Importance of Anterior Commissure in Recurrence of Early Glottic Cancer After Laser Endoscopic Resection

Carlos T. Chone, MD, PhD; Ema Yonehara, MD; Jose E. F. Martins, MD; Albina Altemani, MD, PhD; Agricio N. Crespo, MD, PhD

Objective: To analyze the impact of anterior commissure involvement on rates of local control, recurrence, and laryngeal preservation in patients with early glottic cancer (T1a-T2 lesions, staged according to the TNM staging system) treated with laser microsurgical resection.

Design: Retrospective review.

Setting: A tertiary university referral center.

Patients: Forty-eight patients with early glottic (T1-T2a) cancer.

Intervention: Laser endoscopic resection of glottic cancer.

Main Outcome Measures: Evaluation of local control and larynx preservation rates.

Results: Among 48 patients presenting with early glottic cancer, the anterior commissure was involved in 24 cases. The local control rate was 79% (19 cases), and the larynx preservation rate was 96% (23 cases). In the 24 cases without anterior commissure involvement, the local control rate was 96% (23 cases) and the corresponding larynx preservation rate was 100% (24 cases). The rate of local recurrence with anterior commissure involvement was 21% (5 cases) and was 4% (1 case) when this site was not compromised by the tumor. This difference was not statistically significant (P = .08). When the anterior commissure was compromised by a lesion, more surgical margins taken from the patient after the completion of surgery (additional margins) were compromised by squamous cell carcinoma (SCC) on permanent section (33% [8 cases]) compared with 0% from patients with anterior commissure involvement (P = .003), despite the fact that these margins were negative for disease on frozen section. Cases with additional margins compromised by SCC on permanent section (P = .004) and T1 lesions (P = .009) had a higher rate of recurrence.

Conclusions: This study shows the tendency toward greater additional margins compromised by SCC and a higher rate of tumor recurrence in lesions with anterior commissure involvement after laser microsurgery for early glottic carcinoma. Higher recurrence rates were observed in cases with compromised additional margins and in T1 cases.

Arch Otolaryngol Head Neck Surg. 2007;133(9):882-887
with anterior commissure involvement is still controversial. One reason may be the fact that the endoscopic exposure of the tumor is more difficult in such cases and requires considerable surgical experience. Primary radiotherapy and open surgical procedures, such as frontolateral partial laryngectomy or supracricoid partial laryngectomy, are other possible therapeutic options, but they carry a greater risk of surgical morbidity. In contrast, primary radiotherapy may lead to good functional results in terms of voice quality but at the risk of a higher recurrence rate. Open partial laryngectomies are oncologically safe but functionally less favorable in terms of voice quality than laser microsurgery.

The objective of this study was to compare the rates of local recurrence and larynx preservation according to the presence or absence of the lesion in the anterior commissure in cases of early glottic cancer. We also compared these rates in respect to other factors, such as clinical stage, adjuvant treatment, histopathological risk factors, and additional margins compromised by tumor.

METHODS

From January 1998 to September 2003, all patients with clinically diagnosed T1 and T2 glottic cancer were evaluated for the protocol of laser endoscopic resection of their cancer. The local institutional review board approved the study protocol. Informed consent was obtained from all patients enrolled in this study. All patients had their disease confirmed by previous histopathological evaluation. Only patients with at least 2 years of postoperative follow-up were included.

All lesions were staged with flexible and rigid endoscopes. When anterior commissure, subglottic, or paraglottic space invasion was suspected (eg, bulky lesions or impairment of vocal fold mobility), computed tomographic imaging with multislice imaging of the larynx was obtained with 1-mm slices. All cases with demonstrated cartilage invasion and paraglottic space invasion reaching the thyroid cartilage were upstaged to T3 lesions, excluded from the protocol, and treated with an external approach. The TNM staging system from 2002 was used for this study.1

Surgical resection was accomplished with a carbon dioxide laser (Sharplan 1040; ESC Medical Systems, Yokneam, Israel) with 4 to 10 W in the continuous mode. When exposing the tumor, the surgical procedures attempted to achieve en bloc tumor resection whenever possible. The glottic lesions were removed with a type I, II, or III cordectomy (subligamentous, transmucosal, or total, respectively), and when necessary the resection was enlarged to encompass the anterior commissure, contralateral vocal fold, vestibular fold, arytenoid, and subglottis. Additional surgical margins in critical areas were obtained from each patient and sent for both frozen section and permanent section. The extension of the resection was enlarged until these additional surgical margins were cleared, and the tissue was sent for frozen and permanent section. Each surgical specimen was attached to a cardboard plate with colored needles for spacial orientation and evaluation of the margins of the specimens. All patients were allowed to eat on the day after surgery and received counseling from a speech-language pathologist. Naso-enteral feeding tubes or tracheotomies were not used in any of the patients.

Postoperative radiotherapy or reoperation with an enlargement of previous margins was indicated when additional surgical margins were found to have squamous cell carcinoma on findings on the frozen section. If a patient did not wish to undergo a repeated surgery or this was not possible for any reason, treatment with postoperative radiotherapy was chosen. The presence of neoplastic emboli or perineural invasion was also an indication for radiotherapy.

Patients were grouped according to the presence or absence of anterior commissure involvement in the lesion, and rates of local control, local recurrence, and larynx preservation were calculated and compared between patients with anterior commissure involvement vs those without. The influence of additional positive surgical margins on permanent section, postoperative radiation therapy, the presence of neoplastic emboli, and clinical tumor stage on local recurrence was evaluated. Statistical analysis was performed with the Fisher exact test.

RESULTS

Of a total 62 patients evaluated during the study period, 14 were excluded because their lesions were upstaged to T3 (5 because they had suspected cartilage invasion and 9 because bulky paraglottic space invasion was detected). Thus, 48 patients were enrolled in this study. The mean duration of follow-up was 44 months (range, 24-90 months).

The lesions of 25 patients were staged as T1a, the lesions of 6 as T1b, and those of 17 as T2. The pathological stage was matched to the clinical stage in all T1a and T1b lesions. Five of the 17 T2 lesions had pathological invasion of the paraglottic space that did not reach the internal perichondrium of the thyroid cartilage (30%), and these were upstaged to T3 lesions. Of the 48 patients, none had cartilage invasion on computed tomographic scans, during surgery, or at histopathological evaluation, despite resection of the cartilage in the anterior commissure to clear the margins because the tumor was close to the cartilage (in 4 T1 lesions and 3 T1a lesions); 7 of the lesions were close to the anterior commissure (30%). There was no recurrence of disease in these 7 cases that were treated more aggressively in the anterior commissure. Recurrence was observed in 6 patients (13%) (5 whose lesions were staged as T1a and 1 whose lesion was staged as T1b). Of those lesions clinically staged as T1 (31), 6 (19%) recurred, but no lesions staged as T2 recurred. There was a higher rate of recurrence (19%; 6 vs 0) in T1 lesions (P = .009). The mean interval from diagnosis to recurrence after surgery in these 6 patients was 15 months (range, 5-39 months). These recurrences were observed in the non–anterior commissure area and were salvaged with another endoscopic resection in 3 cases and open surgical procedures in the other 3 cases: 1 with external frontolateral laryngectomy, 1 with supracricoid laryngectomy with cricothyroidoepiglottopexy, and 1 with total laryngectomy and bilateral modified neck dissection (radical and lateral) with postoperative radiotherapy.

To date, all 6 patients are alive and free of disease. The rates of recurrence for each stage were 20% in T1a lesions (5 lesions), 17% in T1b lesions (1 lesion), and 0% in T2 lesions. Only 1 patient (2%) underwent total laryngectomy after local recurrence during the follow-up period. The rate of local control during the follow-up pe
period was 88% (48 patients), and the total control rate, when the rate of salvage treatment was included, was 100%.

Postoperative radiotherapy after the first surgical procedure was performed in 4 of the 48 patients (8%). One patient’s lesion was staged as T1b, and those of the other 3 were staged as T2. The indication for postoperative radiotherapy was dependent on additional margins compromised by SCC on permanent section in 2 of these 4 cases (50%), even though these margins were free of disease on frozen section in 1 lesion staged as T1b and in another staged as T2. Adjuvant treatment was also indicated when neoplastic emboli were found in the surgical specimens in the other 2 cases (50%), patients with T2 lesions. None of the 4 patients who underwent radiotherapy had recurrent disease in the larynx, but 14% of those who did not undergo adjuvant treatment had recurrent disease (6/44) (there was no significant difference; \( P = .58 \)). No patients with neoplastic emboli had recurrence of their lesions, and 13% of patients without neoplastic emboli did have recurrence (6/46) (there was no significant difference; \( P = .65 \)).

Additional margins compromised by SCC on permanent section were positive in 8 patients (17%): 3 with T1a lesions, 4 with T1b lesions, and 1 with a T2 lesion. None of these additional positive surgical margins on permanent section were in the anterior commissure area. Six of these 8 patients refused any further treatment, and 4 of these 6 experienced recurrence of their lesions (67%) (3 T1a lesions and 1 T1b lesion). The other 2 patients (33%), both with T1b lesions, were free of disease at the follow-up examination. The remaining 2 patients with additional positive surgical margins (1 with a T1b lesion and 1 with a T2 lesion) received radiotherapy and were free of disease after the treatment. Recurrence was also observed in 2 patients whose lesions were staged as T1a, with free additional surgical margins on permanent section. Four of those 8 lesions with additional margins compromised by SCC on permanent section recurred (50%), and only 2 of those 40 lesions without additional margins compromised by SCC on permanent section recurred (5%), with a higher rate of recurrence (50%) in the 4 cases with additional positive margins (\( P = .004 \)).

Twenty-four patients (50%) had lesions involving the anterior commissure and 24 (50%) did not. In patients with lesions in the anterior commissure vs those who did not, the rate of local control was 79% (19 patients) vs 96% (23 patients) (\( P = .08 \)), and the rates of local recurrence were 21% (5 patients) and 4% (1 patient), respectively (\( P = .08 \)). The rates of larynx preservation according to the presence vs absence of lesions on the anterior commissure were 96% and 100%, respectively (\( P = .50 \)). Among 5 cases of recurrences in the anterior commissure compromising lesion (4 patients with T1 lesions and 1 with a T1b lesion), 4 also had additional positive surgical margins (80%) (3 T1a lesions and 1 T1b lesion). The only case that recurred that was not a compromising anterior commissure lesion (T1a) had no additional positive surgical margins (\( P = .33 \)). Thus, the presence of additional positive surgical margins was not related to a higher rate of recurrence in the group of patients with lesions that compromised the anterior commissure. Additional positive surgical margins on permanent section were observed in 8 cases of lesions with anterior commissure involvement (17%); the rate was 0% when this site was not compromised by the tumor (\( P = .06 \)).

**COMMENT**

The ideal treatment of early glottic cancer is still a controversial topic, especially in cases involving the anterior commissure. The behavior of the latter seems to be somewhat different from that of other glottic tumors, and these cases deserve special consideration when treatment modalities are considered. The efficiency of the TNM classification in providing a prognosis in cases of laryngeal cancer is limited by the fact that it does not reflect tumor localization in the anterior commissure. Patients with early glottic cancer represent a nonhomogeneous group, and the extent of the glottic lesion needs to be further described in detail. It has been suggested that the anterior commissure classification should take into account not only the TNM classification of the lesion but also the degree of involvement of the anterior commissure. In a series of 309 patients with laryngeal cancer (T1-T4) extending into the anterior commissure and treated with different modalities (primary radiotherapy, endoscopic cordectomy, open partial laryngectomy procedures, and total laryngectomy), the rate of recurrence increased according to the degree of anterior commissure involvement, whereas no such association was found between the local control rate and the TNM stage. Primary radiotherapy is a widely accepted treatment option for early glottic carcinoma, with reported control rates of 80% to 95% for T1 and T2 tumors and a total local control rate, including salvage laryngectomy, of up to 100%. However, the impact of anterior commissure involvement on the success of primary radiotherapy is less clear. Some investigators could not show an association between anterior commissure involvement and an increased risk of local recurrence. Thus, primary radiotherapy seems to be an effective and voice-preserving treatment modality for glottic tumors involving anterior commissure.

In contrast, other investigators consider anterior commissure involvement to be associated with a decrease in the local control rate when primary radiotherapy is used in early glottic cancer. Marshak et al reported a decrease in the 5-year local control rate (from 89% to 74%) when anterior commissure was involved. Other authors reported that anterior commissure involvement in early glottic cancer adversely affects the prognosis. Treatment with primary radiotherapy for tumors involving the anterior commissure could provide results similar to those obtained by conservation surgery. Radiotherapy, however, is a time-consuming procedure necessitating several weeks of treatment, and it may be associated with debilitating complications, such as chondronecrosis and edema requiring tracheostomy in some cases. It introduces the risk of radiogenic carcinoma, especially in younger patients. A delayed diagnosis of persistent or recurrent tumor may be caused by residual
edema. Total laryngectomy is often needed as a salvage operation. Tumor-related deaths occur more often after radiotherapy than after surgery. Furthermore, besides radiotherapy, diagnostic microlaryngoscopy, a procedure that can be used for curative laser surgery, is also needed.

Because there is no operative exploration, radiotherapy contains a pretherapeutic uncertainty of overstaging or understaging of glottic lesions, and the option of further radiotherapy for a second primary tumor in the head and neck area is usually disregarded. Given the disadvantages of primary radiotherapy, Rucci et al\textsuperscript{42} have advocated open partial laryngectomy procedures for treatment of early glottic cancer with anterior commissure involvement. In a review of 158 patients with anterior commissure cancer, a local control rate of 86% after open partial surgery vs 74% after irradiation was observed. The authors\textsuperscript{42} concluded that conservation surgery was the treatment of choice for early glottic carcinoma with anterior commissure involvement. Zohar et al,\textsuperscript{33} who favor surgery, made a comparison of the results of primary radiotherapy and open partial laryngectomy in 67 patients presenting with T1 and T2 glottic cancer involving the anterior commissure and observed that primary radiotherapy achieved initial control in only 76% of the patients with T1 lesions and in 56% of those with T2 lesions. In contrast, conservation surgery obtained local control rates of 91% for T1 tumors and 89% for T2 tumors. The authors\textsuperscript{43} concluded that conservation surgery is recommended for lesions of the anterior commissure because of the lower control rate achieved with radiation therapy. Talavera Sánchez et al\textsuperscript{44} reported a 14% rate of local recurrences that required total salvage laryngectomy in a series of 62 patients with early glottic cancer by the presence of the lesion in anterior commissure involving the anterior commissure (83%)\textsuperscript{56} vs cases in which it was not (87%) as can be observed in our study (we found local rates of 96% in lesions without anterior commissure involvement vs 79% in lesions with anterior commissure involvement; \(P = .08\)). A slight increase to the local recurrence rate was observed in lesions with anterior commissure involvement (21\% [5 cases]) vs lesions without involvement (4\% [1 case]) (\(P = .08\)) even though the rate of larynx preservation was not affected by the presence of the lesion in anterior commissure (\(P = .52\)). In our study, analysis by staging was not performed because of the small number of cases, but this study demonstrates that anterior commissure involvement is not statistically significant for local control (\(P = .08\)). Greater aggressiveness in dealing with anterior commissure involvement is required even in early and superficial lesions (eg, T1a), with a resection of anterior commissure cartilage requiring that the laser's power be increased or use of a window partial laryngectomy (combining an endoscopic approach with a small external approach for resection of anterior commissure cartilage). Nevertheless, our analysis suggests that laser surgery is an excellent treatment option in patients with early glottic cancer and anterior commissure involvement because most lesions with such involvement in this site were properly resected (79\%).

Four of the 5 recurrences in the 24 lesions with anterior commissure involvement in our study (80\%) had additional positive surgical margins on findings from permanent section. The presence of positive additional surgical margins did not affect recurrence in a group of patients with anterior commissure lesions (\(P = .33\)). The rate of additional positive surgical margins on permanent sec-
When deciding whether to perform laser endoscopic resection of a tumor, one should take into consideration the fact that the rates of local control and local recurrence seem to be affected by the presence of a lesion on the anterior commissure (P = .08). In our study, there was a tendency to have better results when this anatomic site was not involved (P = .08), even though the rate of larynx preservation was not affected (P = .052), and all recurrences were salvaged properly, most of them with another conservative organ preservation surgery.

Cases of recurrence involving anterior commissure lesions had more additional positive surgical margins on permanent section (80%), despite negative findings on frozen section compared with cases that recurred without an anterior commissure lesion (but without a statistically significant difference; P = .33).

The rate of additional positive surgical margins on permanent section were higher when the anterior commissure was compromised by tumor (P = .003).

Additional positive surgical margins and T1 lesions resulted in higher rates of local recurrence (P = .004 and P < .001, respectively). The absence of postoperative radiation treatment and the presence of neoplastic emboli did not adversely affect the rate of local recurrence.

Submitted for Publication: July 17, 2006; final revision received March 15, 2007; accepted April 18, 2007.

Correspondence: Carlos T. Chone, MD, PhD, Av. Heitor Penteado 1541, Campinas, São Paulo, Brazil 13087-000 (carloschone@uol.com.br).

Author Contributions: Drs Chone, Yonehara, Martins, Altemani, and Crespo. Both authors have full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Chone and Crespo. Acquisition of data: Yonehara, Martins, and Altemani. Drafting of the manuscript: Yonehara and Martins. Critical revision of the manuscript for important intellectual content: Altemani and Crespo. Statistical analysis: Chone and Martins. Administrative, technical, and material support: Chone, Altemani, and Crespo. Study supervision: Yonehara.

Financial Disclosure: None reported.

Previous Presentation: This study was presented at the 2006 Annual Meeting and Research Workshop on the Biology, Prevention, and Treatment of Head and Neck Cancer; August 17-20, 2006; Chicago, Illinois.

REFERENCES


