Abstract: Background. Treatment of early glottic malignancies is controversial, particularly if postoperative endoscopy shows minimal/no residual disease.

Methods. In a prospective nonrandomized study, we performed endoscopic laser surgery with curative intent in 59 patients with early glottic carcinoma presenting for radiotherapy after diagnosis elsewhere by random biopsy or cordal stripping. We analyzed outcomes and residual cancer in the specimen.

Results. Clinical staging elsewhere did not correspond to (usually underestimated) the pathologic stage in 60.7%. In 22%, no tumor was identified on pathologic examination. After 35.3 months (mean), 93.2% were alive with no evidence of disease. Local control was achieved in 98.3% of the patients, and 13.5% of the patients required radiotherapy. The larynx was conserved in 98.3%.

Conclusions. Biopsy/stripping are best abandoned for persistent glottic lesions. A single laser endoscopic procedure provides reliable staging and definitive treatment in most cases using fewer resources. Biopsied patients presenting for treatment should be offered laser surgery as an alternative to radiotherapy. © 2005 Wiley Periodicals, Inc. Head Neck 28: 121–125, 2006

Keywords: early cancer; larynx; CO2 laser

The clinical appearance of inflammatory glottic lesions is not a reliable indicator of benign versus precancerous versus early cancerous histology, and microlaryngoscopy with histologic examination is necessary for all persistent glottic lesions. Conventional diagnostic endoscopy in such cases requires multiple random punch biopsies or mucosal stripping, both under general anesthesia. If
squamous cell carcinoma (SCC) is diagnosed, the patient requires further treatment with surgery or radiotherapy.

The use of carbon dioxide (CO₂) lasers and micromanipulators (Microspot, St Louis, MO) makes it possible to evaluate the surgical margins and improve diagnosis. In many cases, endoscopic laser surgery provides definitive treatment for the disease in a single intervention, so that patients avoid radiotherapy and its side effects, whereas control rates and vocal (functional) outcome are similar to those obtained with conventional treatments.¹⁻⁶

Nevertheless, the treatment of patients previously subjected to random biopsy or cordal stripping and found to have malignant histology, remains controversial, particularly when postoperative fibroscopy indicates minimal or no residual disease.

We conducted a prospective nonrandomized study to investigate this problem. From April 1999 to December 2001, patients with early glottic SCC biopsied elsewhere and referred to our institute for external radiation therapy were proposed for endoscopic surgery with the CO₂ laser. We evaluated the radicalness of endoscopic laser surgery in this series by determining the presence or absence of residual cancer in the surgical specimen and analyzing outcomes.

**PATIENTS AND METHODS**

We considered patients in whom multiple biopsy or cordal stripping had been performed elsewhere and were positive for early glottic cancer. Eligibility criteria were:

1. Early glottic SSC (cTis, cT1a, cT1b).
2. No palpable neck nodes (cN0).
3. Adequate access to the glottic region.
4. No contraindications to general anesthesia.
5. Written informed consent.
6. No previous surgical or radiation treatment for the cancer with curative intent.

Preoperative evaluation comprised routine blood tests, chest x-ray, flexible endoscopy, and videolaryngostroboscopy. Laryngeal CT with contrast was performed in the presence of bulky tissue at the anterior commissure and suspicion of involvement of the laryngeal ventricle not assessable by outpatient endoscopy or of deeper infiltration.

Patients were placed under general anesthesia and intubated with laser-safe tubing (Laser Flex Tracheal tube, Mallinckrodt, St Louis, MO). Intraoperative visual assessment was performed using rigid endoscopes with 0° and 70° view angles, the aim being to determine vocal cord rigidity, depth of infiltration, and identification of sites of possible endolaryngeal involvement (anterior commissure, subglottic region, ventricle). A 25-W CO₂ laser (Martin, Germany) with a beam spot of 150 µm was used for resection. Superpulse continual mode was used with output power 0.8 to 2.4 W.

The type of cordectomy performed (European Laryngological Society classification⁷) depended on the preoperative and intraoperative findings. Type II cordectomy (mucosa and vocal ligament) was performed on patients who had had vocal cord stripping and showed no macroscopic evidence of disease. Type III cordectomy (mucosa, ligament, superficial part of vocal muscle) was performed on patients who had received punch biopsy and had a well-circumscribed lesion limited to the vocal cord (without involvement of ventricle or subglottis). Type IV cordectomy (mucosa, ligament, vocal muscle) was performed when macroscopic disease extended to the anterior commissure or infiltrated the vocal muscle. Type V cordectomy (mucosa, ligament, vocal muscle, internal thyroid perichondrium) was performed when the disease involved the anterior commissure, vocal muscle, and floor of Morgagni’s ventricle. For type III–V cordectomies, the specimens were removed en bloc.

**Pathologic Examination.** The specimen was oriented and slide mounted to prevent retraction before formalin fixation and subsequent serial sectioning. The histotype was determined, all resection margins were assessed, and the distance between the tumor and margin was measured. Margins were defined as negative (>1 mm from tumor), close (≤1 mm from tumor), or positive (tumor on margin).

**Subsequent Treatment.** For patients with negative margins, clinical checkups (including flexible laryngoscopy or videostrobolaryngoscopy) were performed every 3 months in the first year and every 4 to 6 months subsequently. For close margins or margins involved by precancerous lesions (low-grade to severe intraepithelial laryngeal neoplasia, LIN I–II), checkups were done monthly for 6 months, every 2 months for the next 6 months, and every 3 months subsequently.
If one margin was positive, a new endoscopic surgery was performed 30 to 40 days later to remove the residual disease; if the resulting resection margins were free, patients were checked every 3 months in the first year and every 4 to 6 months subsequently. Patients with two or more positive margins initially or a positive margin after the second surgery were given radiotherapy.

RESULTS

From April 1999 to December 2001, 74 patients were referred to the Divisions of Head and Neck Surgery or Radiotherapy at the European Institute of Oncology (EIO) for treatment after diagnosis of early glottic cancer in biopsy sample. Thirteen were excluded for previous radiotherapy to the larynx and two for inadequate access to the glottic region. Thus, 59 patients, 53 men, were eligible, and all entered the study. The mean age was 53 years (range, 31–92 years). Mean postoperative hospitalization was 3 days (range, 2–5 days), with 83% of patients discharged on the second postoperative day. There were no intraoperative or postoperative complications, and none of the patients required tracheotomy. No patient was lost to follow-up.

Table 1 shows the clinical stage, as determined by laryngoscopy performed elsewhere (CSE), in relation to the preoperative/intraoperative staging procedures as determined at the EIO (CSEIO). Both were assessed according to Union Internationale Contre le Cancer 5th edition criteria. As expected, CSEIO findings often differed from those found initially, most tumors being assessed by us as smaller (eight were ycT0) than suggested by CSE. Tables 2 and 3 show the relationship between CSE, CSEIO, and final pathologic classification (EIOpT) after cordectomy. The tables show that in 13 patients (22%), no residual disease was present on the surgical specimen (ypT0), and in four patients (6.8%), lesion extent was underestimated by both the CSE and CSEIO procedures (cT1/pT2).

None of the 13 patients with ypT0 disease had a local recurrence during follow-up. In the other 46 (78%) patients with SCC in the specimen, the disease was completely removed (negative margins) in 20 (43.4%), there were close margins in 12 (26%), and there were one (three cases) or more (seven cases) positive margins in 10 (21.7%). In four (6.8%) additional patients, margins showed LIN I–II. The three patients with a single positive margin underwent reoperation; the second specimen from these patients showed granulation tissue only in one case, moderate dysplasia (LIN II) in the second, and SCC with one positive margin in the third. This latter patient and the seven with more than one positive margin underwent radiotherapy, so only eight (13.5%) of the patients initially referred to our institute for radiotherapy had to undergo this treatment.

After the complete therapeutic procedure (laser cordectomy with subsequent radicalization or radiotherapy as necessary), a local recurrence developed in four patients (6.7% of total; 8.7% of the 46 with residual SCC on the specimen). In three of these cases (patients 2, 3, and 4; Table 4), both the CSE and CSEIO underestimated the local extent of the disease. Patient 1 received salvage total laryngectomy; patients 2 and 3 under-
went further conservative treatment. At first, patient 3 refused postoperative radiotherapy, but 4 months after the initial cordectomy, he agreed to have further laser surgery followed by radiotherapy for persistent disease in the anterior paraglottic space. Patient 4 had an inoperable local recurrence 9 months after cordectomy plus radiotherapy and died of his disease after a further 6 months.

The larynx was preserved in 58 of 59 (98.3%) patients. Complete local control was achieved with laser resection alone in 48 (81.3%) patients. Five patients had second primary tumors, one of whom developed metachronous quadruplicity (two liver cancers, two prostate cancers, one lung cancer, one rectal cancer, one urinary bladder cancer, and one skin cancer). After a mean follow-up of 35.3 months (range, 24–55 months), 55 patients were alive with no evidence of laryngeal disease. Of the four patients who had died, three died of second primary cancers without any evidence of laryngeal cancer.

**DISCUSSION**

The first point emerging from this study is that the clinical staging conducted elsewhere did not correspond to the pathologic staging (pTNM) in 34 (60.7%) cases (Table 2) and usually underestimated the true extent of the tumor. Thus random biopsy/cordial stripping seem to be an inaccurate staging procedure. Although our own clinical-intraoperative staging (CSEIO) was more accurate than CSE, it also underestimated or overestimated the extent of the tumor in 24 (42.8%) cases (Table 3), mainly because of alterations (hyperemia, granulation tissue, fibrin, ulceration, scarring, and fibrosis) induced by the previous manipulations. It is possible that more extensive preoperative imaging would increase the accuracy of the clinical-intraoperative staging procedure in such cases.9,10

It is noteworthy that in 13 patients (22%), no tumor was identified (ypT0) on pathologic examination. We expected such a proportion from a previous study.11 In fact, although biopsy/strip- ping can usually identify a malignancy, it is unable to determine whether the lesion has been completely removed. This is why patients are referred for radiotherapy. If these 13 patients had received laser excision at the outset, most would have avoided the second treatment, because the final histologic evaluation would generally have revealed complete excision and clear resection margins.

We performed type III (transmuscular) cordectomy in a high proportion of cases (37 of 56; 62.7%), in accord with our pre-established criteria. This more extensive operation was often used to remove superficial lesions (ypTis, ypT1a, and ypT0). Again, if the laser procedure had been used at the outset, a high proportion would probably have received more conservative treatment (type I or II cordectomy) to achieve oncologic radicality.

The outcomes of this study are in line with published findings that endoscopic laser surgery for clinically Tis–T1 glottic tumors affords similar oncologic radicality and functional outcomes to other methods5,11–14 while using less resources than the two-step treatment approach.15

It is also important to note that in cases of tumor recurrence or new malignancy, a previous endoscopic procedure does not preclude further endoscopic, open surgical, or radiation treatment.16–25 Laryngeal preservation may still be possible during repeat endoscopic17,18 or open19–22 surgery. However, in most cases, total laryngectomy must be performed.23,24 Open surgery would generally be used as a salvage option for recurrence after radiotherapy.

To conclude, our findings suggest that random biopsy and cordal stripping are best abandoned for persistent lesions of the glottic region and

**Table 4. Characteristics of the four patients who had a local recurrence development.**

<table>
<thead>
<tr>
<th>Patient</th>
<th>CSE</th>
<th>CSEIO</th>
<th>EIOpT</th>
<th>Margin status</th>
<th>Treatment (cordectomy)</th>
<th>DFI, mo</th>
<th>Recurrence site</th>
<th>Treatment for recurrence</th>
<th>rTNM</th>
<th>FU, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>T1a</td>
<td>T1a</td>
<td>T1a</td>
<td>–</td>
<td>III</td>
<td>16</td>
<td>PPS</td>
<td>TL</td>
<td>T3N0</td>
<td>15 NED</td>
</tr>
<tr>
<td>2</td>
<td>T1a</td>
<td>T1a</td>
<td>T1b</td>
<td>+</td>
<td>IV</td>
<td>13</td>
<td>AC</td>
<td>Type V + RT</td>
<td>T2N0</td>
<td>33 NED</td>
</tr>
<tr>
<td>3</td>
<td>T1b</td>
<td>T1b</td>
<td>T2</td>
<td>+</td>
<td>IV</td>
<td>4</td>
<td>AP</td>
<td>Type V + RT</td>
<td>T2N0</td>
<td>29 NED</td>
</tr>
<tr>
<td>4</td>
<td>T1a</td>
<td>T1b</td>
<td>T2</td>
<td>Close</td>
<td>IV + RT</td>
<td>9</td>
<td>PPS</td>
<td>CT</td>
<td>T3N0</td>
<td>6 DOD</td>
</tr>
</tbody>
</table>

**Abbreviations:** CSE, clinical staging elsewhere; CSEIO, clinical staging at European Institute of Oncology; EIOpT, final postoperative staging at European Institute of Oncology; DFI, disease-free interval; rTNM, TNM classification of recurrence; FU, follow-up; –, negative; PPS, posterior paraglottic space; TL, total laryngectomy; NED, no evidence of disease; +, positive; AC, anterior commissure; type V, type V cordectomy; RT, radiotherapy; AP, arytenoid process; CT, chemotherapy; DOD, died of disease.
should be replaced by a single laser endoscopy procedure that provides reliable staging and definitive treatment in most cases and is less costly than biopsy/striping followed by radiotherapy.⁵ We acknowledge, however, that many centers cannot perform endoscopic resection, so patients referred for further treatment could be offered CO₂ surgery as an alternative to equally effective radiotherapy; those whose disease is not controlled may require radiation. Biopsy remains acceptable for bulky lesions of the anterior commissure and tumors apparently deeply infiltrating the vocal muscle without fixation of the vocal cords. In the latter cases, the treatment should be enlarged cordectomy (type IV–V). However, this procedure carries high risk of functional sequelae and should be performed only after fully informed consent.

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REFERENCES