Survival and swallowing function outcome impact factors analysis of surgery-oriented comprehensive treatment for hypopharyngeal cancer in a series of 122 patients

Wan-Xin Li, MD¹#, Yan-Bo Dong, MD¹#, Cheng Lu, MD¹, Patrick J. Bradley, MBA, FRCS² and Liang-Fa Liu, MD, PhD¹³

Abstract

Objective: Under current standards of treating highly aggressive hypopharyngeal cancer (HPC), oncological control and functional outcome are still unsatisfactory worldwide. This study explored the surgery-oriented comprehensive treatment approach based on 15 years of practice. Methods: A retrospective cohort of HPC patients treated by the senior author at Chinese PLA General Hospital between Nov 2005 and Aug 2012 and Capital Medical University Beijing Friendship Hospital between May 2014 and Nov 2019 was studied. Oncological control, swallowing function, and quality of life (QoL) were assessed. Results: In total, 122 patients were included in this study, with 11 (9.0%) cases in the early stage and 111 (91.0%) cases in the advanced stage. Five-year overall survival (OS) and disease-free survival (DFS) were 40.0% and 36.1%, respectively. The swallowing outcome was satisfactory in 90 (73.8%) patients. Tracheostomy-free survival was achieved in 55 (45.1%) patients. Multivariate cox regression analysis showed that the size of the surgical defect, local-regional recurrence, and distant metastasis were independent impact factors for OS and DFS ($P < .05$). Multivariate analysis showed that the logistic regression coefficients (standard error) of pharyngo-cutaneous fistula and local-regional recurrence on swallowing function were 1.274 (.532) and 1.283 (.496), respectively ($P < .05$). In addition, the logistic regression coefficients (standard error) of the clinical stage, local-regional recurrence, decannulation, and feeding tube on QoL were $-7.803 (3.593)$, $-7.699 (3.151)$, $13.853 (3.494)$, and $-20.243 (3.696)$, respectively ($P < .05$). Conclusions: Surgery-oriented comprehensive treatment can give rise to good swallowing function without jeopardizing oncological control. The size of the surgical defect, local-regional recurrence, and distant metastasis were independent factors impacting OS and DFS. Pharyngo-cutaneous fistula and local-regional recurrence were independent factors impacting swallowing function. Clinical stage, local-regional recurrence, decannulation, and feeding tube were independent factors impacting QoL.

Keywords

ychyphopharyngeal cancer, surgery-oriented comprehensive treatment, survival, functional outcome, swallowing function

Introduction

Hypopharyngeal cancer (HPC) is reported as one of the most aggressive cancers of the head and neck region.¹⁻⁴ The primary tumor commonly causes intra-luminal obstruction of the upper aerodigestive tract, leading to progressive swallowing problems (dysphagia), hoarseness of voice (dysphonia), and airway
compromise (dyspnea). Most patients present with advanced-stage disease at the initial diagnosis. Early-stage HPC tumors are small in size and volume and manifest nonspecific symptoms, making early diagnosis difficult if not impossible without specialist examination. The prognosis of HPC is poor, with a 5 year overall survival (OS) rate of around 40%.2,4,7

The treatment goals are to achieve local-regional tumor control with preservation of laryngopharyngeal functions: tracheostomy-free breathing, ability to maintain body mass (weight) by a daily oral diet, and ability to vocalize.4 Transoral surgery, including transoral laser microsurgery (TLM) and transoral robotic surgery (TORS), has enabled oncologic surgeons to remove tumors without the need of breaching the neck skin. This treatment modality avoids many of the complications of conventional open neck surgery (scar formation, pharyngocutaneous fistula, infection, and hemorrhage), allowing rapid functional recovery, particularly swallowing. This surgical technique is recommended for selected cases.

Although it was reported that the temporal sequence of surgery and radiotherapy (RT) did not affect prognosis,9 a recent study concluded that patients receiving postoperative radiation alone had superior swallowing outcomes and equivalent speech outcomes relative to the preoperative radiation group.10 Moreover, some authors advocate that primary total laryngo-pharyngectomy remains the “gold standard” treatment for T4 HPC (with extra-laryngeal extension) because it gives rise to satisfactory oncologic and functional outcomes.11

Furthermore, it was reported that patients with advanced-stage HPC treated surgically with adjuvant RT or chemoradiotherapy (CRT) showed a trend toward clinically improved OS compared with patients treated with definitive CRT; however, the difference was not statistically significant.12

In China, surgery followed by RT is the mainstream treatment, and the maximal restoration of pharyngoesophageal continuity and function improves survival in patients whose tumors are excised completely.8 This report reviews the clinical data from a cohort of 122 HPC patients undergoing surgery-oriented comprehensive treatment, including preoperative induction chemotherapy, postoperative intensity-modulated RT (IMRT), chemotherapy, or targeted therapy, focusing on their oncologic control and functional outcome, especially swallowing function outcome.

Methods

Patients

The eligible HPC patients were collected based on inclusion and exclusion criteria. Inclusion criteria: HPC patients undergoing surgery-oriented treatment; a pathological diagnosis of HPC; informed consent obtained or waiver of consent; and follow-up information available.

Exclusion criteria: HPC patients without surgery; a lack of histological diagnosis of HPC; and no follow-up information.

This retrospective study investigated a consecutive series of HPC patients surgically treated by the senior author at Chinese PLA General Hospital from Nov 2005 to Aug 2012 and at Capital Medical University Beijing Friendship Hospital from May 2014 to Nov 2019. All the surgical procedures were performed by a single surgeon to eliminate the surgeon’s bias. The following aspects were analyzed and summarized: patient demographics, presenting symptoms, medical history, treatment, complications, survival, swallowing function outcome, and QoL.

The study protocol was approved by the authors’ institutions, and the requirement for patient consent was waived because of the retrospective nature of the study and anonymized analyses. All the patients or their legal surrogates provided written informed consent to undergo surgery.

Every HPC patient was subjected to a multidisciplinary team (MDT) session to determine the most suitable and individualized course of treatment.

Preoperative therapies

Since 2011, for patients whose lesion was too advanced to preserve the larynx, two sessions of induction chemotherapy (cisplatin, 75 mg/m², d1; 5-fluorouracil, 750 mg/m²), or induction CRT chemotherapy and preoperative radiotherapy (additional RT dose of 40–50 Gy) were administered. Then the patients were re-evaluated to determine further course of treatment: RT for complete remission, RT or surgery for partial remission, and surgery for no response or disease progression.

Patients diagnosed with a synchronous second primary esophageal carcinoma underwent treatment by endoscopic submucosal dissection, RT, CRT, or open surgery, based on the depth of tumor infiltration, distance from HPC, and their general condition, before treatment of the hypopharyngeal lesion.

Surgical procedures

Based on preoperative examination results, the location and size of the primary tumor could be accurately estimated. A variety of surgical procedures have been described in the literature to achieve complete tumor removal. Procedures of larynx preservation surgery (LPS) consisted of partial pharyngectomy13 and partial laryngo-pharyngectomy,14 including extended supra-glottic laryngo-pharyngectomy,15 supra-cricoid hemi-laryngo-pharyngectomy,16 and vertical hemi-pharyngo-laryngectomy.17 When the larynx could not be preserved, the following procedures were performed: total laryngectomy (TL) with partial pharyngectomy, total laryngo-pharyngectomy (TLP), TLP with cervical esophagectomy, and total laryngo-hypopharyngo-esophagectomy.

A functioning contra-lateral “crico-arytenoid unit” was paramount when considering LPS,1,18 while the N status of the patients’ disease generally did not influence the type of LPS surgery undertaken. Furthermore, it was paramount for LPS candidates to have a good pulmonary functional reserve, motivation, and psychological support to ensure that they
could cope with the potentially prolonged period possibly required for swallowing rehabilitation. They could be spigotted day and night for a month. They were suggested to have a liquid diet at first and gradually change it to a soft diet. NG-FT feeding, along with NG-FT feeding, would be tried on the first and gradually change it to a soft diet. NG-FT feeding would be initiated on the first postoperative day. Oral feeding, along with NG-FT feeding, would be tried on the 10th postoperative day for primary cases and on the 14th postoperative day for salvage cases. The patients were suggested to have a liquid diet at first and gradually change it to a soft diet. NG-FT feeding would be removed once patients could take in sufficient food orally (usually the second day of oral feeding), without evidence of pharyngo-cutaneous fistula. After completion of RT, the decannulation of tracheotomy tubes should be planned in a graduated fashion for LPS recipients only. OS was calculated from the date of surgery until all-cause death or last follow-up. All the patients were followed up via routine outpatient appointments: one month, 3 months, and every 3 months after that. Barium swallow x-ray was routinely performed during every follow-up visit, except for patients with apparent aspiration, who would be evaluated with a fiberoptic laryngoscope. Swallowing function outcome and QoL were routinely evaluated commencing from 6 months. The scores of swallowing function outcome and QoL, used for further analyses, were from the individual’s latest evaluation.

The swallowing function was evaluated regarding a functional outcome swallowing scale (FOSS). Symptom criteria ranged from stage 0 (normal function and asymptomatic) to stage V (nonoral feeding for all nutrition). Swallowing function at or above stage III was considered satisfactory because patients could swallow orally, and aspiration was avoided. The functional assessment of cancer therapy-general (FACT-G) questionnaire was used to evaluate patients’ general postoperative QoL. The FACT-G (version 4) consists of 27 items rated on a 0–4 Likert-type scale, divided into four subscales that assess physical well-being, social/family well-being, emotional well-being, and functional well-being. The total score range was 0–108, with higher scores representing better QoL. The status of breath and voice was recorded for LPS recipients only. OS was calculated from the day of surgery until all-cause death or last follow-up.

Statistical analysis
OS and disease-free survival (DFS) were determined by Kaplan–Meier analysis. For postoperative course and functional results, the chi-squared test or Fisher’s exact test was used to compare differences between categorical variables, and the t-test was conducted to compare differences in continuous variables. All the variables associated with \( P < .05 \) on univariate analysis were included in the logistic (qualitative variables) or linear (quantitative variables) regression models (enter) for multivariate analysis (conducted only when more than one factor was significant in univariate analyses). All the statistical analyses were performed by SPSS 26.0 (IBM Corp, Armonk, NY).

Results
Patient demographics and baseline characteristics
In total, 122 patients were included in this study, with a median age of 58 years (range = 39–83); 117 (95.9%) patients were...
male, and five (4.1%) were female. Only 11 (9.0%) patients had an early-stage HPC (stages I and II), and 111 (91.0%) had advanced-stage HPC (stages III and IV), as shown in Table 1. In addition, since 2014 (66 cases in total), examination of the esophagus with a gastroendoscope and barium swallow imaging was routinely included in the assessment of patients with HPC, which identified a second primary esophageal carcinoma in seven (10.6%) male patients, with a median age of 52 years (range = 48–65).

The location of the primary tumor by the subsite of HPC: 95 (77.9%) in the pyriform sinus, 22 (18.0%) in the posterior hypopharyngeal wall (PHPW), and five (4.1%) in the postcricoid region. Classification of disease using the TNM system and clinical staging was based on the American Joint Committee on Cancer (AJCC, eighth edition, 2017). There were 30 (24.6%) cases of T1/T2 disease and 92 (75.4%) cases of T3/T4 disease (Table 2).

**Table 1.** Characteristics of our cohort of patients with hypopharyngeal cancer.

| Characteristic                        | Number of patients (%) |
|---------------------------------------|------------------------|
| Age (Median)                          | 39–83 (58)             |
| Sex                                   |                        |
| Male                                  | 117 (95.9)             |
| Female                                | 5 (4.1)                |
| Smoking history                       | 83 (68.0)              |
| History of alcohol drinking           | 74 (60.7)              |
| Primary site                          |                        |
| Pyriform sinus                        | 95 (77.9)              |
| Posterior hypopharyngeal wall         | 22 (18.0)              |
| Postcricoid area                      | 5 (4.1)                |
| T stage                               |                        |
| T1                                    | 4 (3.3)                |
| T2                                    | 26 (21.3)              |
| T3                                    | 46 (37.7)              |
| T4                                    | 46 (37.7)              |
| N stage                               |                        |
| N0                                    | 29 (23.8)              |
| N1                                    | 24 (19.7)              |
| N2                                    | 62 (50.8)              |
| N3                                    | 7 (5.7)                |
| M stage                               |                        |
| M0                                    | 122 (100)              |
| M1                                    | 0                      |
| Clinical stage                        |                        |
| I                                     | 2 (1.6)                |
| II                                    | 9 (7.4)                |
| III                                   | 24 (19.7)              |
| IV                                    | 87 (71.3)              |

Li et al. 535

Treatment

Thirteen patients underwent induction chemotherapy (five cases) or induction CRT chemotherapy and preoperative radiotherapy (eight cases). As there was no objective evidence of tumor shrinkage up to partial remission, the patients were informed, who agreed to surgical treatment (eight LPS cases and five TL cases). Salvage surgery was performed on four additional cases due to the failure of tumor control after definitive RT, whose HPC tumor has remained stable following a total dose of 70 Gy.

LPS was performed for 64 (52.5%) patients, while 58 (47.5%) patients received TL (Table 3). For LPS recipients, decannulation was successful in 55 (85.9%) patients, and median tracheostomy-free survival was 38 months.

The final hypopharyngeal surgical defect measurement ranged between 5 cm² and 110 cm², with a median size of 16 cm². Primary closure was achieved in 62 (50.8%) patients, while reconstruction was necessary in 60 (49.2%) patients. Reconstruction methods included 25 cases of the submental flap, 5 cases of RFFF (see Figure 1), 3 cases of the gastric pull-up, 1 case of ALT free flap, and various other methods.

Neck dissection was necessary in 120 (98.4%) patients. Forty-three (35.2%) patients experienced complications. There were 27 (22.1%) cases of PCF (including 3 salvage cases), 6 (5.0%) cases of postoperative pneumonia, 4 (3.3%) cases of postoperative hemorrhage, 4 (3.3%) cases of local infection, 1 (.8%) case of chylous fistula, and 1 (.8%) case of neopharyngeal stenosis. To manage PCF, conservative treatment was successful in 23 cases, a pecto-deltoid flap was used for two other cases, and a pectoralis major musculocutaneous flap was used for yet another case. In one salvage case, the PCF could not be repaired.

IMRT was undertaken within 6 weeks for 90 (73.8%) patients: 5 days a week, 2 Gy/day over 7 weeks, reaching a total dose of 60–70 Gy; among them, 23 patients also received alternating chemotherapy (cisplatin, 75 mg/m², d 1; 5-fluorouracil, 750 mg/m², d 1–d 5; docetaxel, 75 mg/m²), with four receiving additional targeted therapy (cetuximab, 400 mg/m²). PCF resulted in delayed RT in 18 (14.6%) patients. Three (2.5%) patients rejected any postoperative adjuvant therapy.

**Survival**

The follow-up ranged between 9 months and 136 months. Recurrence occurred in 45 cases: 25 patients had local recurrence; 12 patients had regional recurrence; 1 patient had both local and regional recurrence; and 7 patients had local and regional recurrence, with distant metastasis. All these patients chose chemotherapy and targeted therapy and died subsequently. There were 12 other distant metastasis cases alone, including lung, liver, brain, and cervical vertebrae. In addition, two patients died of second primary lung cancer, one patient died of second primary nasopharyngeal carcinoma, and another patient died of second primary esophageal carcinoma. Furthermore, 14 other patients died of unrelated causes, including four cases of pneumonia, two cases of cardiac infarction, two cases of cerebral infarction, one case of pulmonary embolism, and various other reasons.
Table 2. Analysis of sub-groups of patients and primary tumor subsites.

|                        | T 1+2 | T 3+4 | Stage I+II | Stage III+V | PS | PHPW | PCR | Total |
|------------------------|-------|-------|------------|-------------|----|------|-----|-------|
| Number of patients     | 30    | 92    | 11         | 111         | 95 | 22   | 5   | 122   |
| 3-year OS              | 70.5% | 42.7% | 90.0%      | 45.3%       | 53.9% | 40.9% | 20% | 49.9% |
| 5-year OS              | 61.1% | 32.0% | 90.0%      | 34.1%       | 43.3% | 32.7% | 20% | 40.0% |
| 3-year DFS             | 67.3% | 42.4% | 90.9%      | 43.9%       | 52.1% | 42.3% | 20% | 48.8% |
| 5-year DFS             | 54.7% | 28.7% | 90.9%      | 29.4%       | 38.4% | 33.9% | 20% | 36.1% |
| Satisfactory swallowing| 24/30 | 66/92 | 9/11       | 81/111      | 75/95 | 12/22 | 3/5 | 90/122 |
| (%)                    | (80%) | (71.7%) | (81.8%) | (73.0%)   | (78.9%) | (54.5%) | (60.0%) | (73.8%) |
| QoL (SD)               | 75 (22.41) | 56 (19.39) | 82 (21.12) | 65 (21.93) | 69 (22.02) | 59 (22.22) | 54 (16.86) | 66 (22) |

OS: overall survival, DFS: disease-free survival, SD: standard deviation, PS: Pyriform sinus, PHPW: posterior hypopharyngeal wall, PCR: postcricoid area.

Table 3. Comparison between patients receiving laryngeal preservation surgery (LPS) and total laryngectomy (TL).

|                        | LPS | TL | P-value |
|------------------------|-----|----|---------|
| Number of patients (men) | 64 (62) | 58 (55) | NA |
| Median age (range)      | 57.5 (39–74) | 59 (40–83) | NA |
| Postoperative complications (%) | 16 (25%) | 27 (46.6%) | .015 |
| Pharyngo-cutaneous fistula (%) | 8 (12.5%) | 19 (32.8%) | .009 |
| Local-regional recurrence (%) | 17 (26.6%) | 33 (56.9%) | .001 |
| Distant metastasis (%)  | 13 (20.3%) | 7 (12.1%) | .328 |
| 5-year survival rate (%) | 47.3 | 33.0 | .003 |
| Satisfactory swallowing (%) | 50 (78.1%) | 40 (69.0%) | .305 |
| QoL (SD)                | 75.08 (22.94) | 56.59 (16.65) | <.001 |

SD, standard deviation; NA, not applicable.

Figure 1. Preoperative examination, intraoperative photo, and postoperative follow-up of a hypopharyngeal cancer patient with surgical defect reconstructed by radial forearm free flap (RFFF). (A) Preoperative enhanced CT shows a massive right hypopharyngeal mass (yellow arrow) (B) Preoperative enhanced MRI T1WI sagittal view shows a massive right hypopharyngeal mass (yellow arrow) (C) Preoperative barium swallow x-ray shows a massive right hypopharyngeal filling defect, indicating a giant mass (D) The RFFF was sutured into a tube with skin lining the lumen before being inserted into the surgical defect (E) Surgical defect reconstructed by the RFFF tube (F) Barium swallow x-ray two months postoperatively shows the smooth flow of barium through the hypopharynx into the esophagus (G) Barium swallow x-ray 10 months postoperatively shows the smooth flow of barium through the hypopharynx into the esophagus.
According to Kaplan–Meier analysis, 3 year and 5 year OS rates were 49.9% and 40.0%, respectively, while 3 year and 5 year DFS rates were 48.8% and 36.1%, respectively (Figure 2). Interestingly, the OS of stage I+II was very good, with 5 year OS at 90.0% (Table 2). Further analysis showed that the difference between the OS of stage I+II and stage III+IV was statistically significant (HR = 11.60, 95% CI: 5.908 to 22.77, log-rank \( P = .0018 \); Figure 2C), and the difference between the OS of T1+2 and T3+4 was also statistically significant (HR = 2.585, 95% CI: 1.550 to 4.311, log-rank \( P = .0024 \); Figure 2D). However, the differences in OS and DFS were not statistically significant between different primary sites.

The 5 year OS rates of LPS and TL recipients were 47.3% and 33.0%, respectively (Table 3), and this difference was statistically significant (HR = 2.036, 95% CI: 1.229 to 3.375, log-rank \( P = .0029 \); data not shown). Furthermore, the differences in postoperative complications, PCF, and local-regional recurrence were statistically significant between LPS and TL recipients. We assumed these differences were because TL recipients had more advanced disease than LPS recipients, although the difference in distant metastasis between LPS and TL recipients was not statistically significant (Table 3).

Univariate analysis showed that T stage, N stage, clinical stage, size of the surgical defect, pathological risk factors, local-regional recurrence, and distant metastasis were factors impacting OS and DFS. Further multivariate analysis showed that the size of the surgical defect, local-regional recurrence, and distant metastasis independently impacted OS and DFS (Table 4).

**Functional outcome**

**Swallowing function.** The duration from surgery to full oral food intake was 10–150 days (average time = 24.02 days, while the median was 14 days). Swallowing was deemed “satisfactory” in patients with FOSS Grade 0–III: 17 cases of Grade 0, 20 cases of Grade I, 26 cases of Grade II, and 27 cases of Grade III. In total, swallowing function was satisfactory in 90 (73.8%) patients. Unsatisfactory swallowing was recorded in 28 cases of Grade IV and 3 cases of Grade V. The differences in swallowing function between different primary sites were not statistically significant (Table 2).

Univariate analysis showed that the size of the surgical defect (categorized as a binary variable with a cutoff value of 16 cm² for its median), presence of PCF, and local-regional recurrence were factors that impacted swallowing function. Further multivariate analysis showed PCF and local-regional recurrence independently impacted swallowing function (Table 5).

**Quality of life.** The QoL score was between 16 and 105 (median score = 70; mean ± SD = 66.29±22.153; normally distributed).
The distribution was wide because these cases varied significantly in tumor stage and postoperative function such as breath, swallowing, and phonation. Different primary sites did not correlate with QoL significantly. Univariate analysis showed that clinical stage, surgical defect size, presence of PCF, presence of local-regional recurrence, decannulation, and feeding tube impacted QoL. Further multivariate analysis showed that clinical stage, local-regional recurrence, decannulation, and feeding tube independently impacted QoL (Table 6).

**Discussion**

HPC is one of the most aggressive cancers of the head and neck region. Treatment strategy varies according to the tumor stage and institutional experience. In China and some Asian countries, skilled surgeons prefer surgery-oriented treatment to remove the lesions completely, and the prognosis is not worse than those undergoing chemoradiotherapy. Hence, this study focused on the survival and function outcomes and the impact factors of surgery-oriented comprehensive treatment for hypopharyngeal cancer in a series of 122 patients. We hope that our findings will contribute to the treatment of the disease and improve the prognostic expectations for HPC patients.

We presented the patient demographics, individual treatment strategies, survival, and functional outcomes in the present study. The OS of patients with early-stage HPC and advanced-stage HPC were statistically significant. The results showed that the treatment outcomes of early HPC by surgery-
oriented comprehensive treatment were satisfactory, while the
treatment effect of advanced HPC was not, indicating that
early diagnosis and treatment improved the treatment out-
comes for advanced-stage HPC.

Univariate and multivariate analyses were used to identify
the impact factors for OS, DFS, swallow function outcome,
and QoL. The results revealed that the size of the surgical
defect, local-regional recurrence, and distant metastasis were
independent predictors for OS and DFS; PCF and local-
regional recurrence were independent predictors for the
overall survival; and PCF and swallowing function were indepen-
dent predictors for QoL in HPC patients.

Overall swallowing performance is the most important
functional outcome for a patient’s health and QoL before and
after treatment.22 In order to provide HPC patients with a
chance to maintain oral swallowing, every effort was made to
remove the space-occupying lesion and reconstruct a passage
for food, which might include the reconstruction of the hy-
popharynx, oropharynx, and/or esophagus, depending on the
extent of the surgical defect, after making sure of secure
margins. Much of this surgical progress has been achieved by
innovative surgeons using free tissue transfer, accurate
placement surgery, reconstruction of neo-glottis, and per-
flecting the pharyngo-esophageal anastomosis.19 Compared
with non-surgical treatment,12,23–25 our surgery-oriented
comprehensive treatment resulted in comparable 5 year OS,
functional larynx preservation, and better swallowing
function.

Based on our experience, some detailed surgical skills were
helpful to preserve the swallowing function. When the hy-
popharyngeal defect is too large, too much mobilization of the
mucosa and direct suturing will lead to too much tension on
the neo-hypopharyngeal wall and postoperative PCF, which is
a significant negative factor for swallowing function, as shown
by our results. Defects affecting the PHPW can be closed
primarily if the extent of the defect is <50%; otherwise, re-
construction is required and is best repaired by a flap.19

Sometimes, the width of the surgical resection margin is
crucial for primary closure. A wide resection margin of 2 cm,
and up to 3 cm for inferior margin, has been suggested.23
Adequate tumor extirpation, with less extensive and invasive
procedures preserving unaffected normal tissue, contributes to
more tumor control and less morbidity.26 Furthermore, for the
reconstruction of PHPW, relatively thin flaps (like RFFF, free
jejunals patch graft, or free skin graft) can lead to better
swallowing function. In contrast, thick flaps (like the pecto-
ralis major musclocutaneous flap) will narrow the hypo-
pharyngeal passage and dampen swallowing, possibly
resulting in aspiration.27 When pyriform sinus lesions are
surgically removed, the morphological characteristics of
piform sinus can be regained by reconstruction with different
flaps, which is good for the rehabilitation of swallowing
function and prevention of aspiration.

Based on our results, PCF is an independent factor im-
pacting swallowing function. Hence, its prevention and proper
management are crucial for better outcomes. Comorbidity can
predispose patients to PCF, including hypertension, diabetes,
cardiovascular disease, hypoalbuninemia, anemia, throm-
bocytosis, poor nutritional status, liver disease, peripheral
vascular disease, chronic obstructive pulmonary disease, and
immunosuppressive medication,28–30 which should be dealt
with or optimized before surgery. A review of the literature
concludes a clear advantage in using vascularized tissue from
outside the radiation field in the surgical defect. Some studies
show a clear reduction in PCF rates, while others suggest that
the fistulae are smaller and rarely need repair.31 However,
using vascularized tissues, especially those from outside the
irradiated field, will definitely be more time-consuming,
prolonging the operative time (>10 hours), which is inde-
pendently associated with postoperative wound complica-
tions.32 In our experience, the most important technique of
closure of the hypopharyngeal surgical defect is continuous
submucosal suture as the first suture line between realigned
healthy residual mucosal edges or between residual mucosa
and various kinds of flaps (pedicled or free). Moreover, there

| Clinical factors | B (s.e.) |
|------------------|---------|
| Age              | 5.806 (4.067) |
| Smoking history  | -7.331 (4.328) |
| History of alcohol drinking | -7.138 (4.142) |
| Clinical stage   | -17.929 (4.165)*** - 7.803 (3.593)* |
| Size of defect   | -9.459 (3.990)/0.600 (3.099) |
| Pharyngo-cutaneous fistula | -16.761 (4.624)*** - 1.779 (3.891) |
| Local-regional recurrence | -18.821 (3.754)*** - 7.699 (3.151)* |
| Decannulation    | 24.825 (3.419)*** / 13.853 (3.494)*** |
| NG-FT/G-FT       | 17.929 (4.165)*** - 7.803 (3.593)* |
| R² of multiple linear regression | 0.532 |

B, Regression coefficient. s.e. Standard error. * with statistical difference (P < .05); ** with statistical difference (P < .01); *** with statistical difference (P < .001). NG-FT: nasogastric feeding tube; G-FT: gastric feeding tube. R², determination coefficient.
should be no tension on the first suture line. Furthermore, this neo-hypopharynx will be strengthened with adjacent muscles, mainly inferior pharyngeal constrictor and strap muscles, even if they have been irradiated. For us, time-saving surgical technique is preferred.

**Conclusion**

HPC is highly aggressive, and at present, the survival of HPC patients is not satisfactory, which is why we try our best to improve their functional outcome and QoL. Surgery-oriented comprehensive treatment can give rise to good swallowing function without jeopardizing oncological control. The size of the surgical defect, local-regional recurrence, and distant metastasis were independent factors impacting OS and DFS. Pharyngo-cutaneous fistulae and local-regional recurrence were independent factors impacting swallowing function. Clinical stage, local-regional recurrence, decannulation, and feeding tube were independent factors impacting QoL.

**Declaration of Conflicting Interests**

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**ORCID iD**

Liang-Fa Liu [https://orcid.org/0000-0002-3296-5371](https://orcid.org/0000-0002-3296-5371)

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