

Original Article

Treatment selection for tonsillar squamous cell carcinoma

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Abstract

Background: The optimal treatment for tonsillar squamous cell carcinoma (SCC) remains controversial. The purpose of this study was to evaluate long-term treatment outcomes of patients with tonsillar SCC, in order to aid in appropriate treatment selection.

Methods: We conducted a retrospective chart review of 105 patients with curatively treated tonsillar SCC between January 1996 and December 2005. Forty-three patients (41.0%) underwent primary surgery with or without adjuvant therapy (primary surgery group), and 62 patients (59.0%) were treated with radiotherapy/chemoradiotherapy (RT/CRT, organ preservation group). Twenty patients (19%) received tumor tonsillectomy before definitive RT/CRT and were grouped into the organ preservation group.

Results: No significant differences were observed between the primary surgery and organ preservation groups in terms of local control ($p = 0.212$), regional control ($p = 0.684$), distant metastasis ($p = 0.627$), 5-year disease-specific survival (DSS, $p = 0.774$), and overall survival rates (OS, $p = 0.667$). The rates of major complication ($p = 0.216$), long-term dependency on feeding tubes ($p = 0.876$), and tracheostomy ($p = 0.401$) were also similar. Advanced T classification (T3–4) was the only factor associated with significantly worse DSS ($p = 0.007$) and OS ($p = 0.012$). However, there was also no difference in final treatment outcomes in T3–4 patients regardless of whether they were treated with primary surgery or RT/CRT. In the organ preservation group, tumor tonsillectomy before RT/CRT did not improve local control ($p = 0.520$) or other treatment outcomes, including 5-year DSS ($p = 0.707$) and OS ($p = 0.745$).

Conclusion: Both primary surgery and RT/CRT organ preservation are effective treatments for tonsillar SCC. Single modality treatment, either surgery or RT/CRT, can typically be provided for stage I–II diseases. Although RT/CRT organ preservation is used more frequently for stage III–IV tonsillar SCC in recent years, primary surgery combined with adjuvant therapy still achieves equivalent outcomes. Multidisciplinary pretreatment counseling and the facilities and personnel available are therefore important for decision-making. In addition, if RT/CRT organ preservation is selected as the primary treatment, tumor tonsillectomy is not indicated.

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1. Introduction

Tonsillar squamous cell carcinoma (SCC) is the most common type of oropharyngeal cancer and is relatively radio-sensitive.¹ Multiple treatment modalities are thus available,

including primary surgery with or without adjuvant therapy and radiotherapy/chemoradiotherapy (RT/CRT) organ preservation. Early tonsillar SCC can be effectively treated with either RT or surgery alone.² Many patients, however, present at advanced stages, and a combination of primary surgery and postoperative radiotherapy (PORT) is the traditional treatment of choice.^{3,4}

Over the past decade, however, there has been a paradigm shift toward RT/CRT organ preservation because surgical

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excision for advanced tonsillar SCC is technically demanding and frequently associated with post-treatment cosmetic and functional sequelae.^{5,6} The combination of chemotherapy with RT in organ preservation treatment has been demonstrated to improve the efficacy of RT alone for advanced oropharyngeal SCC, offering comparable treatment outcomes to primary surgery with PORT.^{7–9} However, high rates of acute grade 3–4 toxicities and late treatment sequelae can be observed under intense CRT treatment, including xerostomia, dysphagia, soft tissue fibrosis, and radionecrosis.¹⁰ So far, no randomized studies have compared the treatment outcomes of CRT and primary surgery for tonsillar SCC, and therefore, the optimal treatment selection remains unsettled.^{5,11}

Another controversial issue is the benefit of tumor tonsillectomy before RT/CRT organ preservation. Surgical excision of the primary tumor reduces tumor burden and can theoretically provide better local tumor control. Yildirim et al¹² demonstrated that gross primary tumor removal by tonsillectomies followed by RT achieved excellent treatment outcomes. However, no control group without tonsillectomy was available for comparison in their study, and the benefit of tumor tonsillectomy remains unclear.

The purpose of this study was to compare the treatment outcomes, major complication rates, and functional results of patients with tonsillar SCC treated with either primary surgery or RT/CRT organ preservation. Furthermore, we also investigated the role of tumor tonsillectomy before RT/CRT organ preservation.

2. Methods

2.1. Study population

Between January 1996 and December 2005, 105 patients with histologically confirmed tonsillar SCC were curatively treated at the Department of Otolaryngology, Taipei Veterans General Hospital, Taiwan. None of the patients had radiologic evidence of distant metastasis at presentation, and those with a previous history of cancer were excluded unless they had been disease free for at least 2 years.

Pretreatment evaluations included a physical examination, panendoscopy tumor mapping and biopsy, computed tomography (CT) or magnetic resonance imaging of the primary tumor and the neck, chest X-ray or chest CT, and routine laboratory studies. Treatment records were reviewed, and the patients were categorized into two groups: surgery with or without adjuvant therapy (primary surgery group) and RT/CRT (organ preservation group). After treatment completion, the patients entered a monthly follow-up program for the 1st year, and every 3 months thereafter. Patients were staged according to the 2002 criteria of the American Joint Committee on Cancer. This study was approved by the hospital's Institutional Review Board.

2.2. RT and CRT regimens

PORT was delivered at 2 Gy per fraction, 5 days per week, at a total dose of 60–66 Gy to the primary site and/or positive

neck levels and 50 Gy to the N0 neck levels. Patients in the organ preservation group received RT under the same RT schedule with a total dose of 70 Gy to the primary site and gross lymphadenopathy (≥ 1 cm), and 50 Gy to the N0 neck. Both sides of the neck were included in treatment portals and RT was administered with 6-MV X-rays from a linear accelerator. Most of the RT techniques used were initial 2D followed by 3D boost after 56 Gy. Ten patients received intensity-modulated RT, and accelerated fractionation was not used.

Cisplatin-based induction chemotherapy was given mainly to those patients with bulky T3–4 primary tumors and/or neck diseases. In primary concurrent chemoradiotherapy (CCRT) treatment, weekly cisplatin (20 mg/m²) and 5-fluorouracil (400 mg/m²) were delivered concurrently with the RT. In postoperative concurrent chemoradiotherapy (POCCRT) treatment, the chemotherapy regimen consisted of weekly cisplatin (30 mg/m²) and daily oral tegafur–uracil (250 mg/m²) concurrently with PORT.

2.3. Statistical analysis

Local and regional controls were defined as no evidence of disease at the primary site and the neck. Differences in the pretreatment and treatment variables between the two groups were determined using the Chi-square or Fisher exact test and *t* test. The rates of disease-specific survival (DSS) and overall survival (OS) were calculated using the Kaplan–Meier product limit method and compared by the logrank test. Follow-up times were defined as the duration between the date of treatment initiation and the events or last contact. DSS was defined as the time to death from cancer or treatment-related events. Functional results were evaluated by long-term dependency on feeding tubes for nutrition and tracheostomy for breathing. Major complications were defined as treatment-related events that necessitated a second operation, prolonged hospitalization, or were life-threatening. All analyses were performed using the Statistical Package for the Social Sciences software version 17.0 (SPSS Inc., Chicago, IL, USA). All tests were two sided, and results were considered significant at $p < 0.05$.

3. Results

3.1. Patient characteristics

The characteristics of the patients are summarized in Table 1. Of the 105 patients in our study, 40 (38.1%) had locally advanced T3–4 tumors and 71 (67.6%) had advanced stage III–IV disease at initial diagnosis. Forty-three patients (41.0%) were treated with primary surgery with or without adjuvant therapy, and 62 patients (59.0%) were treated with RT/CRT organ preservation. There were no differences between the two groups in terms of age, gender, T and N classifications, TNM stage, and histological differentiation. The treatment paradigm changed significantly at our institute before and after 2002. Only 35.3% of the patients underwent

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