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Current management strategy of hypopharyngeal carcinoma

Jimmy Yu Wai Chan *, William Ignace Wei

Division of Head and Neck Surgery, Department of Surgery, University of Hong Kong Li Ka Shing Faculty of Medicine, Queen Mary Hospital, Hong Kong Special Administrative Region

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ABSTRACT

Objectives: Squamous cell carcinoma (SCC) of the hypopharynx represents a distinct clinical entity among other cancers of the head and neck region. Despite recent advances in chemoradiotherapy, surgery remains the preferred therapeutic option for locally advanced disease and salvage for failure after chemo-radiotherapy. In this article, several aspects of surgical and non-surgical approaches in the management of hypopharyngeal cancer are discussed.
Methods: A search in pubmed was made for publications with regard to the management of hypopharyngeal carcinoma.
Results: In early-staged hypopharyngeal cancer, the overall and disease-specific survival rates after organ-preserving radiotherapy is comparable to that after surgery. However, for advanced staged disease, the results initial surgery with post-operative adjuvant radiotherapy was superior to chemoradiotherapy alone. The incidence of occult nodal metastasis is found to be more than 20%. Selective neck dissection removing cervical lymph node level II–IV is the procedure of choice for patients with clinically N0 neck. Contralateral nodal clearance may also be considered in tumors involving the medial wall of the pyriform recess, post-crioid region or the posterior wall, and those with ipsilateral palpable nodal metastasis and clinical stage IV disease. Transoral robotic surgery (TORS) has the potential value as the minimally invasive procedure for the management of carcinoma of the hypopharynx.
Conclusions: The treatment strategy for carcinoma of the hypopharynx has been evolving with time. Organ preserving chemoradiotherapy has been the treatment of choice for early stage disease, with surgical resection and reconstruction reserved for advanced and recurrent tumors.

1. Introduction

Squamous cell carcinoma (SCC) of the hypopharynx represents a distinct clinical entity among other cancers of the head and neck region. It is less prevalent than other head and neck cancers, accounting for 3–5% of all SCC in the region [1,2], yet it presents unique therapeutic challenges to clinical oncologists as well as ablative and reconstructive surgeons. These patients usually present late, with 60–80% of the patients having ipsilateral nodal metastasis [3] and up to 40% of them have contralateral occult nodal tumor deposits [4] on presentation. Furthermore, systemic metastasis is reported to occur in up to 60% of the patients [5], either at presentation or during follow up. The overall survival is relatively poor with high rates of regional and systemic metastasis early in the course of the disease, despite aggressive surgical and adjuvant treatment. There is no level-one evidence on the best treatment [6], or agreement on treatment [7,8]. With the global trend toward organ-preserving therapy, chemo-radiotherapy has gained increasing popularity over primary surgical therapies for early stage hypopharyngeal carcinoma [9,10]. Nevertheless, surgery remains the preferred therapeutic option for those with locally advanced disease as well as salvage for failure after chemo-radiotherapy. Reconstruction is often required in order to restore the swallowing function after surgery. However, there has been no consensus on the best reconstructive option for repairing such a defect. In this article, several aspects of surgical and non-surgical approaches in the management of hypopharyngeal cancer are discussed.

2. The nature of disease

In an epidemiological study of the largest series of patients with hypopharyngeal cancer, 2939 cases from 769 hospitals across the United States of America [8], with the diagnosis made from 1980 to 1985 and 1990 to 1992, were investigated. In 1990 to 1992, the mean age of the patients was around 65.8 years with 76.0% male.

* Corresponding author at: Division of Head and Neck Surgery, Department of Surgery, University of Hong Kong Li Ka Shing Faculty of Medicine, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong Special Administrative Region.
Tel.: +852 2255 4394; fax: +852 2819 3780.
E-mail address: chanjyw@gmail.com (J.Y.W. Chan).

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Over 90% had smoked and over 50% were heavy drinkers. Synchronous primary tumors occurred in 7.4% of the patients, and 16.1% had a history of previous cancer. The clinical TNM stage on presentation was 10.5%, 12.1%, 23.0%, and 52.6% for stages I–IV, respectively. Regarding treatment, 48.2% of the patients had surgery ± radiotherapy (RT), 26.1% had RT alone, 15.8% had RT with chemotherapy, and 4.4% had no treatment. Among the patients in 1980–1985, the locoregional failure after treatment and metastases was 16.8% and 8.8%, respectively. The overall 5-year disease-specific survival was 33.4%, which segregated to 63.1% (stage I), 57.5% (stage II), 41.8% (stage III), and 22% (stage IV). Similar findings were reported in a population-based study in Holland [11].

3. Treatment options

The treatment of hypopharyngeal cancer has evolved with time. Radiotherapy was the main choice of treatment in the 1940s and 1950s, but it was soon replaced by surgery. Laryngopharyngectomy and reconstruction, followed by chemoradiotherapy has been and remains the mainstay of treatment for carcinoma of the hypopharynx at present. However, surgical treatment is inevitably associated with severe speech and swallowing disability. With the global trend toward organ preservation, primary chemoradiotherapy, as in laryngeal cancer, has gained increasing popularity as the definitive treatment of tumors in the hypopharynx. Unfortunately, unlike carcinoma of the larynx, the value and feasibility of organ preservation in hypopharyngeal cancer has not been thoroughly evaluated, precluding conclusions regarding the optimal treatment modality to be made [12,13]. Furthermore, it is important to note that 'organ preservation' does not always equal to 'function preservation'. There are patients who are permanently dependent on tracheostomy for airway protection and nasogastric tube for feeding after radical chemoradiotherapy. In these patients, function may even be better preserved after removing the organ, allowing aspiration free swallowing and better prosthetic speech restoration than by preserving a functionless larynx.

3.1. Primary chemoradiotherapy

In early-staged hypopharyngeal cancer, the overall survival and disease-specific survival rates achieved with definitive radiotherapy is comparable to that after surgery [14–17]. However, for advanced staged disease, the results of primary radiotherapy followed by salvage surgery if tumor persists/recurs are inferior to those after initial surgery with post-operative adjuvant radiotherapy [18]. It must be emphasized that many chemoradiotherapy trials had different mix of patients with laryngeal and hypopharyngeal cancers, making interpretation and meaningful comparisons difficult. A randomized phase III trial comparing the results of surgical versus non-surgical treatment for hypopharyngeal cancer was conducted by the European Organization for Research and Treatment of Cancer (EORTC) [19]. One hundred and ninety-four patients were randomized between surgery followed by postoperative adjuvant radiotherapy versus induction chemotherapy (cisplatin followed by fluorouracil) and radiotherapy. There was no statistically significant difference between the 2 groups with regard to local or regional recurrence and disease free survival rates at 5 years. The 5-year estimate of retaining a functional larynx was 35%.

For patients with locoregionally advanced tumor (TNM stages III and IV), the addition of cetuximab (IgG monoclonal antibody against epidermal growth factor receptor (EGFR)) to radiotherapy significantly improves the overall survival at 5 years when compared to radiation alone (45.6% vs. 36.4%, respectively) [20].

3.2. Primary surgery

3.2.1. Laryngopharyngectomy

The aim of the surgery is to resect the tumor with microscopically clear margins. In order to achieve this, the presence of submucosal tumor extension has to be taken into account. Pathological studies by the examination of the resected specimens showed that the extent of submucosal involvement measured from the edge of the tumor was different when examined superiorly and inferiorly, ranging from 10 to 20 mm and 10 to 30 mm, respectively [21–23]. The incidence of submucosal extension is up to 58% [24]. From information gained in the step serial pathological study of the resected specimens, recommended resection margins are 3 cm inferiorly and 2 cm both superiorly and laterally. Therefore, depending on the location and extent of the primary tumor, the following types resection of the hypopharynx may be performed:

- Laryngeal preservation surgery

  For a selected group of patients with early-stage hypopharyngeal cancer, laryngeal preserving surgery can be performed with good functional results. Attention has to be paid for the possibility of chronic or life threatening aspiration after operation. Endoscopic approach is suitable for small, favorably located and easily accessible lesions. Partial pharyngectomy for posterior pharyngeal or small lateral pharyngeal tumors can be approached through a lateral or transhyoid pharyngotomy. For tumors of the pyriform sinus invading the lateral wall of the hypopharynx, partial laryngopharyngectomy can be performed. Contraindications to the procedure include those tumors which invade the pyriform sinus apex or the post-cricoid region, and presence of vocal cord paralysis. Studies on the use of supracricoid hemilaryngopharyngectomy [25,26] had been performed on 147 patients over a 19-year period. The 5-year actuarial local control rate was 90% and the overall laryngeal preservation rate was 91%, showing that the procedure is safe with good functional and oncological outcome for patients with early hypopharyngeal cancer.
- Total laryngectomy and partial pharyngectomy

  For patients with small tumors located at high level (pyriform sinus) and the risk of postoperative aspiration is high, total laryngectomy is required with the tumor resected with adequate margins, while leaving a strip of full thickness pharyngeal wall between the oropharynx and the cervical esophagus. The width of the remaining pharyngeal wall is insufficient to allow direct closure. Additional tissue is required to reconstruct the pharyngeal defect to facilitate swallowing in the future.
- Total laryngectomy and circumferential pharyngectomy

  For large tumor involving the posterior wall or the post-cricoid region, resection with adequate margins will result in a circumferential defect. The continuity of the upper digestive tract between the oropharynx and the esophagus is disrupted and the resultant defect is circumferential.
- Pharyngo-laryngo-esophagectomy

  For tumors that have extended to the cervical esophagus, pharyngo-laryngo-esophagectomy is required. The defect is most commonly reconstructed by gastric pull-up where there is only one anastomosis in the upper neck
- Manubrium resection and mediastinal tracheostomy

  In the presence of locally advanced tumor with major esophageal or tracheal invasion, or in those patients with level VI nodal metastasis, or when tumors recur in the parastomal region after previous surgery, manubrium resection provides a better exposure to ensure complete tumor clearance with better marginal control [27,28]. With attention to surgical details, it is a useful adjunct to tumor resection with minimal morbidities [29].