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# Healing the gap: the evolution of esophageal substitute and quality of life in patients undergoing total pharyngolaryngoesophagectomy with reconstruction

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## Abstract

**Aim:** Hypopharyngeal squamous cell carcinoma is reportedly one of the most aggressive primary cancers, and surgical resection continues to be the standard therapeutic choice. In patients with hypopharyngeal cancer involving the esophagus or synchronous hypopharyngeal and esophageal cancer, total pharyngolaryngoesophagectomy (TPLE) is indicated to control both malignancies at the same time. Reconstruction remains challenging with regard to the length of the substitute for the esophagus as well as the donor site morbidity. We reported our long-term follow-up and the outcome of the quality of life (QoL).



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**Methods:** We retrospectively reviewed the records of all patients who underwent TPLE between January 2012 and December 2020. Information was collected on sex, age, surgical indications, operative time, postoperative complication, swallowing function, hospital stay, and survival. Quality of life scores were acquired by World Health Organization Quality of Life-Brief (WHOQOL-BREF) questionnaires and completed at the outpatient clinic. Gaussian kernel-smoothing was applied to estimate the dynamic changes of QoL function.

**Results:** A total of 40 patients undergoing oncologic pharyngolaryngoesophagectomy were enrolled in this study. There were 26 patients (65%) undergoing gastric tube reconstruction with direct anastomosis to the oropharynx (GP group), 7 patients (18%) undergoing additional free jejunal flap to bridge the gap between the gastric tube and oropharynx (GP-JF group), 4 patients (10%) undergoing additional free anterolateral thigh flap to bridge the gap and resurface the neck skin (GP-ALT group), and 3 patients (8%) undergoing colon interposition (CI group). The leakage rate in each group was 50% for GP group, 29% for GP-JF group, 50% for GP-ALT group, and 67% for CI group. The mean operation time was  $1010 \pm 195$  min. Although the overall leakage rate was 47.5%, only 15% of the patients needed further surgical intervention. One patient (2.5%) died with persistent leakage and pneumonia. In terms of life quality assessment, the response rate for the QoL questionnaire was 50%. We found the overall QoL deteriorated for the first year after operation, but it gradually improved and even surpassed the patient pretreatment scores by the end of the second year after operation.

**Conclusion:** The gap caused by TPLE in patient, perioperative morbidity, and postoperative quality of life could be managed by the evolution of esophageal substitute, surgical techniques, perioperative wound care, and evaluation of the quality of life.

**Keywords:** Total pharyngolaryngoesophagectomy, negative pressure wound therapy, quality of life

## INTRODUCTION

There are approximately 80,000 patients with newly diagnosed hypopharyngeal cancer and 35,000 deaths annually in the world<sup>[1]</sup>. In Taiwan, 1209 patients were newly diagnosed as having hypopharyngeal cancer in 2018, and the age-standardized incidence rate was 3.25 per 100,000 person-years. Hypopharyngeal cancer tends to be locally advanced at diagnosis because of the lack of alarming symptoms. Fewer than 50% of hypopharyngeal cancers are confined to the hypopharynx and more than 80% of patients have stage III or IV disease at diagnosis<sup>[2-4]</sup>. Because of its late diagnosis with high rate of metastasis, the disappointing survival and functional outcome were well-known. Although organ-preserving multi-modality treatment for hypopharyngeal cancer has been prevailing, surgical resection continues to be the standard therapeutic choice<sup>[5-7]</sup>.

It is not uncommon for hypopharyngeal cancers to have multisite involvement and extension into adjacent mucosal areas. Postcricoid tumors usually extend through the cricoid cartilage or involve the cervical esophagus<sup>[5]</sup>. For those patients with advanced hypopharyngeal cancers, total pharyngolaryngoesophagectomy (TPLE) with postoperative radiotherapy (RT) is usually recommended for disease eradication and prevention from local recurrence. Chemoradiation for extensive disease with organ dysfunction is likely to preserve the organ without preservation of function. Although salvaging the TPLE after a failed RT therapy always produces a high morbidity<sup>[6]</sup>, radical surgery with subsequent reconstruction and adequate adjuvant treatment are more likely to have an acceptable oncologic and functional outcome in such circumstances<sup>[7]</sup>. Routine endoscopic screening of the upper alimentary tract at the diagnosis of hypopharyngeal cancer contributes to the frequent association of hypopharyngeal cancer with esophageal cancer because of commonly shared risk factors such as cigarette smoking and alcohol consumption<sup>[8-11]</sup>. In patients with synchronous hypopharyngeal and esophageal cancer, TPLE with esophagectomy is indicated to control both malignancies at the same time.

Reconstructing the alimentary tract after TPLE is challenging. The goal of reconstruction should be directed to single-stage surgery with low morbidity and mortality, shortened hospital stay, and rapid restoration of oral alimentation<sup>[12]</sup>. Different substitutes for the esophagus have been proposed, including gastric tube pull-up or colon graft interposition, free jejunal flap transfer, and supercharge of graft with microvascular anastomosis<sup>[13-18]</sup>. Gastric pull-up is the oldest technique still in use for reconstruction after TPLE. When introduced in 1960, the procedure was characterized by its a one-stage operation, low mortality, and the patients not being worse off than before the operation<sup>[19]</sup>. However, the limited extension of gastric tube might put the anastomosis under tension if the resection margin was too high in the oropharynx or nasopharynx. Additional flap would be required to bridge this gap<sup>[20]</sup>. In this study, we report our long-term follow-up and share our experience about the management of complication.

## METHODS

### Patient enrollment

This retrospective study was conducted to review the medical records of patients who underwent oncologic TPLE between January 2012 and December 2020. There were 41 patients; 38 patients were reconstructed with gastric pull-up and the other 3 were reconstructed with colon interposition. Among the 38 patients with gastric pull-up, 26 patients had their gastric tube directly anastomosed to the oropharynx (GP group). Another 7 patients had free jejunal flap to bridge the gap between the gastric tube and the oropharynx (GP-JF group). Another 4 patients had free anterolateral thigh flap to bridge this gap with concomitant reconstruction of the neck skin defect (GP-ALT group). One patient was reconstructed with pedicled pectoralis major myocutaneous flap to bridge this gap. Because he did not follow our algorithm, he was excluded for the following analysis.

### Algorithmic approach for TPLE reconstruction

The gastric pull-up was of higher priority as the esophageal substitute than the colon interposition in our institution. Colon interposition was only considered if the stomach was previously operated. The gastric tube was pulled up via a posterior mediastinal route to reach the pharyngeal defect. The tension between the gastric tube and the resection margin at the oropharynx was evaluated. The additional free flap would be transferred by a plastic surgeon if gap between the gastric tube and the resection margin could not be resolved using Kocher maneuver. The priority of free jejunal flap was higher than anterolateral thigh flap to avoid donor site immobilization. If there was an additional neck skin defect, the anterolateral thigh flap was otherwise harvested. The surgical procedure was detailed in our previous study<sup>[20]</sup>.

### The evaluation of the quality of life

Patients in this study were invited to complete the World Health Organization Quality of Life-Brief (WHOQOL-BREF) questionnaires at the outpatient clinic. The WHOQOL-BREF questionnaire is a generic psychometric instrument<sup>[21]</sup>. It contains 28 items to evaluate in the four domains: physical, psychological, social relations, and environment. Each item is scored from 1 to 5, where a higher score indicates a better Quality of Life (QoL). By multiplying the average scores of all items in the same domain by four, a domain score is calculated. Each domain score ranges from 4 to 20 points. The validity of its use in oral cancer has been confirmed by Rasch models, confirmatory factor analysis, and Pearson correlations<sup>[22]</sup>. For each QoL assessment, the “time after treatment” was defined as the period between the operation date and the date of assessment. To estimate the dynamic changes of QoL function, Gaussian kernel smoothing was applied<sup>[23]</sup>. Namely, the estimation of the mean QoL at a particular time  $t$  was the weighted average of QoL assessments, where the weights were determined by a parameter named bandwidth. The bandwidth was set at 0.1 in this study. The relevant confidence intervals for the mean function estimations of QoL was constructed by a bootstrap approach. Each patient was the unit used for bootstrapping. At each time point, a 95% confidence interval was constructed using the 2.5 and 97.5 percentiles of 76 mean QoL estimated

from bootstrapping. This study was approved by our institutional review board (A-ER-108-525).

### Statistical analysis

For the numerical variables, the data are mean  $\pm$  standard deviation and were analyzed using the Wilcoxon test because the normality tests (Kolmogorov-Smirnov test and Shapiro-Wilk test) rejected the null hypothesis and concluded that these data did not come from normal distribution. For the categorical variables, the data were analyzed using Pearson's  $\chi^2$  test or Fisher's Exact test, as appropriate. Significance was set at  $P < 0.05$  (two-tailed). Statistical software, MedCalc (version 19.5), was used to perform statistical analysis of data and results.

## RESULTS

A total of 40 patients undergoing oncologic TPLE were further analyzed [Table 1 and 2]. All but one was male. The indication for 18 patients (45%) was hypopharyngeal or laryngeal cancer with esophageal extension, while indication for the rest of the 22 patients (55%) was synchronous hypopharyngeal or laryngeal cancer and esophageal cancer. Twenty-four patients (60%) were primarily treated with surgery, and the rest of the 16 patients (40%) were treated with salvage operation. The mean operation time was  $1010 \pm 195$  min, and the mean duration of hospitalization was  $41 \pm 31$  days. The distribution of hypopharyngeal cancer stages was the following: 1 (2.5%) was stage I, 2 (5%) were stage II, 8 (20%) were stage III, 23 (57.5%) were stage IVa, and 6 (15%) were stage IVb. The overall survival time were  $45 \pm 7$  months [Figure 1]. The mean survival time was  $43 \pm 16$  months for stage III,  $50 \pm 9$  months for stage IVa, and  $12 \pm 3$  months for stage IVb [Figure 2]. There was no difference in survival time between those primarily treated with surgery (mean 42 months; 95%CI: 27-58 months) and those treated with salvage operation (mean 41 months; 95%CI: 19-63 months) ( $P = 0.940$ ) [Figure 3].

Thirty-seven patients were reconstructed using gastric pull-up [Table 2]. Among them, 26 patients (70%) had the gastric tube directly anastomosed to the oropharynx (GP group). Another 7 patients (19%) used additional free jejunal flap to bridge the gap between gastric tube and oropharynx (GP-JF group). The rest 4 patients (11%) had additional free anterolateral thigh flap to bridge the gap and resurface the neck skin (GP-ALT group). The operation time was significantly lower in the GP group ( $918 \pm 152$  min) than the GP-JF ( $1166 \pm 164$  min) and GP-ALT group ( $1166 \pm 90$  min) ( $P < 0.001$ ). Successful swallowing was achieved by more than 70% patients in gastric pull-up group, and the GP-JF group had the highest rate as 85% (6/7) patients swallowed successfully. Other than gastric pull-up, we had 3 patients who underwent colon interposition (CI group). However, only one patient in the CI group swallowed successfully in the end.

Regarding surgical complications, anastomosis leakage occurred in 19 patients (47.5%). The leakage rate was as high as 50% (13/26) in the GP group, but as low as 29% (2/7) in the GP-JF group, but there was no statistical significance ( $P = 0.413$ ). However, most of the leakage was managed conservatively. Two patients in the GP group had partial necrosis of the gastric tube. One was salvaged by deltopectoral flap, and the other was salvaged by pectoralis major flap. In the GP-JF group, there was one jejunal flap partial necrosis with leakage, salvaged by deltopectoral flap. In the GP-ALT group, 2 patients (50%) had leakage from anastomosis between flap and gastric tube. One was salvaged by simple closure, and the other one closed with pectoralis major flap. In the CI group, 2 patients (67%) had colon graft necrosis. One was salvaged by pectoralis major flap, and the other one had persistent leakage even though pectoralis major and deltopectoral flaps were used. Unfortunately, the patient died of pneumonia as the only intrahospital mortality (2.5%, 1/40) in the study cohort. One patient in the GP group and one in the CI group developed tracheoesophageal fistula at the outpatient clinic. The former was salvaged by tracheal stent, and the latter, salvaged by tracheal stent along with deltopectoral flap.

**Table 1. Characteristics of patients underwent total laryngopharyngoesophagectomy and reconstruction**

Case	Age	Sex	Dx	Recon.	Complication	Oral intake	Follow up	Outcome
1	47	F	HCa-ECa	GP	Leakage	Failed	13	Bleeding; died
2	72	M	HCa	GP		POD 15	23	Renal failure; died
3	53	M	HCa	GP		POD 15	12	Pneumonia; died
4	59	M	HCa	GP		POD 15	107	NER; survived
5	50	M	HCa	GP	Leakage	Failed	15	Pneumonia; died
6	51	M	HCa	GP	Leakage	POD 50	14	Pneumonia; died
7	62	M	HCa	GP		POD 30	5	Pneumonia; died
8	68	M	HCa	GP	Leakage	POD 54	90	NER; survived
9	53	M	HCa-ECa	GP	Leakage, stricture	POD 39	86	NER; survived
10	48	M	HCa	GP		POD 19	83	NER; survived
11	56	M	HCa	GP	Leakage	Failed	5	Bleeding; died
12	55	M	HCa-ECa-TCa	GP	Leakage	POD 180	80	NER; survived
13	43	M	HCa-ECa	GP		POD 31	15	UTI; died
14	63	M	HCa	GP	Leakage	Failed	3	Pneumonia; died
15	53	M	HCa-ECa	GP		POD 23	53	Recurrence; died
16	51	M	HCa-ECa	GP		POD 20	19	Recurrence; died
17	60	M	HCa	GP	T-E fistula	POD 25	20	NER; survived
18	39	M	HCa-ECa	GP	Leakage, stricture	POD 47	18	Liver mets; died
19	64	M	LCa-ECa	GP	Leakage	POD 41	38	NER; survived
20	63	M	LCa-ECa	GP	Gastric tube necrosis; PM salvage	Failed	27	NER; survived
21	57	M	LCa-ECa	GP		POD 60	24	NER; survived
22	46	M	LCa-ECa	GP	Leakage	Failed	7	Pneumonia; died
23	52	M	HCa-ECa	GP		POD 17	7	Bleeding; died
24	52	M	HCa-ECa	GP	Leakage, DP salvage	POD 90	17	NER; survived
25	66	M	HCa-ECa-TCa	GP	Chylous leakage	Failed	5	NER; survived
26	79	M	HCa	GP		POD 37	7	NER; survived
27	70	M	HCa-ECa	CI	Leakage; PM, DP salvage	Failed	3	Pneumonia; died
28	50	M	LCa-ECa	CI	Empyema, chylo, T-E fistula	POD 58	81	NER; survived
29	61	M	HCa-ECa	CI	Leakage, PM salvage	Failed	4	NER; survived
30	59	M	HCa-ECa	GP-JF		POD 76	12	Pneumonia; died
31	45	M	HCa-ECa-MFCa	GP-JF		POD 28	29	Died
32	41	M	HCa	GP-JF		POD 38	8	Pneumonia; died
33	57	M	HCa	GP-JF	Leakage	Failed	7	Lung mets; died
34	46	M	HCa-ECa	GP-JF		POD 28	20	Bleeding; died
35	58	M	HCa-ECa-PCa	GP-JF		POD 28	33	Recurrence; died
36	58	M	HCa	GP-JF	Leakage; DP salvage	POD 62	22	LN, bone mets; died
37	55	M	LCa	GP-ALT		POD 30	106	NER; survived
38	51	M	HCa-ECa	GP-ALT	Leakage	POD 36	73	Died
39	55	M	HCa	GP-ALT		POD 42	9	Bleeding; died
40	56	M	HCa	GP-ALT	Leakage; PM salvage	Failed	7	NER; survived

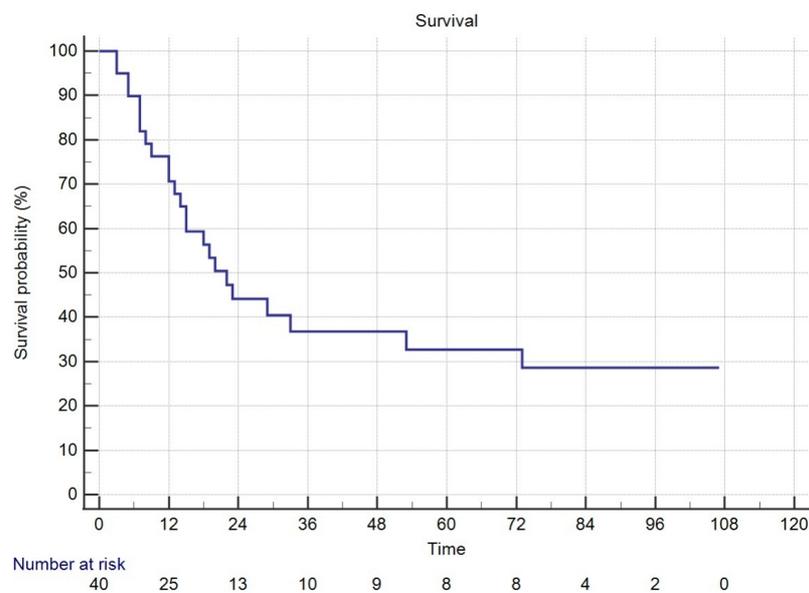
HCa: Hypopharyngeal cancer; ECa: esophageal cancer; LCa: laryngeal cancer; TCa: tongue cancer; MFCa: mouth floor cancer; PCa: palatal cancer; Recon.: reconstruction type; GP: pure gastric pull-up; CI: colon interposition; GP-JF: gastric pull-up with free jejunal flap; GP-ALT: gastric pull-up with free anterolateral thigh flap; GP-PM: gastric pull-up with pectoralis major myocutaneous flap; POD: postoperative day; NER: no evidence of recurrence; Mets: metastasis; LN: lymph node; UTI: urinary tract infection; Chylo: chylothorax; PM: pectoralis major myocutaneous flap; DP: deltopectoral flap.

Twenty patients (50%) had been assessed for their QoL at least one time [Figure 4]. The overall QoL and general health (Q1) deteriorated for the first year after the index operation. However, it gradually improved

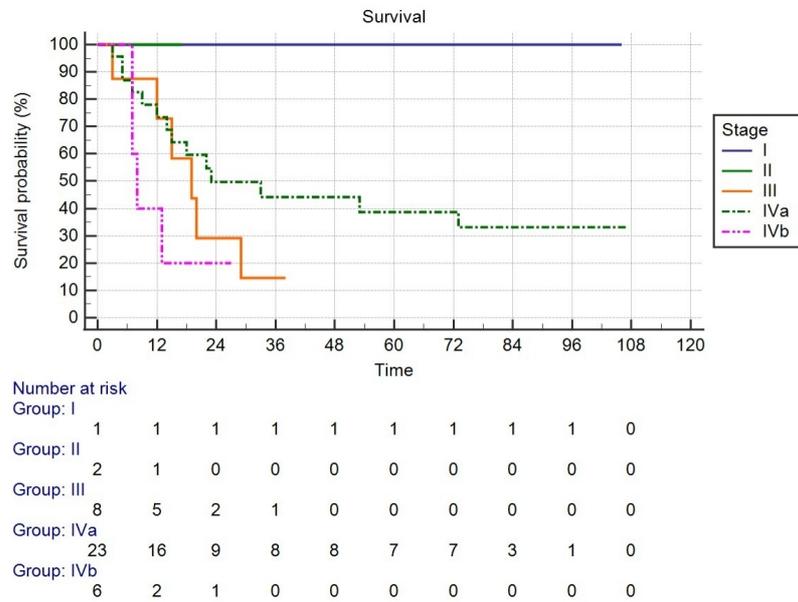
**Table 2. Patients underwent different reconstruction after total laryngopharyngoesophagectomy**

	Total	GP	GP-JF	GP-ALT	CI
<i>n</i>	40	26	7	4	3
Sex, M/F	39/1	25/1	7/0	4/0	3/0
Age, y/o (SD)	55.6 (8.5)	56.2 (9.2)	52.0 (7.7)	54.3 (2.2)	60.3 (10.0)
Indication					
Esophageal extension, <i>n</i>	18	12	3	3	0
Double cancer, <i>n</i>	22	14	4	1	3
Primary, <i>n</i>	24	17	3	3	1
Salvage, <i>n</i>	16	9	4	1	2
Operation time, min	1010 (195)	918 (152)	1166 (164)	1166 (90)	1230 (207)
Leakage, <i>n</i> (%)	19 (47.5)	13 (50)	2 (28.6)	2 (50)	2 (66.7)
Stricture, <i>n</i> (%)	2 (6.9)	2 (10.5)	0	0	0
Successful swallowing, <i>n</i> (%)	29 (72.5)	20 (73.1)	6 (85.7)	3 (75.0)	1 (33.3)
Hospitalization length, mean day (SD)	41 (31)	29 (10)	51 (44)	81 (58)	70 (5)
Follow-up time, mean months (SD)	30 (32)	31 (31)	19 (10)	49 (49)	29 (45)

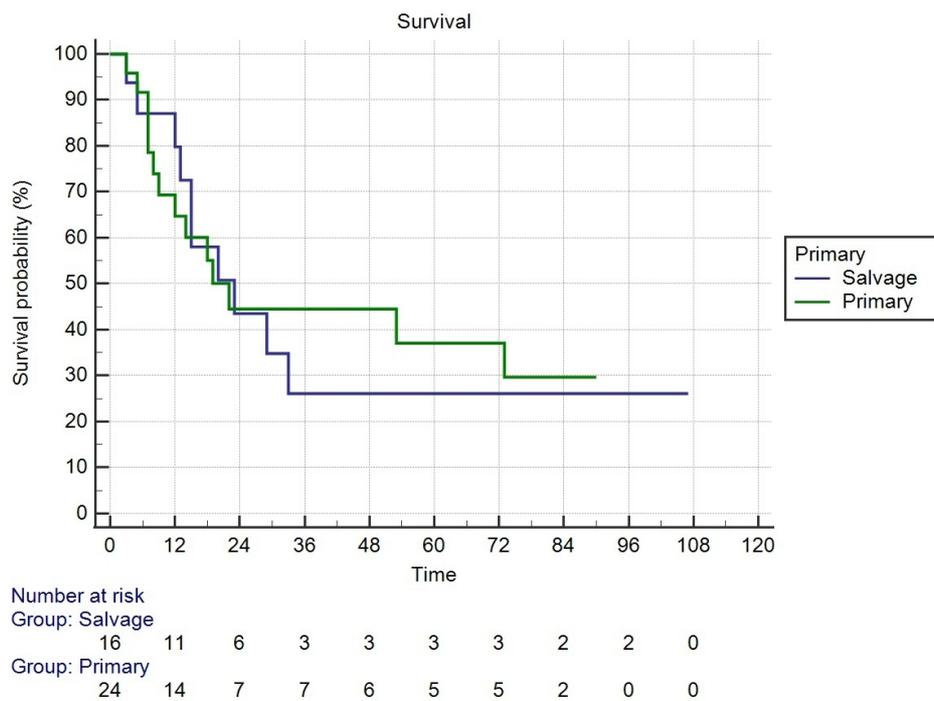
GP: Pure gastric pull-up; CI: colon interposition; GP-JF: gastric pull-up with free jejunal flap; GP-ALT: gastric pull-up with free anterolateral thigh flap; SD: standard deviation.



**Figure 1.** The overall survival time for the entire cohort were  $45 \pm 7$  months.

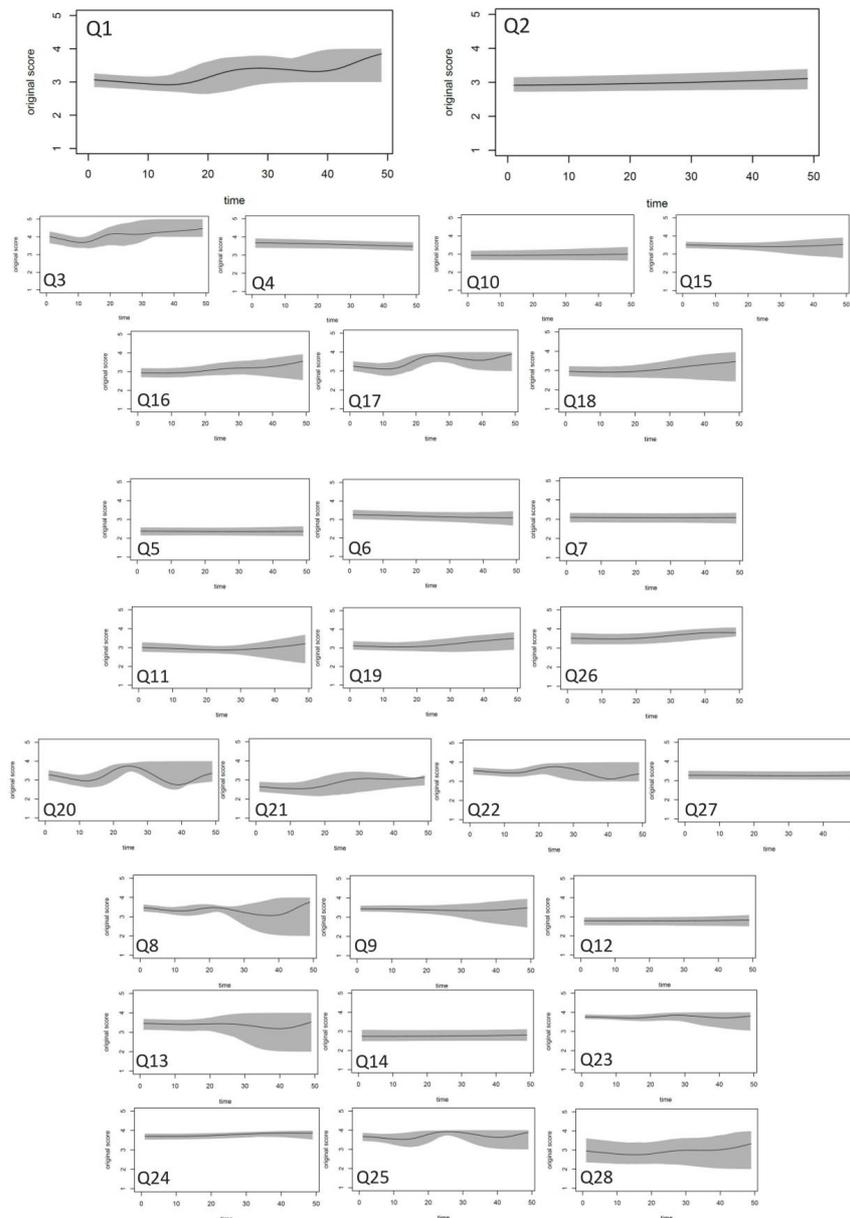


**Figure 2.** The hypopharyngeal cancer stage distribution was as follows: 1 (2.5%) was stage I, 2 (5%) were stage II, 8 (20%) were stage III, 23 (57.5%) were stage IVa, and 6 (15%) were stage IVb. The mean survival time was  $43 \pm 16$  months for stage III,  $50 \pm 9$  months for stage IVa,  $12 \pm 3$  months for stage IVb.



**Figure 3.** There was no difference between those primarily treated with surgery (mean 42 months; 95%CI: 27-58 months) and those treated with salvage operation (mean 41 months; 95%CI: 19-63 months) ( $P = 0.9396$ ).

and even surpassed their pretreatment QoL score by the end of the second year after the index operation. Since then, the QoL reached a constant level. Similar curve could be found in pain and discomfort (Q3), activities of daily living (Q17), work capacity (Q18), negative feeling (Q26), and sexual activity (Q21). Sleep



**Figure 4.** The World Health Organization Quality of Life - Brief (WHOQOL-BREF) questionnaire contains 28 items to evaluate four domains. The Q1 and Q2 represent overall QoL and general health. The physical domain consists of pain and discomfort (Q3), dependence on medical substances and medical aids (Q4), energy and fatigue (Q10), mobility (Q15), sleep and rest (Q16), activities of daily living (Q17), and work capacity (Q18). The psychologic domain consists of positive feelings (Q5), spirituality/religion/personal beliefs (Q6), thinking/learning/memory/concentration (Q7), bodily image and appearance (Q11), self-esteem (Q19), and negative feelings (Q26). The social relations domain consists of personal relationships (Q20), sexual activity (Q21), practical social support (Q22), and being respected/accepted (Q27). The environment domain consists of freedom, physical safety, and security (Q8), physical environment (Q9), financial resources (Q12), opportunities for acquiring new information and skills (Q13), participation in and opportunities for recreation/leisure activities (Q14), home environment (Q23), health and social care: accessibility and quality (Q24), transport (Q25), and eating/food (Q28). The overall QoL and general health (Q1) deteriorated in the first year after operation. However, it gradually improved and even surpassed their pretreatment QoL score by the end of the second year after operation. Since then, the QoL reached a constant level. Similar curve could be found in pain and discomfort (Q3), activities of daily living (Q17), work capacity (Q18), negative feeling (Q26), and sexual activity (Q21). Otherwise, sleep and rest (Q16) and self-esteem (Q19) slowly improved during follow up after surgery. However, substances and medical aids (Q4), and spirituality/religion/personal beliefs (Q6), deteriorated after surgery and did not recovered in the end. Interestingly, some QoL, like personal relationships (Q20), practical social support (Q22), freedom/physical safety/security (Q8), transport (Q25), and eating/food (Q28), showed regular oscillation after surgery with year.

and rest (Q16) and self-esteem (Q19) slowly improved during the follow up visits after surgery. However, substances and medical aids (Q4) and spirituality/religion/personal beliefs (Q6) deteriorated after surgery and did not improve in the end of the follow up. Interestingly, some QoL, like personal relationships (Q20), practical social support (Q22), freedom/physical safety/security (Q8), transport (Q25), and eating/food (Q28), demonstrated regular annual oscillation after surgery.

## DISCUSSION

### Rationale for esophageal substitute

The surgical option of esophageal substitute varies and depends on the individualized basis of the surgeon's preference and the patient's physical feasibility. Gastric tube pull-up has been advocated and proved as an effective measure for reconstruction of the alimentary tract after TPLE, but it comes with a reportedly high rate of anastomotic leakage and surgical complications<sup>[24-26]</sup>. The combination with free jejunal flap interposition overcomes the gap between the gastric tube and the resection margin. Since Asamura *et al.*<sup>[17]</sup> documented the first case, it has been reported to decrease the tension of anastomosis and the leakage rate<sup>[27]</sup>. Colon graft interposition is another choice for alimentary tract reconstruction especially in patients who were previously operated on for peptic ulcer. Vascular supply, however, greatly impacts on the postoperative graft viability and patient outcome. It has been reported that the colon is the most preferred and safest organ for esophageal reconstruction, whereas the stomach is a vascular and muscular organ with lower risk of ischemia<sup>[28]</sup>. Moreover, the study on the QoL after esophagectomy reported that the functional results with a colon interposition were better than those with a gastric tube<sup>[29]</sup>.

Reconstruction of the alimentary tract using visceral organs avoids strict postoperative immobilization of the extremity and enables early ambulation and rehabilitation, compared to the use of the free flap harvested from the extremities. For the long-segment gap between the gastric tube and resection margin, the redundancy of free jejunal flap should be taken into consideration to avoid swallowing difficulty. Nonetheless, the superior healing ability of jejunal mucosa minimizes the incidence of anastomotic leakage and complications requiring further surgery<sup>[30]</sup>.

Occasionally, cancer invasion of the skin results in skin defect in the neck region that will expose the great vessels postoperatively. The use of a free anterolateral thigh flap to reconstruct the gap between the gastric tube and the oropharynx and the coexisting neck skin defect is optimal. We proposed the "butterfly" design, which made the anastomosis externalized at the body surface<sup>[20]</sup>. By this design, it is easy to detect any leakage from the anastomosis, and it is also safe because the leakage would not accumulate in the neck. Therefore, we provided an algorithmic approach to reconstruct the defect of the TPLE. Gastric pull-up is simple and effective to restore alimentary continuity. When tension existed between the gastric tube and the oropharynx, an additional free jejunal flap is vital to solve the problem. If there is concomitant skin defect in the neck, the combined use of gastric pull-up and free anterolateral thigh flap would be ideal. The colon interposition should be reserved for patients with previous gastric surgery or disease. Alternatively, a pedunculated gastric conduit using a Roux-en-Y anastomosis precludes the need for a second flap, but it requires an additional anastomosis in the abdomen<sup>[30,31]</sup>. Additional use of pectoralis myocutaneous flap other than gastric pull-up is also optimal if the patient is unsuitable for microvascular surgery<sup>[32]</sup>.

### Negative pressure wound therapy

A substantial proportion of patients with hypopharyngeal cancer undergoing TPLE were previously irradiated<sup>[33,34]</sup>, portending the risk of anastomotic leakage and vascular fistula secondary to soiling of saliva around the anastomosis and secretion of digestive tract<sup>[35]</sup>. Anastomotic leakage constitutes a major proportion of surgical complications in patients undergoing TPLE for hypopharyngeal cancer<sup>[36-38]</sup>. The

accumulated saliva and localized abscess resulted in vascular erosion and even aspiration pneumonia if the abscess drained out of the wound into the permanent tracheostomy. The continuous vacuum-assisted drainage adopted right after surgery evacuated the saliva as soon as it leaked, forming a controlled enterocutaneous fistula. The continuous negative pressure was created using suction tube embedded in the Penrose drain and connected to the bedside wall suction unit [Figure 5]. The application of vacuum-assisted drain decreased the frequency of wound dressing change, facilitated the postoperative wound care, reduced the risk of saliva soiling, and enhanced early bedside mobilization.

Anastomosis leakage of the intestinal mucosa in abdominal surgery was initially managed with drainage<sup>[39,40]</sup>. Because of the positive pressure in the abdomen, intra-abdominal abscess transformed into enterocutaneous fistula after the drainage<sup>[41-43]</sup>. The anatomical difference with the lack of positive pressure in the neck area resulted in abscess formation secondary to the anastomotic leakage despite of adequate drainage. The negative pressure in the conventional negative-pressure drainage device gradually decreased as the drainage amount in the device increases<sup>[44]</sup>. The continuous negative pressure in the vacuum-assisted drainage created steady suction pressure, evacuated the leakage, and provoked adhesion around the anastomosis<sup>[45,46]</sup>. In patients with microvascular anastomosis, a conventional negative-pressure drain was placed around the pedicle instead. Nonetheless, a negative-pressure drain could still be applied on the other side.

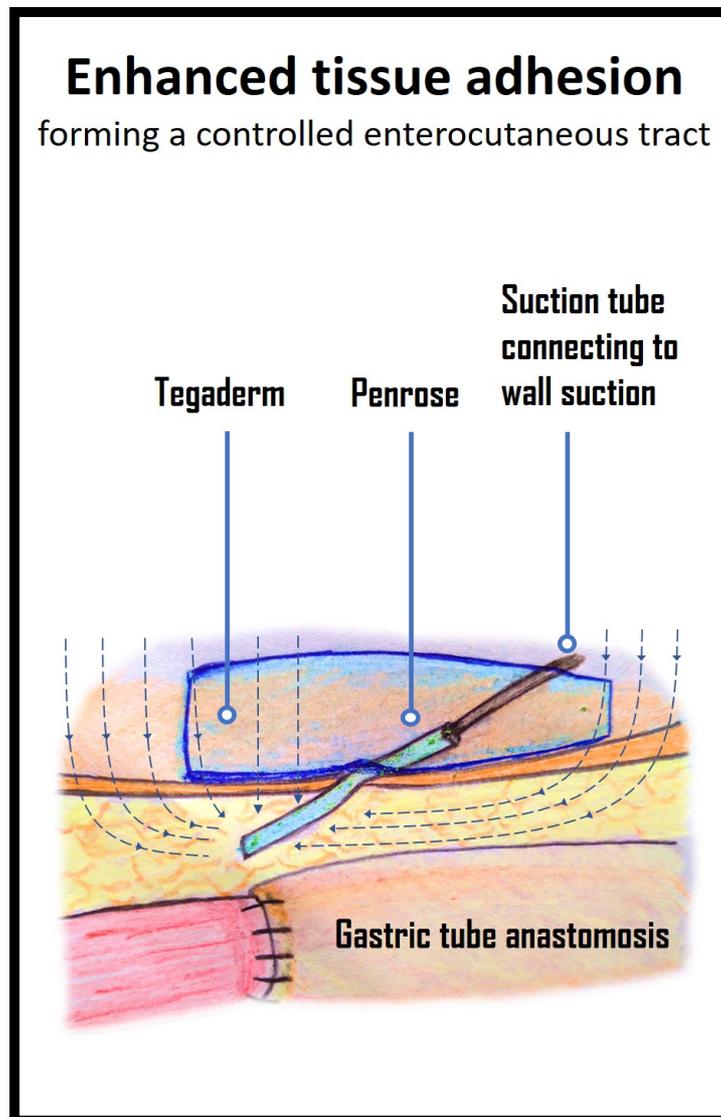
#### **Outcome evaluation of head and neck cancer reconstruction: QoL**

Defect of the head and neck poses a significant functional and emotional impact. Head and neck reconstruction should focus not only on wound resurfacing, but also function restoration. It is fundamental to evaluate the outcome with respect to both the clinical aspect and the QoL perceived by patients. In 2009, the United States' Food and Drug Administration approved the patient-reported outcome as a validated measure of treatment benefit or risk in clinical trials<sup>[47]</sup>. It is widely used in the fields of breast cancer and lung cancer<sup>[48,49]</sup>. Dissecting the outcome evaluation like the QoL in the head and neck reconstruction helps us acquire what is optimal in some inconclusive reconstruction.

Although our patient numbers were still not large enough to test our thesis in detail or subgroup analysis, the dynamic changes of the QoL in patients undergoing TPLE still gave us some clinical implications. The deterioration of the overall QoL and general health right after surgery for one year may result from surgical complication, adjuvant therapy, and the frustration from the sense of well-being. This period seemed longer than those of other head and neck patients, which usually lasts for 3 to 6 months<sup>[50]</sup>. Higher rate of surgical complication might also be responsible for this difference. However, the QoL recovered or even surpassed the pretreatment scores during the second year. This result supported the proof of the concept that surgical resection remained the standard therapeutic choice.

Two factors of the QoL constantly deteriorated after surgery despite addressing the patients' complications and having the patients acclimate to this disease. One factor is "How much medical treatment the patient needs to function in his or her daily life"? We might attribute it to the assistive device for voice rehabilitation or tube feeding due to failed swallowing function. The other factor is "How meaningful is life to the patient"? The results of these two factors are quite discouraging; however, we must factor in the significance of the psychological aspects that these patients face in such a devastating disease.

The response rate for the QoL was 50% in this study. Patients responded in the outpatient clinic, which implied that they were the patients with the better outcome than those who did not respond. The representation for the outcome of the QoL might be biased and overestimated. Nonetheless, the patients'



**Figure 5.** The negative pressure wound therapy (NPWT) facilitates formation of a controlled enterocutaneous fistula and avoids saliva soiling with subsequent abscess formation. Continuous and steady negative pressure was applied with connection of the suction tube to the bedside wall suction unit.

reported outcome was important and reflected their psychological well-being and resilience.

In summary, the evolution of esophageal substitute follows the improvement of surgical techniques and perioperative care. Different measures have been taken to heal the gap between the gastric tube pull-up and the resection margin in the oropharynx or even the nasopharynx. The postoperative QoL is becoming an issue worthy of serious consideration as long as complications after TPLE could be successfully tackled. The gap caused by TPLE in patients, perioperative morbidity, and postoperative QoL could be managed by the evolution of esophageal substitute, surgical techniques, perioperative wound care, and QoL evaluation.

## DECLARATIONS

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### Authors' contributions

Data acquisition, data analysis, interpretation, study design, and manuscript writing: Chang TY, Chang CC, Yen YT

Figure 5 illustration and manuscript writing: Tang WR

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### Availability of data and materials

Not applicable.

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None.

### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

This study has been approved by Institutional Review Board of National Cheng Kung University Hospital (A-ER-108-525).

### Consent for publication

Not applicable.

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