

## Original Article

# Surgical management of cervical esophageal carcinoma with larynx preservation and reconstruction

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Received August 5, 2014; Accepted August 28, 2014; Epub September 15, 2014; Published September 30, 2014

**Abstract:** Objectives: There is no generally accepted treatment strategy for cervical esophageal carcinoma. The purpose of this study was to evaluate the operative outcomes of reconstruction after resection of cervical esophageal and hypopharynx-esophagus junction carcinoma with larynx preservation. Methods: We retrospectively reviewed the data of 79 patients with carcinoma of the hypopharynx-esophagus junction and cervical esophagus. Transhiatal total esophagectomy without thoracotomy was carried out in 67 patients who underwent gastric pull-up (GP) or colon interposition (CI) techniques. Transcervical limited pharyngo-cervical esophagectomy was performed in the patients with the pectoralis major flap alone or combined with the split graft (PMF/CWSG) for reconstruction. Seventy-two patients received postoperative adjuvant therapy. Results: The 3-year and 5-year overall survival rates were 66.4% and 45.5%, respectively. The average time to resumption of oral feeding was 25.2 days. All patients had preserved laryngeal function. The overall incidence of complications was 29.1% (23/79), which included cervical fistula, abdominal wound dehiscence, liquefaction necrosis of abdominal fat, and pleural effusion. Conclusions: Surgical resection of cervical esophageal carcinoma and laryngeal preservation is possible. Complete esophagectomy should be performed when the resection extends below the thoracic inlet. The reconstruction methods we performed were safe and effective for the immediate restoration of alimentary continuity after resection of cervical esophageal and pharyngo-cervical esophageal carcinoma; and the patients with PMF/CWSG reconstruction had a better survival than those with GP or CI reconstruction. Combined with radiotherapy, the resectability rate and survival rate of cervical esophageal carcinoma can be improved.

**Keywords:** Carcinoma, cervical esophagus, gastric pull-up, colon interposition, larynx preservation, oral cancer

## Introduction

Esophageal cancer is the sixth most common cause of death from cancer worldwide [1]. In China, esophageal cancer is the fourth most common cancer and the most common cause of cancer death, with an age-adjusted mortality of up to 140 deaths per 100,000 [2]. It has been estimated that fewer than 5% of all esophageal cancers occur in the cervical portion of the esophagus [3]. The cervical esophagus is defined as the upper part of the esophagus between the cricopharyngeal muscle and the thoracic inlet. Cervical esophageal cancer frequently spreads submucosally upwards to

involve the hypopharynx and downwards to involve the thoracic esophagus. Cervical esophageal and hypopharyngeal cancers are often analyzed together because of the anatomic similarities between the 2 and because hypopharyngeal cancers frequently spread submucosally downward to involve the cervical esophagus. In addition, carcinomas of the cervical esophagus can easily infiltrate the trachea, thyroid gland, recurrent laryngeal nerves, and other accessory regions [4, 5].

Multimodality treatment of cervical esophageal cancer that includes surgery together with radiation therapy or concurrent chemotherapy has

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**Table 1.** Patients and tumor characteristics

Characteristics	GP (n=48)	CI (n=19)	PMF/CWSG (n=12)
Age (years), mean $\pm$ SD	56.9 $\pm$ 10.5	54.2 $\pm$ 8.7	65.7 $\pm$ 10.1
Gender (male/female)	43/5	17/22	11/1
Tumor location			
Cervical esophagus	43	13	0
Hypopharynx-esophagus junction	5	6	12
Tumor size			
$\leq$ 4 cm	16	2	4
$>$ 4 cm	32	17	8
Extraesophageal invasion			
Thyroid gland	4	1	1
Recurrent laryngeal nerve	3	2	1
Cervical trachea	3	2	2
Lymphadenopathy			
Positive	12	8	2
Negative	36	11	10
Grade of differentiation			
Well	9	3	2
Moderate	27	10	8
Poor	12	6	2
Depth of tumor invasion			
T1-T2	9	0	0
T3-T4	39	19	12
Adjuvant therapy			
Radiotherapy	40	14	9
Chemoradiotherapy	5	3	1
Decannulation rate	43/47 (91.5%)	17/19 (89.5%)	10/12 (83.3%)

GP=gastric pull-up for reconstruction; CI=colon interposition for reconstruction; PMF/CWSG=pectoralis major flap alone or combined with split graft for reconstruction.

been shown to result in good local control, to prolong patient survival, and to improve quality of life, particularly through preservation of the larynx [6-9]. Because of the close proximity of anatomical structures and the different tumor biology, outcomes, and chemoradiotherapy regimens for cervical esophageal cancer and hypopharyngeal carcinoma, reconstruction of the upper digestive tract after cervical esophageal cancer resection is a difficult problem. Due to the poor prognosis of these patients, it is important to offer a safe, 1-stage procedure with low morbidity and acceptable operative mortality, as well as good functional rehabilitation, permitting a reasonable quality of life [10-12]. Historically, techniques used to achieve a safe and functional reconstruction after resection of the cervical esophagus have included local skin flaps; deltopectoral flaps; reversed gastric tube esophagoplasty; pectoralis major

myocutaneous flaps; visceral interposition with stomach or colon; and free tissue autografts utilizing colon, jejunum, or tubed radial forearm flaps [13]. The goal of surgery is a single-stage reconstruction with low morbidity and mortality, a short hospital stay, early restoration of swallowing and adequate oral intake, and preservation of intelligible laryngeal speech. However, surgical ablation of advanced tumors of the cervical esophageal region with restoration of digestive continuity and preservation of the larynx is among the most challenging oncologic operations because of the large area involved in the surgical field, the routes selected, and the difficulty in maintaining an adequate blood supply to the segment of the gut used for reconstruction [10, 11, 14].

The purpose of our study was to analyze outcomes of our institution's 23-year experience

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**Table 2.** Complications of the surgical reconstruction methods

Complications	GP (n=48)		CI (n=19)		PMF/CWSG (n=12)	
	N	%	N	%	N	%
Total	14	29.4	8	42.2	1	8.3
Types of complications						
Cervical fistula	3	6.3	3	15.8	1	8.3
Abdominal wound dehiscence	2	4.2	1	5.3	0	0
Liquefaction necrosis of abdominal fat	2	4.2	1	5.3	0	0
Pleural effusion	1	2.1	0	0	0	0
Chylorrhea	1	2.1	0	0	0	0
Dysphagia	1	2.1	2	10.5	0	0
Recurrent nerve palsy	1	2.1	0	0	0	0
Anastomotic leakage	1	2.1	0	0	0	0
Pneumonia	1	2.1	0	0	0	0
Infection	1	2.1	1	5.3	0	0

with reconstruction after ablative surgery with larynx preservation for cervical esophageal and hypopharynx-esophagus junction carcinoma.

### Materials and methods

We retrospectively searched the patient records of the Department of Otorhinolaryngology, Qilu Hospital, Shandong University and identified patients with cervical esophageal or hypopharynx-esophagus junction carcinoma who were surgically treated between March 1988 and October 2011. Patients with biopsy-proven squamous cell carcinoma with or without local lymph node metastases (clinical/enhanced computed tomography T1-4 cNx cMO in the tumour node metastasis (TNM) classification) were eligible for the study. Follow-up data were obtained through personal interviews and examinations and telephone contacts with patients and families, which was done as part of the current study. We recorded and analyzed the following data: patient and tumor characteristics, diagnosis and staging, reconstruction method, adjuvant treatment, swallowing outcomes, complications, and survival.

We used the SPSS (SPSS Inc., Chicago, IL) statistical package for the statistical analysis of the data. The survival analysis was performed using the Kaplan-Meier method for computing actuarial survival.

### Results

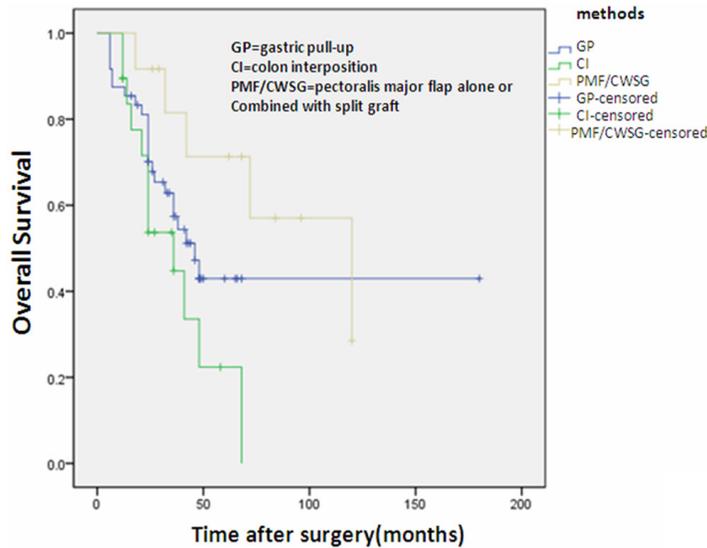
Seventy-nine patients with a diagnosis of cervical esophageal or hypopharynx-esophagus jun-

ction carcinoma were identified. None of the patients received any preoperative treatment. The preoperative workup included a barium esophagogram, endoscopic examination and biopsy, a full blood count with routine serum chemistry, chest radiography, cardiologic examination, and respiratory function tests in smokers and patients over 70 years old. The diagnosis was confirmed by histological

examination of the biopsy tissues. Additionally, neck and chest computed tomography was performed in all patients. The preoperative histologic diagnosis of the 79 patients was all squamous cell carcinoma. All study patients were staged before and after surgery according to the criteria of the International Union Against Cancer (UICC) [15]. All the Patients and the tumor characteristics were summarized in **Table 1.**

Of these 79 patients, 67 patients underwent transhiatal total esophagectomy with gastric pull-up (GP) (n=48) or colon interposition (CI) (n=19) reconstruction. The original esophageal bed in the posterior mediastinum was used for esophageal substitution in 63 patients, and the substernal route was used in 4 patients. The remaining 12 patients whose tumors were located in both the cervical esophagus and hypopharynx underwent transcervical limited esophagectomy with pectoralis major flap alone or pectoralis major flap combined with the split graft (PMF/CWSG) reconstruction. Ipsilateral neck dissections were performed on all patients. Hemithyroidectomy was performed in 35 patients on the side where the main tumor bulk was located. Every effort was made to preserve the parathyroid glands whenever possible. The sternocleidomastoid myoperiosteal flap was used for reconstruction of the posterior cervical tracheal wall in 4 patients. Seventy-eight patients underwent temporary tracheotomy. The operations were performed by otolaryngologists and thoracic surgeons.

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**Figure 1.** Overall survival by surgical reconstruction methods.

Sixty-three patients were treated with adjuvant postoperative radiotherapy (1.8-2 Gy/fraction/day, 5 times/week for 5-6 weeks). Radiation was administered via a 10-mV X-ray linear accelerator. The bilateral lower neck, supraclavicular nodes, and upper mediastinum were also included in the radiation field. Nine patients received adjuvant postoperative chemoradiotherapy, and the remaining 7 patients underwent surgery alone.

The most common sites of tumor extension were the lymph nodes (n=22, 27.8%), posterior wall of the cervical trachea (n=7, 8.9%), thyroid gland (n=6, 7.6%) and recurrent laryngeal nerve (n=6, 7.6%).

The average time until resumption of oral feeding was 25.2 days following the operation (range, 11-65 days). Only 3 patients (3.8%) were not able to swallow after recovering from the procedure because of necrosis of the anastomotic stenostomia and cervical fistula, respectively. All 3 patients underwent gastrostomy.

The mean hospital stay in this series was 27.4 days (range, 13-140 days) for the whole population, 25.6 days (range, 13-140 days) for patients with pharyngogastric anastomoses, 34.2 days (range, 20-65 days) for patients with pharyngocolic anastomoses, and 23.8 days (range, 19-31 days) for patients with transcervical limited esophagectomy and hypopharyngectomy.

Seventy (89.7%) of the 78 patients who underwent tracheotomy were successfully decannulated from 13 to 60 days postoperatively. Laryngeal function was preserved in all patients, and most of them had good speech preservation.

The overall incidence rate of complications was 29.1% (23/79). The most common postoperative complication at initial evaluation was cervical fistula, which occurred in 7 patients. Five of those cases were spontaneously cured, 1 case was repaired with a pectoralis major myocutaneous flap, and 1 required gastrostomy because of necrosis of the anastomotic stenostomia. Other complications included abdominal wound dehiscence, liquefaction necrosis of abdominal fat, pleural effusion, chylorrhea, dysphagia, recurrent nerve palsy, anastomotic leakage, pneumonia, and infection (Table 2). Abdominal wound dehiscence and liquefaction necrosis of abdominal fat occurred in 6 cases and was cured within 2 weeks by dressing change and relaxation of the suture. Pleural effusion occurred in 1 patient and resolved in 1 week after closing drainage of the pleural cavity. Chylorrhea occurred in 1 patient and was cured by dressing change.

The mean follow-up time was 38.4 months (range, 6-180 months). The Kaplan-Meier actuarial 3-year and 5-year survival rates were 66.4% and 45.5%, respectively. Figure 1 shows overall survival by reconstruction methods. The patients with PMF/CWSG reconstruction had a better survival than those with GP or CI reconstruction (log-rank,  $p=0.032$ ).

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### Discussion

In summary, on the whole, aggressive surgical resection with restoration of alimentary continuity is an effective therapy for cervical esophageal carcinoma. GP, CI interposition, and PMF/CWSG are safe and effective methods for the immediate restoration of alimentary continuity after resection of cervical esophageal and pharyngo-cervical esophageal carcinoma. They are promising treatment strategies for pursuing the preservation of laryngeal function. Combined with adjuvant therapy, these techniques can

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improve the resectability rate and survival rate of cervical esophageal carcinoma.

Debate continues over whether primary resection, adjuvant treatment, or definitive chemoradiotherapy is most effective for the treatment of esophageal squamous cell carcinoma [16-18]. Here we show that satisfactory results can be obtained using primary resection combined with postoperative adjuvant therapy. Postoperative radiotherapy or chemoradiotherapy were given to 72 patients in our study, which may have contributed to the high survival rates [9, 13, 19]. However, longer follow-up is needed to explore the survival.

The actuarial 5-year survival rates for patients with cervical esophageal cancer reported in the literature range from 18% to 33% [9, 13, 20]. Ott et al. and Hiroshi et al. reported higher 5-year survival rates of 47% and 43%, respectively, after limited resection followed by reconstruction with a free jejunal graft. In our series, the overall 5-year survival rate (45.5%) was similar to theirs [7, 11].

Many surgical techniques have been devised to reconstruct the defect left after total laryngopharyngoesophagectomy [7, 10, 21, 22]. These techniques have included prostheses, a variety of skin and myocutaneous graft flaps, visceral reconstruction with a free jejunal graft and stomach or segment colon interposition. Over the past several decades, with the development of the pectoralis major myocutaneous flap and microvascular free jejunal transfer, partial and circumferential pharyngeal defects created after adequate tumor ablation could be adequately reconstructed [7, 11, 22, 23]. However, when the resection extends below the thoracic inlet, visceral interposition with the stomach or colon is the best choice for reconstruction of the cervical esophagus.

Following total esophagectomy, a pharyngogastrostomy is the preferred method of most surgeons because only 1 anastomosis is required, the stomach has an excellent blood supply, it is relatively easy to prepare, and swallowing after the operation is more likely because of low rates of stricture and fistula formation [10]. GP is a safe and effective method for the immediate restoration of alimentary continuity after pharyngoesophagectomy. The procedure can be performed with low mortality, acceptable

morbidity, and a short hospital stay. The technique of GP has other advantages: 1) long segments of the alimentary tract can be reconstructed; 2) the operation is done in a single stage by 2 teams working simultaneously; and 3) the alimentary tract remains lined exclusively by native mucosa, which is not prone to ulceration or stricture. However, the main disadvantage of this technique is that it can cause reflux when oral feeding resumes if the anastomosis is close to or higher than the throat plane, which can result in aspiration pneumonia. Intraoperative pyloroplasty promotes gastric emptying and can prevent or reduce regurgitation. The most common postoperative complication associated with GP in the present study was cervical fistula (3/48), which differs from that reported by Ferahkose et al and Triboulet et al [10, 13]. Both of them reported pneumonia was the most common postoperative complication in the GP group.

The colon is also used for esophageal replacement following resection [13, 24]. Ensuring that the transplanted colon has a healthy and complete marginal artery arch is the most important factor associated with the success of this technique. The major advantages of using long-segment colon for esophageal replacement are that a greater length of viscus is available, mobilization is easy, and acid regurgitation with anastomotic ulceration rarely occurs. The use of an isoperistaltic segment is physiological and, in the retrosternal position, gives a better functional result in most cases than the use of the presternal subcutaneous route. An advantage of reconstruction via the retrosternal route is that the risk of local recurrence interfering with the conduit is diminished and radical radiation therapy can be administered without compromise to a transposed viscus in the posterior mediastinum. Although colon interposition has the advantage of providing a long segment, its disadvantages include the need for 3 intestinal anastomoses, the frequency of breakdown of the cervical anastomosis, and a tenuous blood supply. In our study, the most common postoperative complications of this technique were cervical fistula (3/19) and dysphagia (2/19) because of cervical anastomotic stenosis, which resulted in undergoing esophagectasia in both cases.

Ariyan [25] reported that 8 patients who underwent reconstructions of the pharyngoesopha-

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gus with a pectoralis major flap had good therapeutic results. The pectoralis major myocutaneous flap has the following characteristics: 1) it is an axial flap with an abundant blood supply; 2) it can provide a large area of skin and thick muscle tissue to cover a larger wound and fill the defect; 3) it has a long enough pedicle to cover defects that are some distance away; 4) the donor site can be directly closed without skin grafting; and 5) flap nerve transfer avoids atrophy and contracture of the flap after the operation. The flap is suitable for lesions not lower than the upper thoracic level. Over 2 cm width of the hypopharynx and esophagus continuous mucosa can not only reduce the post-operative anastomotic stenosis but also is conducive to the recovery of swallowing function.

For cervical esophageal ring defects, the pectoralis major flap can be combined with the split skin graft for reconstruction. Our experience is as follows: the prevertebral fascia of the paries posterior mucosa of the pharyngeal and esophageal stump are sutured together. The two side edges of the split graft are sewn to the prevertebral fascia, and upper and lower edge, respectively, are connected with the end wall of the hypopharynx and esophagus mucosa suture. Making a midline vertical incision of 1~2 cm in the front and rear walls of the esophagus respectively can enlarge the lumen to prevent stricture. The pectoralis major myocutaneous flap transfers to the neck to reconstruct the front wall and 2 side walls of the pharyngo-esophageal defect. In our study, 12 patients underwent reconstruction with a PMF/CWSG for reconstruction; only 1 patient had a complication: a cervical fistula that was spontaneously cured.

With improvements in microsurgical techniques, free jejunal transfer has become well accepted for the reconstruction for proximal lesions when resection includes the pharynx, larynx, hypopharynx, and cervical esophagus above the thoracic inlet [7, 11, 22, 23]. Free jejunal transfer avoids a mediastinal dissection, can be used in irradiated fields or when the stomach is unavailable, and allows for reconstruction of more proximal defects. However, when large defects extend below the thoracic inlet or when total esophagectomy is required, free jejunal grafts may not be a reasonable choice for reconstruction because the use of long lengths of jejunum occasionally

results in indigestion. In addition, this technique is limited by the need for a microvascular anastomosis, which is associated with significant rates of necrosis with anastomotic breakdown, fistula, and stricture [20, 26].

The reported larynx preservation rate in patients who undergo surgical resection for cervical esophageal cancer varies widely [7, 11, 20, 27]. The most important problem in larynx preservation is the surgical margin of the tumor residue in the proximal and distal sites. Some investigators have reported that total esophagectomy with larynx preservation might be proposed in carefully selected patients with cervical esophageal cancer to obtain a proximal surgical margin of at least 2-3 cm [28]. Although preservation of the larynx depends on the extent of the upward extension of the cervical tumor, there are no definitive criteria for larynx-preserving surgery. Ott et al. [7] preserved the larynx in 89 (81.7%) of their 109 patients who underwent limited resection with a free jejunal graft for cervical esophageal cancer. Hiroshi et al. [11] reported larynx preservation was possible in 33 (56.9%) of 58 patients who underwent limited resection with a free jejunal graft. In our study, all patients had preserved laryngeal function, including 33 patients (44.7%) with pathological T4 tumors.

Difficulty in swallowing and aspiration to varying degrees seem to be the most severe problems associated with laryngeal-preserving procedures to treat cervical esophageal cancer. Laryngeal suspension appears to decrease the chance of aspiration, and cricopharyngeal myotomy appears to improve swallowing difficulties [28]. In the present study, preserving laryngeal function in 8 patients (10.1%) who were not decannulated prevented aspiration and preserved voice function at the expense of laryngeal respiratory function. In four patients, resection of the tumor involving the posterior tracheal wall was reconstructed with a myoperiosteal flap consisting of the sternocleidomastoid muscle, and clavicular periosteum was successfully used in the repair of the deficient laryngeal and cervical tracheal wall. The sternocleidomastoid myoperiosteal flap uses clavicular periosteum on a muscle pedicle to provide vascularity. Clavicular periosteum is fibrous and durable and will conform to the shape of the trachea, forming bone to provide stability to the airway. The procedure is relatively simple

and involves single-stage reconstruction [29]. In our patients, complete epithelialization took place with no granuloma formation. This flap proved to be rigid enough to form a noncollapsed wall at times of alternative pressure changes. The method described consists of a 1-stage procedure where the donor site is in the same surgical field as the defect. There is no interference with any vital function and no apparent cosmetic defect [30].

## Acknowledgements

This work was supported by the Taishan Scholars Program (No. tshw20130950), Shandong province, and Department of Science & Technology of Shandong province (No. 2009GG10002018).

## Disclosure of conflict of interest

None.

## Abbreviations

GP, gastric pull-up for reconstruction; CI, colon interposition for reconstruction; PMF/CWSG, pectoralis major flap alone or combined with split graft for reconstruction.

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