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Margin Photocoagulation in Laser Surgery for Early Glottic Cancer: Impact on Disease Local Control

Marco Lucioni, MD1, Andy Bertolin, MD1, Luca D’Ascanio, MD1, and Giuseppe Rizzotto, MD1

Abstract

Objective. Assess the impact of surgical margin CO2 laser photocoagulation (LPC) on disease local control in patients submitted to endoscopic surgery for early glottic cancer in comparison with subjects treated with laser cordectomy without borders LPC.

Study Design. Historical cohort study.

Setting. Regional referral cancer center.

Subjects and Methods. A total 281 patients with early glottic cancer (T1a, T1b, T2) were treated with endoscopic laser cordectomy according to the European Laryngological Society Classification between 1999 and 2006. Among the patients, 123 (treated between 2003 and 2006) were submitted to postresection LPC of surgical margins (group 1), whereas 158 (operated between 1999 and 2002) underwent laser cordectomy without margin LPC (group 2). Median follow-up was 51 months (range, 36-101 months).

Results. Local recurrence was found in 43 of 281 (15.3%) subjects (18 with T1a, 13 with T1b, 12 with T2). A significant difference in recurrence rate was found among patients treated with margin LPC in comparison with group 2 (P = .022). In particular, a lower recurrence rate in LPC patients was noticed in case of close (≤1 mm), nondefinable, and positive margins with infiltration of the superficial border. No significant difference was noticed in the case of negative edges (>1 mm) or involvement of either deep margin or both superficial and deep edges.

Conclusions. Surgical margin LPC increases disease local control in the case of close and superficial margin positivity. In such cases, no further treatment (surgical revision or radiotherapy) seems to be required in LPC patients. In case of deep border involvement, surgical revision or radiotherapy should be performed.

Keywords

laser; photocoagulation; endoscopic surgery; laryngeal cancer, glottic tumor
submitted to postresection margin photocoagulation in comparison with patients treated with laser cordectomy for early glottic cancer before the introduction of routine LPC.

**Materials and Methods**

**Patient Selection and Staging**

We retrospectively reviewed the charts of consecutive patients treated in our department for a history of vocal cord biopsy positive for squamous cell carcinoma or with a clinically suspicious lesion of the glottis staged as cT1a, cT1b, or cT2 and clinically negative neck (cN0) between 1999 and 2006. Inclusion criteria were (a) early glottic carcinoma (cT1a, cT1b, or cT2) with cN0; (b) adequate glottic exposure; (c) no tumor extension to the subglottis or paraglottic spaces; (d) no infiltration of the thyroid cartilage; (e) ability to understand and desire to sign a written informed consent to take part in the study; and (f) no contraindication to general anesthesia. Patients who had been previously treated (radiotherapy or surgery) for the same lesion or previous cancer were excluded. Basing on the aforementioned criteria, 281 patients (242 males, 39 females; mean age, 65.7 years; age range, 36-87 years) operated at the Department of Otolaryngology–Head and Neck Surgery, Veneto Regional Laryngeal Cancer Center, Vittorio, Veneto, Italy, for glottic cancer were enrolled in the study (Table 1). Patients recruited in the early period (1999-2002) had their cancers reclassified according to the latest International Union Against Cancer classification. The therapeutic protocol, its risks and benefits, and possible alternative treatments were discussed with the patient before obtaining informed consent. Preoperative evaluation included physical examination, routine blood tests, chest radiography, and video-laryngoscopy with flexible endoscope. Computed tomography (CT) of the neck with contrast was performed for bulky lesions, suspected deep infiltration of the anterior commissure or paraglottic spaces, and possible extension to arytenoids or subglottis. Among our patients, 172 (61.21%) were staged as cT1a, 73 (25.98%) as cT1b, and 36 (12.81%) as cT2 (Table 1). The study was approved by Vittorio Veneto Hospital review board.

**Surgical Treatment**

Laser treatment was always preceded by intraoperative visual evaluation of the larynx using rigid endoscopes with 0°, 30°, and 70° angles of view, with examination of both vocal cords, ventricles, and subglottis to assess tumor extension. All surgical procedures were performed under general anesthesia after orotracheal intubation using a laser-safe

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**Table 1. Pathologic Stage, Type of Cordectomy, Margin Status, and Recurrence Rate in Both Groups**

<table>
<thead>
<tr>
<th>Pathological stage</th>
<th>Group 1: LPC (n = 123), No. (%)</th>
<th>Group 2: No LPC (n = 158), No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1a</td>
<td>66 (53.66)</td>
<td>106 (67.09)</td>
</tr>
<tr>
<td>T1b</td>
<td>36 (29.27)</td>
<td>37 (23.42)</td>
</tr>
<tr>
<td>T2</td>
<td>21 (17.07)</td>
<td>15 (9.49)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of cordectomy</th>
<th>Group 1: LPC (n = 123), No. (%)</th>
<th>Group 2: No LPC (n = 158), No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>18 (14.64)</td>
<td>13 (8.23)</td>
</tr>
<tr>
<td>II</td>
<td>30 (24.39)</td>
<td>29 (18.35)</td>
</tr>
<tr>
<td>III</td>
<td>27 (21.95)</td>
<td>58 (36.71)</td>
</tr>
<tr>
<td>IV</td>
<td>12 (9.75)</td>
<td>24 (15.19)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Margin status</th>
<th>Group 1: LPC (n = 123), No. (%)</th>
<th>Group 2: No LPC (n = 158), No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative (&gt;1 mm)</td>
<td>72 (58.54)</td>
<td>98 (62.03)</td>
</tr>
<tr>
<td>Close (≤1 mm)</td>
<td>3 (2.43)</td>
<td>9 (5.70)</td>
</tr>
<tr>
<td>Nondefinable</td>
<td>3 (2.43)a</td>
<td>23 (14.56)a</td>
</tr>
</tbody>
</table>

Positive

<table>
<thead>
<tr>
<th>Only superficial margin</th>
<th>Group 1: LPC (n = 123), No. (%)</th>
<th>Group 2: No LPC (n = 158), No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only deep margin</td>
<td>30 (24.40)</td>
<td>22 (13.92)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Recurrence</th>
<th>Group 1: LPC (n = 123), No. (%)</th>
<th>Group 2: No LPC (n = 158), No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/123 (9.76)b</td>
<td>31/158 (19.62)b</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: LPC, surgical margin laser photocoagulation.

*aStatistically significant at P < .001.

bStatistically significant at P = .023.
endotracheal tube Laser-Flex Mallinckrodt (Athlone, Ireland) or Laser Shield II (Xomed, Jacksonville, Florida) with internal diameters ranging from 4.5 to 5.5 mm. The larynx was exposed as widely as possible with suspension laryngoscopy and counterpressure on the cricoid cartilage as required for optimal visualization of the anterior commissure region. Laryngoscopes of different sizes and shapes were used to obtain adequate laryngeal exposure; the Bouchayer-Microfrance laryngoscope with wide proximal diameter (Xomed) was used most often. Between 1999 and 2002, a Wild Heerbrugg M 655 microscope (Jena, Germany) with 400-mm focal lens coupled with Lasertronics Paragon 50 model CO2 laser (San Jose, California) and UniMax Model 2000 micromanipulator (Reliant Technologies, Foster City, California) was used. Since 2003, a Leica M520 F40 microscope (Leica Microsystems, Heerbrugg, Switzerland), coupled with an Ultra Pulse Surgitouch with an Acuspot 71 micromanipulator (Lumenis Ltd, Yokneam, Israel), has been used. Superpulse and 270-μm spots were used. Pulsed energy, mean power in watts, and excision depth were tailored to carcinoma localization and cordectomy type. Cordectomy was usually preceded by homolateral vestibulectomy to improve tumor site exposure.

En bloc endoscopic resection was performed by the same surgeon (M.L.) in accordance with cordectomy classification proposed by the European Laryngological Society. The choice was based on the superficial and deep extension of the tumor evaluated during operation by visual examination and tissue palpation with microforceps. Of the 281 laser cordectomies performed, 31 (11.03%) were type I, 59 (21.00%) type II, 85 (30.25%) type III, 36 (12.81%) type IV, 25 (8.90%) type Va, 19 (6.76%) type Vb, 12 (4.27%) type Vc, 6 (2.13%) type Vd, and 8 (2.85%) type VI (Table 1). Each surgical specimen was oriented, and margins were marked with ink. Fixation in 10% buffered formalin followed. Five-micrometer-thick serial sections were obtained and stained using hematoxylin–eosin for histological examination carried out by a pathologist with prominent experience in laryngeal diseases. All the edges were assessed, and the distances between tumor and specimen margins were measured. Negative borders had more than 1 mm between margin and tumor, close margins had 1 mm or less between border and tumor, and positive margins had tumor on an examined edge. Margins were considered nondefinable if abundant artifacts prevented a reliable assessment of specimen borders. No frozen section was performed.

In the 123 patients treated between 2003 and 2006 (group 1), laser photocoagulation of the surgical margins was performed after resection. The procedure consisted of vaporizing the microscopically healthy tissue (with an extent of about 1.6 mm) around the resection margins with a CO2 laser with the purpose to destroy any residual cancer cell and avoid local recurrence. Laser settings for LPC were as follows: circular spot shape, spot diameter 1.6 mm, laser depth for each pulse 0.3 mm, power 16 W (Figures 1-3). LPC was not performed in the 158 patients treated between 1999 and 2002 (group 2). No fatalities occurred. No patient underwent prophylactic neck dissection or tracheotomy. Patients were discharged from the hospital on the first or second postoperative day and received only a single perioperative dose of antibiotics.

Follow-Up

Each patient was examined every 3 months for the first year and subsequently every 4 to 6 months depending on the patient’s progress and requirements. Flexible videonasolaryngoscopy was performed at each follow-up visit. In concordance with the experience of Peretti et al, Mortuaire et al, and Brøndbo et al, patients in whom the histological margins were positive, close, or suspicious were not retreated or submitted to radiotherapy but were strictly and regularly followed. Three months postoperatively, all
patients completed the Voice Handicap Index (VHI) via a self-evaluation form consisting of 30 questions covering 3 domains (functional, physical, and emotional) translated from the original work in English by one of the authors. Each question was assigned a score of 0 to 4 (from least disability to most). In each item, the maximum score was 40 points, and we classified them as mild disability (<20), moderate disability (21-30), and severe disability (>30). When the 3 scores were added together, the maximum total score ranged from 0 (no disability) to 120 (greatest disability).

Neck CT with contrast was carried out in patients at higher risk of recurrence (eg, neoplasm extension, difficult surgical exposure). Routine repeated rigid laryngoscopy using general anesthesia was not performed. The length of follow-up ranged from 36 to 101 months, with a median follow-up period of 51 months.

**Data Collection and Statistical Analysis**

Data relating to the initial lesion, including stage, size, anatomical site, and type of cordectomy performed, were documented and reviewed retrospectively with additional information on histopathological findings and follow-up. Patients’ characteristics were represented as frequencies and percentages. The comparison between different variables in the 2 groups was assessed using Student t test for unpaired data and Kaplan-Meier analysis. The overall survival time was defined as the interval between the date of surgery and recurrence or last follow-up. Statistical analysis was performed using SPSS 10.0 for Windows (SPSS, Chicago, Illinois). A value of $P < .05$ was considered as statistically significant.

**Results**

A summary of pathological, surgical, and histological details in the 2 groups is presented in Table 1. No significant difference was noticed in tumor pathological stage between the 2 groups. Types II and III were the most common cordectomy procedures performed in our patients. Type VI cordectomy for isolated involvement of the anterior commissure was performed in 8 cases.

Local recurrence was found in 43 of 281 (15.30%) subjects (18 T1a, 13 T1b, 12 T2), with a median time interval between surgery and recurrence diagnosis of 16 months (range, 5-58 months). Among them, 21 patients were managed with a new laser treatment, 8 with supracricoid laryngectomies, and 3 with radiotherapy alone. The 3-year actuarial overall survival was 91.46%. Among the 24 patients who died, 6 deaths were related to the glottis tumor. The rate of cause-specific survival was 97.86%. The 3-year disease-free survival was 84.70%.

A statistically significant difference in recurrence rate was found among patients treated with margin LPC in comparison to group 2. Kaplan-Meier analysis of potential prognosis factors with impact on disease-free survival shows that LPC of surgical margins influences local control (Figure 4). In particular, a lower recurrence rate in LPC patients with respect to group 2 subjects was noticed in patients with close, nondefinable, and positive margins (Table 2). In patients with involved resection borders, a significantly lower recurrence rate was found in group 1 only for infiltration of the superficial margin, whereas no significant difference was noticed in patients with involvement of either deep edge or both superficial and deep borders. No significant difference in recurrence rate was found between the 2 groups in patients with negative margins. As to functional outcomes, 5 patients showed changes in fluid deglutition without requiring temporary nasogastric feeding; 7 subjects presented postoperative glottic synchiae requiring laser excision. As to postoperative voice quality, no significant difference ($P = .11$) in 3-month postoperative VHI score was noticed between the 2 groups (group 1, 23.61 ± 13.18; group 2, 21.06 ± 13.33).

**Discussion**

Laser-assisted transoral laryngeal surgery is now accepted as a valid treatment for glottis cancer; however, the approach to obtain intraoperative safe surgical margins with minimal impairment of voice quality is still a matter of controversy. Even though a systematic use of intraoperative frozen sections has been proposed, the cost-efficiency of such procedure in laryngeal laser surgery is still debated. According to our experience, the disease-free survival of our patients (84.70%) was comparable to that reported in other studies on early glottic cancer laser treatment (80%-94%). In particular, the recurrence rate of the subgroup with what we considered free margins (>1 mm) was similar to the data published by other authors. This finding...
supports the idea of considering the rather narrow border of 1 mm as free. According to our experience, results in case of free surgical edges are not influenced by margin LPC. On the contrary, our data show a role for surgical margin photocoagulation in reducing local recurrence rate in case of close, nondefinable, and positive margins. Such results may be related to the destruction of possible neoplastic cells that remained in the surgical field in proximity to resection borders. In case of involved resection edges, however, our data suggest an efficacy of margin LPC in the prevention of recurrences for infiltration of superficial surgical margins. In patients with infiltration of deep surgical borders, no significant difference in recurrence rate was noticed between LPC subjects and non-LPC patients, thus suggesting that in these cases photocoagulation was unable to destroy the tumor cells that possibly remained in the surgical field.

Despite the amount of studies in the literature regarding the impact of resection margins in early glottic cancer treated by endoscopic laser surgery, this topic is still controversial. According to some authors, positive or suspicious margins are unrelated to recurrence rate, whereas others report a correlation between local disease recurrence and positive surgical margins. Interestingly, our data in non-LPC patients with positive margins show a recurrence rate (42.85%) lower than expected (on the basis of edges positivity). Such results in subjects with positive boundaries may be related to specimen shrinkage, which can prevent an adequate histological assessment of surgical borders.

Our experience shows that margin LPC can further reduce the risk of local recurrence in patients submitted to laser surgery for early glottic cancer, also in patients with positive margins, without affecting voice quality. Even though these oncological and functional results may be influenced by increased surgeon experience and technological changes in microscope and laser over the years, our preliminary findings on the efficacy of surgical borders LPC are encouraging.

The absence of difference in vocal function between the 2 groups is likely related to the very limited extension (1.6 mm) of margin LPC, which does not cause significant damage to vocal folds. Even though margin LPC may be considered an overtreatment in patients with negative margins, the lack of significant difference in postoperative voice quality between the 2 groups seems to justify routine surgical edges LPC in patients submitted to laser cordectomy.

The efficacy of LPC in recurrence prevention, however, is restricted to those patients with border involvement limited to vocal cord superficial layer. Such results suggest that no further treatment should be undertaken in patients with histological positivity of superficial surgical edge after laser surgery for glottic cancer. On the contrary, our findings suggest carrying out a second procedure (laser treatment or radiotherapy) for patients with deep surgical border involvement at postoperative histological examination. Even though intraoperative margin LPC does not seem in accordance with the traditional rules of oncological surgery, it may represent an additional technique to be considered by laryngeal laser surgeon. Further studies are needed for a better understanding of the effects of margin LPC and standardization of this procedure.

**Conclusion**

Early glottic carcinomas are tumors of excellent prognosis in terms of overall survival, disease-free survival, and quality of life. Three modalities of treatment are recommended.
with comparable oncological results: radiotherapy, partial open surgery, and endoscopic laser cordectomy. Laser treatment is associated with time- and cost-effectiveness, a low morbidity, and excellent retreatment options. Furthermore, high magnification available in endoscopic laser equipment can help preserve normal tissue while removing the tumor, thus improving postoperative voice quality. Laser photocoagulation of surgical margins can be useful during endoscopic surgery to increase disease local control. In case of close or superficial margin positivity at postoperative histological examination, no further treatment seems to be required in LPC patients.

**Author Contributions**

Marco Lucioni, conception and design, acquisition of data, analysis and interpretation of data, drafting the article, final approval of the version to be published; Andy Bertolin, conception and design, acquisition of data, analysis and interpretation of data, final approval of the version to be published; Luca D’Ascanio, conception and design, analysis and interpretation of data, drafting/revising the article, final approval of the version to be published; Giuseppe Rizzotto, conception and design, acquisition of data, analysis and interpretation of data, revising the article critically, final approval of the version to be published.

**Disclosures**

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**References**


