Management of the clinically negative neck (N0) of T2N0M0 supraglottic laryngeal carcinoma: a retrospective study

T Jin* 

Abstract

Introduction

The most effective therapeutic approach for the cN0 patients with T2N0M0 supraglottic laryngeal carcinoma remains a subject of much debate. The purpose of this study was to answer the following question: among patients with T2N0M0 supraglottic laryngeal carcinoma, are the survival rates significantly different between patients who received neck dissection and those who had another therapeutic treatment (radiotherapy, ‘wait and see’ policy)?

Methods

A retrospective analysis of 101 consecutive T2N0M0 cases of squamous cell carcinoma of the supraglottic larynx, treated between 1993 and 2009, was performed. Overall survival, loco-regional control, local disease-free survival and neck disease-free survival (NDFS) were estimated using the Kaplan-Meier method. Log-rank test was employed to identify significant prognostic factors for overall survival, loco-regional control, local disease-free survival and neck disease-free survival.

Results

For treating the primary tumour, the 5-year overall survival, loco-regional control and neck disease-free survival of cT2 tumour and/or cN0 neck. The aim of this study was to report our results and try to identify, in a retrospective analysis, potential prognostic factors and possible guidelines in tailoring the most appropriate conservative treatment for patients with T2N0M0 supraglottic carcinoma.

Materials and methods

Patient enrolment criteria

Between 1993 and 2009, 3193 consecutive patients with neoplasms of the larynx were observed at the Sun Yat-sen University Cancer Center and Zhejiang Cancer Hospital, China. Of these, 1035 (32.4%) had supraglottic cancer.

Discussion

The most effective therapeutic approaches for the cN0 neck in SGLC are: (a) partial or total supraglottic laryngectomy; (b) radiotherapy and (c) combination of supraglottic laryngectomy and irradiation. The therapeutic choices for the management of cT2 tumour in supraglottic laryngeal carcinoma (SGLC) are: (a) partial or total supraglottic laryngectomy; (b) radiotherapy and (c) combination of supraglottic laryngectomy and irradiation.

Results

For treating the primary tumour, the 5-year overall survival, loco-regional control and neck disease-free survival were not significantly different between patients in the neck dissection treatment group, neck radiotherapy group, and ‘wait and see’ group. \( \chi^2 = 2.422, P = 0.298; \chi^2 = 1.576, P = 0.455; \chi^2 = 0.003, P = 0.998 \).

Conclusion

Our result suggests that neck dissection is not superior to radiotherapy or a ‘wait and see’ policy in terms of survival and control of neck disease. A ‘wait and see’ policy may be the best choice for these patients.

Introduction

Management of the clinically negative (N0) neck in supraglottic laryngeal cancer (especially the early stage) is still controversial. Compared with the glottis, the supraglottis is characterized by a rich lymphatic network and carcinoma of this area has a strong tendency to develop regional metastases. The incidence of nodal metastases presents a wide variation from 10% to 50%, depending on the clinical, imaging and histopathological methods that are used. With the clinical stage of T2N0M0, some researchers have reported that the incidence of nodal metastases varies from 13.7% to 23.9%.

The therapeutic choices for the management of cT2 tumour in supraglottic laryngeal carcinoma (SGLC) are: (a) partial or total supraglottic laryngectomy; (b) radiotherapy and (c) combination of supraglottic laryngectomy and irradiation. The therapeutic choices for the management of cN0 neck in SGLC are: (a) neck dissection; (b) radiotherapy; (c) combination of neck dissection and neck irradiation and (d) ‘wait and see’ policy. Neck dissection, and especially selective neck dissection of levels II–IV, has become the procedure of choice for surgical treatment of the clinically negative neck of patients with SGLC, as most supraglottic tumours metastasize to these levels. Radiation therapy is an alternative that is considered to be as effective as surgery in preventing neck recurrence. The treatment, whether it is surgery or radiotherapy, may cause morbidity or theoretically remove an immunological barrier to the spread of disease. For this reason, the ‘wait and see’ policy has been proposed as an alternative for the treatment of the cN0 neck.

This retrospective study reviews a series of 101 consecutive early-stage supraglottic cancer (T2N0M0) observed at our institutions and managed with the aforementioned therapeutic choices for cT2 tumour and/or cN0 neck. The aim of this study was to report our results and try to identify, in a retrospective analysis, potential prognostic factors and possible guidelines in tailoring the most appropriate conservative treatment for patients with T2N0M0 supraglottic carcinoma.
tomography (CT), and/or magnetic resonance imaging (MRI). Among these 331 patients, the enrolment criteria were as follows: (a) each patient’s complete clinical and pathological data including age, gender, blood style, stage, smoking index, alcohol consumption, histological differentiation, and treatment status; (b) patients were restaged according to the guidelines of the 2002 Union for International Cancer Control by the cancer staging system; (c) the primary tumours were restaged as cT2 and (d) no patient had distant metastasis at the time of initial staging. Because this was a retrospective study, no informed consent from individual patients was needed in our jurisdiction.

A total of 101 patients were evaluated in this analysis according to the above criteria. Patient characteristics are summarized in Table 1.

### Treatment

For the treatment modality of the primary site, partial supraglottic laryngectomy was performed in 67.3% (n = 68) and total laryngectomy in 14.9% (n = 15) of our patients. Surgical margins of resection at the primary site were negative in 68 of 83 patients (81.9%), close (<5 mm) in 8 (9.6%) and positive in 7 (8.4%). All patients with close or positive surgical margins received post-operative radiotherapy. In the surgical treatment of the neck, elective bilateral neck node dissection (functional or modified radical neck dissection, routinely including levels 2–4) was performed in 83 patients. The radiotherapy was delivered in 30 parallel fields as 60Co or 6 MV photons. The radiotherapy was delivered in 18 patients and post-operative radiotherapy, the median total dose was 68 (range, 64–70) Gy. For the patients who received post-operative radiotherapy, the median total dose was 60 (range, 40–70) Gy. Low doses (<50 Gy) were given to patients whose clinical condition demanded premature termination of treatment (e.g., local progression during radiotherapy, deteriorating performance status and intercurrent disease) or to those who refused completion of treatment.

### Follow-up time and method

Follow-ups were conducted mainly via outpatient check-ups. The follow-up examination was started after treatment. Patients were seen every 2 months during the first year, every 3 months for the subsequent 2 years and then every 6 months thereafter until death. All loco-regional tumours were diagnosed by clinical examination, MRI or intensive CT, fibroptic endoscopy and biopsy. Distant metastases were diagnosed by clinical symptoms, physical examinations and imaging methods, including chest X-ray, bone scan, abdominal sonography, MRI, intensive CT or positron emission CT.

### Statistical analyses

Overall survival (OS) was measured from the onset of treatment to the date of death or the survival status at the last date of follow-up. The local disease-free survival (LDFS) was the interval from the onset of treatment to the date of local recurrence. The neck disease-free survival (NDFS) rate was the interval from the onset of treatment to the date of regional recurrence. The loco-regional control (LRC) was the interval from the onset of treatment to the date of recurrence. Recurrence was defined as local tissue invasion by the primary tumour or regional lymph node involvement.

### Results

There were 95 male and 6 female patients. The median age at diagnosis was 63 (range, 46–83) years. Follow-up examination was started after treatment. The last follow-up was on 29 June 2010, with a median follow-up time of 62 months (range, 6–176 months). No patients were lost during the follow-up. Eleven patients recurred at the primary site and 12 patients recurred at the regional site. Five patients had both local and regional relapse. Seven patients developed distant metastases (5 in the lungs, 1 in the bone and 1 in the liver).

Overall 3, 5 and 10 year survival rates for the entire group were 83.2%, 71.9% and 42.7% respectively (Figure 1A). For treating the primary tumour, the 5-year OS rates of the surgery group, radiotherapy group and surgery plus radiotherapy group were 68.6%, 68.8% and 79.2% respectively ($\chi^2 = 4.441$, $P = 0.109$) (Figure 1B). For treating the neck, the 5-year OS rates of the ‘wait and see’ group, surgery group and radiotherapy group were 72.4%, 65.8% and 83.3% respectively ($\chi^2 = 2.422$, $P = 0.298$) (Figure 1C).

The 3, 5 and 10 year LRC rates for the entire group were 74.9%, 72.0% and 63.2% respectively (Figure 1D). For treating the primary tumour, the 5-year LRC rates of the surgery group, radiotherapy group and surgery plus radiotherapy group were 75.1%, 47.9% and 79.7% respectively ($\chi^2 = 2.256$, $P = 0.324$) (Figure 1E). For treating the neck, the 5-year LRC rates of the ‘wait and see’ group, surgery group and radiotherapy group were 74.0%, 74.3% and 65.7% respectively ($\chi^2 = 0.003$, $P = 0.998$) (Figure 1F).

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For treating the neck, the 5-year NDFS rates of the ‘wait and see’ group, surgery group and radiotherapy group were 87.3%, 78.5% and 83.3% respectively ($\chi^2 = 1.576, P = 0.455$) (Figure 1G).

For treating the primary tumour, the 5-year LDFS rates of the surgery group, radiotherapy group and surgery plus radiotherapy group were 83.4%, 64.3% and 90.0% respectively ($\chi^2 = 1.181, P = 0.554$) (Figure 1H).

**Discussion**

The optimal conservative management for early-stage (T2N0M0) SCC of the supraglottic larynx is still controversial. National Comprehensive Cancer Network guidelines version 2.2011

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**Table 1** Patient characteristics and univariate analysis of prognostic factors for loco-regional control rate and overall survival

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<th>Prognostic factor</th>
<th>No. of patients</th>
<th>5-year LRC (%)</th>
<th>$\chi^2$</th>
<th>$P^a$</th>
<th>5-year OS (%)</th>
<th>$\chi^2$</th>
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LRC, loco-regional control; OS, overall survival.
$^a$Log-rank test.
$^b$Patients were divided into two groups according to the median age.
$^c$Smoking index is defined as the number of cigarettes used per day × total smoking time (years).

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about cancer of the supraglottic larynx recommend that endoscopic resection +/- neck dissection or open partial supraglottic laryngectomy +/- neck dissection or definitive radiotherapy can be the first choice for treating early-stage SCC of the supraglottic larynx.

It has been reported that supraglottic laryngectomy and definitive radiotherapy are both suitable in terms of local control rates and larynx preservation. These results were substantially confirmed by our study. Our univariate analysis showed that not only the 5-year LRC rates but also the 5-year LDFS and OS rates of the surgery group and the radiotherapy

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group were not significantly different between the surgery group, radiotherapy group and surgery plus radiotherapy group \((\chi^2 = 2.256, P = 0.324; \chi^2 = 1.181, P = 0.554; \chi^2 = 4.441, P = 0.109)\). When surgical margins of resection at the primary site were close or positive, patients receiving post-operative radiotherapy can get the same outcome as patients with negative margins. Clearly, tumour characteristics are not the only factors influencing the therapeutic decision as a host of other related variables could play an important role. The choice of treatment modality depends on anticipated functional outcome, the patient’s wishes, reliability of follow-up and general medical condition.

The management of the neck in early supraglottic carcinoma is an important issue, since uncontrolled cervical metastasis is the most common source of treatment failure. The rich lymphatic network of the supraglottic level, in combination with the presence of unrecognized occult metastases, raises the question of what may be the appropriate therapeutic approach of these carcinomas. At present, selective neck dissection is considered in several institutions as the treatment of choice for patients with a clinically negative neck, as it can serve therapeutic as well as diagnostic purposes¹⁶–²⁵.

For the above reasons, in our research, neck dissection was compared with radiotherapy and a ‘wait and see’ policy for the treatment of cN0 in T2N0M0 cases of SGLC. The 5-year OS rates of the ‘wait and see’ group, surgery group and radiotherapy group were 72.4%, 65.8% and 83.3% respectively \((\chi^2 = 2.422, P = 0.298)\). The 5-year LRC rates of the ‘wait and see’ group, surgery group and radiotherapy group were 87.3%, 78.5% and 83.3% respectively \((\chi^2 = 1.576, P = 0.455)\). Our results showed that not only the 5-year OS rates but also the 5-year LRC and 5-year LDFS rates were not significantly different between the surgery group, radiotherapy group and ‘wait and see’ group. Our conclusion was also confirmed by other researchers. Orús et al.²⁶ reported a 78% disease-specific survival (DSS) rate for patients who received neck dissection and 87% for those who received neck radiotherapy (rate difference \(-10.8\%, 95\% CI \sim 31.0 \text{ to } +4.3\) ). In the study of Sessions et al.,²⁷ the DSS rate was 75.5% in the dissection treatment group and 66.1% in the radiotherapy group (rate difference \(+9.4\%, 95\% CI \sim 4.6 \text{ to } +23.8\) ). OS rate was also reported in the Orús et al. study²⁶ and was 55% in the neck dissection group and 71% in the radiotherapy treatment group, without being significantly different \((P = 0.4)\). The NDFS rate and the site of neck recurrence did not differ significantly between patients who received neck dissection and those who had neck radiotherapy in the above two studies.²⁶,²⁷ The comparison of neck dissection with the ‘wait and see’ policy was the subject of research in some studies. The conclusion was similar to that obtained in our study. In the study of Sessions et al.,²⁷ the DSS rate was 75.5% in the neck dissection group and 79.9% in the ‘wait and see’ group; these rates were not significantly different (rate difference \(-4.4\%, 95\% CI \sim 16.0 \text{ to } +8.3\) ). In the study of Baredes et al.,²⁸ the rate of OS in the neck dissection group was 46.4% and 50% in the ‘wait and see’ group; these rates were not greatly different (rate difference \(-3.6\%, 95\% CI \sim 34.9 \text{ to } +28.2\) ). The NDFS rate and the site of neck recurrence did not differ significantly between patients who received neck dissection and those who had a conservative approach in any of the two studies.

Conclusion

Above all, our result suggests that among patients with T2N0M0 SGLC, supraglottic laryngectomy and definitive radiotherapy are both suitable in terms of survival and local control rates. When surgical margins of resection at the primary site were close or positive, patients receiving post-operative radiotherapy can get the same outcome as patients with negative margins. Neck dissection does not seem to be superior to radiotherapy or a ‘wait and see’ policy in terms of survival and control of neck disease.

References