Implication of Margin of Glottic Cancer: Laser Surgery

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Background and Objectives

An involved resection margin in a head and neck malignant neoplasm is one of the most important factors affecting local recurrence. The aim of this study is to assess the clinical impact of resected margin status in laser surgery for glottic cancers on local recurrences and larynx preservation.

Materials and Methods

Sixty four patients of glottis cancer from January 1994 to December 2013 were included in this study. The records were evaluated for disease recurrence rate, follow up duration, additional treatment modality, and laryngeal preservation. Pathologic reports with resection margin status were reviewed in all cases. Resection margins were evaluated in anterior, posterior, superior, inferior, and deep directions.

Results

Local recurrence was not associated with positive mucosal margin. The number of positive margins was also not associated with local recurrence ($p=0.24$). Only deep margin status showed association with local recurrence ($p<0.05$). The laryngeal preservation rate was 97%. All patients who underwent salvage laryngectomy had a positive deep margin.

Conclusion

Unlike other studies, in this study, mucosal margin did not have a significant impact on clinical outcome in laser surgery for early glottic cancer. However, a deep margin should be carefully evaluated during surgery and more study is needed.

Key words

Glottic cancer; Margin status; Laser surgery

INTRODUCTION

Squamous cell cancer of the glottis is the most common laryngeal malignancy. Because of clear symptoms, sparse lymphohematologic drainage and solid anatomic boundaries, glottic cancer is commonly diagnosed in its early stage and is associated with an excellent cure rate. The goals of treatment of such lesions are cure of cancer with a low risk of complications, laryngeal preservation and good voice quality.

Despite the good prognosis of glottic cancer, repeated surgery even laryngectomy is needed for local recurrence. An involved resection margin in malignant neoplasms of the head and neck is one of the most important factors affecting local recurrence.¹⁻⁴ However, the impact of margin status on the local recurrence of early glottic cancer remains controversial. Ansarin⁵ reported that patients with close or positive margins had greater recurrence risk. The few studies⁶⁻⁹ that have addressed the impact of margin status on local control in malignant vocal cord neoplasms have provided contrasting results.

The aim of this study is to assess the clinical impact of resection margin status in laser surgery for early glottic cancers on local recurrence and larynx preservation.

MATERIALS AND METHODS

This retrospective chart review and pathologic study was approved by the Ethics Committee and the Institutional Review Board at Korea University College of Medicine, Seoul, Korea.

From January 1994 to December 2013, the records of 64 consecutive patients confirmed to have squamous cell carcinoma of the glottis were identified (Table 1). The patients underwent laser surgery using a CO₂ laser (Lumenis 30C, Yokneam, Israel) under general anesthesia. The CO₂ laser was used in regular pulse continuous mode, spot size less than 3 mm, with an output

power set at 1.5 to 3.5 W.

Histological resection margin analysis was performed in all cases with the same technique and criteria. Surgical specimens were fixed in 4% formaldehyde for 72 hr, and inked on their superficial and deep mucosa with two different colored inks. The formaldehyde-fixed specimens were entirely embedded in paraffin. Sections (4 µm) were mounted on glass slides and hematoxylin and eosin stained. Resection margins were analyzed in anterior, posterior, superior, inferior and deep directions. Positive margins were defined by in situ or invasive carcinoma in contact with the margin. All patients were followed-up with office-based fiberoptic or videostrobe-laryngoscopy monthly for the first 6 months and then every 2 months for the following 6 months. In the second year, patients were followed-up with office-based laryngoscopy every 3 to 4 months, and 4 to 6 months thereafter. Routine computed tomography and chest X-rays were scheduled every year for at least 3 years post-operation. The records of consecutive patients were evaluated for disease recurrence rate, duration, additional treatment modality and laryngeal preservation.

Patient characteristics are presented as frequencies and percentages for categorical variables and as medians and ranges for continuous variables. The effect of margin status on recurrence rate was assessed using a multivariate Cox proportional hazards regression model. Statistical analysis was performed using SAS for Windows statistical software, version 8.2 (SAS Institute Inc., Cary, North Carolina, USA). A p value of less than 0.05 was considered to be statistically significant.

RESULTS

All laser surgery specimens were evaluated for surgical margin status by a pathologist. Margin status was analyzed in superior, inferior, anterior, posterior and deep directions. Surgical margins were positive in 47 patients. Local recurrence was observed in 17% of patients with a positive margin but was not statistically significant. Of 47 patients, six were judged positive at the superior margin. Among these, one patient experienced local recurrence. Of 27 patients with a positive inferior margin, eight had local recurrence. Eight of 23 patients who were had a positive anterior margin experienced local recurrence. Local recurrence was not observed in patients with a positive posterior margin. Only deep margin status was associated with local recurrence and was statistically significant ($p < 0.05$) (Table 2). The superior margin positive population had the following values: 12.5%, 91.07%, 16.7%

Table 1. Patients and tumor characteristics

Characteristic	Value
Age, median (range)	59 (32-77)
Sex (%)	
Male	58 (84.4)
Female	6 (15.6)
Clinical stage	
Tis	12
T1a	27
T1b	21
T2	4

Table 2. Local recurrence according to margin status

Margin Status		Recurrence(n=8)		P value
		Positive	Negative	
Superior	Positive	1	5	0.092
	Negative	7	51	0.342
Inferior	Positive	8	19	0.084
	Negative	0	37	N/A
Anterior	Positive	8	15	0.054
	Negative	0	41	N/A
Posterior	Positive	0	8	N/A
	Negative	8	48	0.067
Deep	Positive	6*	11	0.002
	Negative	2	45	0.405

*Statistically significant.

and 87.9% for the sensitivity, specificity, PPV and NPV, respectively. The inferior and anterior margin positive populations had similar results. However, the deep margin positive population had the following results: 75%, 80.4%, 35.3% and 95.7% for the sensitivity, specificity, PPV and NPV, respectively. The sensitivity and NPV in the deep margin positive population are higher than those of the superior margin positive population. The sensitivity and NPV in the inferior and anterior margin positive populations are higher than those of the deep margin positive population, but their specificity and PPV are lower than those of the deep margin positive population.

DISCUSSION

Laser resection of glottic cancer was developed in the 1970s.¹⁰ It is based on the same principle of en bloc resection as partial laryngectomy, but laser surgery shortens hospital stay and simplifies postoperative course, notably avoiding tracheotomy.¹¹ Since the initial reports from the 1970s, laser surgery has evolved to be a widely accepted operation in the treatment of early laryngeal carcinoma. Currently, laser surgery is recognized as an effective and safe standard management option for patients with early glottic cancer. When performing laser surgery to treat early glottic cancer, resection with a narrow tumor margin is usually the goal in order to preserve as much tissue as possible. The peculiarities of laryngeal embryologic development and the scarce glottic submucosal lymphatic network suggest that the resection margins can be narrower than required in other head and neck cancers.

The present study sought to assess the margin status in terms of local recurrence in laser surgery for early glottic

cancer. In our results, there is a discrepancy between pathology reports with a high percentage of unclear resection margins and a low incidence of recurrence. Forty-seven patients with a positive margin were either violated or showed tumor-suspect areas in the laser carbonized zone with thermal artifact. In this group, only eight patients experienced recurrence; however, no instances of recurrence were observed when the surgical margins were negative on permanent pathologic reports although this was not statistically significant. This finding suggests that mucosal margins do not have a significant influence on clinical outcomes. We assumed that there were no tumors in the resection margin even if positive margins were revealed in the pathologic report or there were burns and artifacts in the margin which did not allow an exact conclusion. Deep margin status, however, was associated with local recurrence. Six of 17 patients who were judged positive at the deep margin experienced local recurrence ($p<0.05$). The high rate of local recurrence observed in this group could be explained by conservative resection of the lesion, which was due to an attempt to save the vocalis muscle and achieve good phonatory results. The other reason was that the deep plane of excision was the most difficult part of the operation, especially if it was uncertain whether the vocal ligament was affected or not. On the other hand, the superior, inferior, anterior and posterior margins were not associated with local recurrence.

Laser excision of early glottic cancer has several advantages over other treatment modalities. The procedure is brief with shorter hospital stay, lower morbidity, and fewer side effects. In addition, organ preservation is the best advantage. In this study, the organ preservation rate was 97%. The local control rate with laryngeal preservation was similar to that seen in other studies. But two patients who had positive deep margin required salvage total laryngectomy after radiation therapy. Even though our data supported that deep margin should be carefully evaluated during operation, this study was primarily limited by the number of T2 patients. There might be some other limiting factors, such as histologic characteristics and laser cordectomy type, which were not classified nor taken into consideration in the analysis, although they could also potentially affect local recurrence. Finally, the retrospective nature of the results was a limitation.

The margin status in early glottic cancer was important for local recurrence. But mucosal margin did not have a significant impact on clinical outcome unlike other studies. Only positive deep margin was significantly

correlated with local recurrence and larynx preservation. Deep margin should be carefully evaluated during operation and the more study was needed.

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