications for pharyngo-esophageal reconstruction (40). Another study by Chen et al. detailed a single surgeon's experience using the free ileocolic flap after a total pharyngolaryngectomy. Out of 205 patients, 191 underwent free ileocolic flap reconstruction, while the remaining 14 received pedicled flaps. The overall 5-year survival rate was 52%. It was concluded that using the ileocolic free flap could prevent vocal tube obstruction due to the natural secretions and spontaneous peristalsis of the intestinal flap, although it could potentially lead to vocal prosthesis obstruction (41).

The use of the ileocecal free flap offers several specific advantages over other flaps, including easily accessible vascular pedicles and large caliber vessels for reliable and fast anastomosis. The caliber of the ascending colon matches well with the hypopharynx diameter, requiring minimal trimming. When the gastrointestinal (GI) tract is reconstructed with a GI flap, it closely resembles the original tract with mucosal lining. The terminal ileum can be used as an external monitor to assess flap viability, providing an advantage that other myocutaneous flaps lack. The vascular pedicle's length is sufficient to reach the base of the neck and transverse cervical artery and vein for anastomosis in non-radiated areas. Additionally, the appendix can be used for anastomosis between the neopharynx and the membranous portion of the trachea, creating a trachea-esophageal fistula for voice reconstruction. However, it's worth noting that flap harvest requires a midline laparotomy, and there is the necessity for one GI anastomosis, potentially leading to subsequent complications. Vascular anastomosis should also be performed more quickly compared to cutaneous free flaps due to the intestinal mucosa's increased sensitivity to ischemia.

Our study had a few limitations. Firstly, it was a descriptive study, so we were unable to make direct comparisons between different reconstruction methods. Additionally, the relatively small sample size may have influenced the results observed during our 10-year experience. Therefore, more extensive studies are needed to comprehensively address the best treatment options for reconstruction after oncologic resection of head and neck malignancies.

5.1. Conclusions

In our experience, in cases where pharyngectomy is performed without esophagectomy, preserving a tumor-free lower pharyngeal margin, the recommended reconstructive approach for optimal function and a lower risk of stricture is the use of a free jejunal flap. We suggest reserving myocutaneous flaps for partial defects in patients who may not be ideal candidates for free flaps, or as a salvage treatment in cases where free flap reconstruction has failed. On the other hand, in cases involving tumoral infiltration of the lower pharyngeal margin where esophagectomy is warranted, GPU yields good functional results and low complication rates. Furthermore, colon transfer is reserved for cases not suitable for the GPU.

Ultimately, it's important to note that the choice of reconstruction method does not impact survival or recurrence rates, but it significantly influences the

patient's quality of life. Many reconstructive techniques have been introduced to restore hypo-pharyngeal function, each with its own advantages and limitations. It seems that in the future, the ileocecal free flap holds the potential to become the treatment of choice for hypo-pharyngeal reconstruction.

Footnotes

Authors' Contribution: Study concept and design: A.J., and M.S.; analysis and interpretation of data: A.S, and S. K.; drafting of the manuscript: A. S and S.K.; critical revision of the manuscript for important intellectual content: M.S, and A.J.; statistical analysis: A.S.

Conflict of Interests Statement: Authors have declared that there is no conflict of interest

Data Availability: Data will be available upon request from corresponding author.

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