CO₂ LASER SURGERY: A LARYNX PRESERVATION ALTERNATIVE FOR SELECTED HYPOPHARYNGEAL CARCINOMAS

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Abstract: Background. Transoral CO₂ laser surgery (TLS) has demonstrated good oncologic results and low morbidity in the treatment of selected laryngeal carcinomas, but experience in hypopharyngeal carcinomas (HC) is limited. The aim of this study was to evaluate the usefulness of TLS in the treatment of selected HC.

Methods. Twenty-eight patients with HC were treated with TLS and neck dissection. Tumors with preoperative invasion of thyroid cartilage at CT, deep growth into the cervical space or tongue base, and tumors crossing the posterior midline or involving the cervical esophagus were excluded. Postoperative radiation to the neck was administered when more than one lymph node was involved, when the metastasis diameter was greater than 2 cm, or when extranodal spread was found at the pathologic study.

Results. The sample included two T1, 16 T2, nine T3, and one T4 tumors. Stage classification was: II, 21.4%; III, 28.6%; and IV, 50%. Four-year overall and disease-specific survival rates were 43.4% and 59.4%, respectively, with 78.5% function preservation. Nine patients (32.1%) did not need a nasogastric feeding tube. The mean duration of the feeding tube in the remaining patients was 15.27 ± 27.3 days. We had two postoperative bleeding episodes that required endoscopic coagulation and three postoperative pneumonias caused by aspiration.

Conclusions. TLS is an alternative for the treatment of selected HC associated with a high larynx preservation rate. © 2004 Wiley Periodicals, Inc. Head Neck 26: 953–959, 2004

Keywords: hypopharyngeal carcinoma; CO₂ laser surgery; organ preservation

Hypopharyngeal carcinoma (HC) has a very poor prognosis even if treated with combined radical surgery and postoperative radiation.¹–⁶ Although surgery has long been the preferred approach in the management of HC, the poor prognosis suggested that combined strategies should be applied to treat these patients. After years of treatment with neoadjuvant chemotherapy, survival rates did not improve; however, chemotherapy improved the disease-free interval and changed the strategies for head and neck cancer.⁷–¹⁰ Thus, in many centers, response to chemotherapy is used as a selection criteria for organ preservation protocols.⁹ Moreover, new treatment modalities with concurrent chemoradiation have been established in the past decade in an effort to increase disease control and the percentage of larynx preservation.¹¹–¹³ A recent meta-analysis showed...
a 3% survival absolute benefit in favor of these protocols, although they did not reach statistical significance.7

Since Strong and Jako14 reported their early clinical experience with the CO2 laser in 1972, indications for laser surgery have widely extended. The technologic improvement of the CO2 laser, with a smaller spot and reduced thermal damage, has also changed the surgical treatment of upper airway malignancies. The use of the CO2 laser for transoral resection of malignant tumors is gaining support, especially in Europe, because of its minimally invasive approach and the increasing possibilities of function preservation. Experience to date is small, but it seems to indicate that the oncologic results in properly selected cases are comparable with those achieved with extralaryngeal surgery, the functional results are better, and most patients do not require a tracheotomy or a postoperative feeding tube.15–23 Furthermore, the reduced morbidity resulting from preservation of sensory pharyngeal nerve branches and the larynx framework allows older patients to be surgically treated.24,25

The aim of our study was to evaluate the survival and functional follow-up of a selected group of patients with HC treated with curative intention with endoscopic CO2 laser surgery.

PATIENTS AND METHODS

Twenty-eight patients with previously untreated HC were treated with curative intention between March 1998 and September 2001 by transoral removal of the tumor with CO2 laser by use of the technique previously described by Steiner.15 Laser surgery was followed by radical or modified neck dissection in the same intervention.

Dissections included the levels II, III, IV, and V of the neck. Radiotherapy to the primary site was not initially considered in our protocol. When definitive histologic margins were positive, a transoral surgical revision to enlarge the resection was done. However, when negative histologic margins could not be achieved and surgical enlargement was not possible because of piriform sinus obliteration, postoperative radiotherapy to the primary site was performed. Postoperative radiotherapy to the neck was performed only in the affected necks if there was more than one lymph node involved, the metastasis diameter was greater than 2 cm, or the nodes showed extracapsular spread at the pathologic study. Because of technical aspects, in those patients with bilateral positive necks, a considerable dose of radiation to the primary site may be assumed.

Tumors were classified according to the 1997 Union Internationale Contre le Cancer (UICC) staging system.26 All tumors except those with preoperative invasion of the thyroid cartilage at CT, deep growth into the cervical space or tongue base, tumors crossing the midline of the posterior commissure or posterior pharyngeal wall, and tumors involving the cervical esophagus were included. No age limit was considered for surgery.

Complications were classified either as major (requiring intensive medical treatment, blood transfusion, surgery, or intensive care unit admission) or minor (resolving spontaneously or with conventional ambulatory treatment without sequelae). Postoperative functional assessment was based on clinical parameters and transnasal flexible endoscopies during the follow-up. A minimum follow-up period of 5 months was selected to establish the status of deglutition, and the number of patients with remaining and functional larynx was counted.

We also compared our data with previous results achieved at our own institution,10 analyzing the follow-up and functional outcome of a stage-matched control group of 25 patients treated with two courses of neoadjuvant cisplatin (120 mg/m2) plus bleomycin (20 mg/m2/day 1 to 5) in continuous perfusion, followed by conventional surgery with or without postoperative radiotherapy or by radical radiotherapy alone.

Statistical Analysis. Survival and organ preservation rates were calculated from the date of onset of therapy with the product-limit estimator of Kaplan-Meier. Disease-specific survival was calculated on deaths from HC, and overall survival was calculated on deaths from all causes. Differences between laser surgery and historical patients at our institution were assessed with the log-rank test. The chi-square test, analysis of variance, and Mann-Whitney U test were used, as appropriate, to assess the correlation between different variables. All analysis were done with SPSS (version 10.0 for Windows: Chicago, IL). A p value of .05 was considered statistically significant.

RESULTS

Twenty-seven men (96.4%) and one woman (3.6%), with a mean age of 56.6 ± 7.32 years (range, 43–69 years) met the inclusion criteria. Three patients (10.7%) had arterial hypertension,
and six (21.4%) had diabetes mellitus. Laser resection was the first treatment in all patients. Tumor approach was considered adequate in 89.3% of cases and difficult in 10.7%. The postoperative tumor classification and node involvement are expressed in Table 1. Stage distribution was as follows: stage I (0%), stage II (21.4%), stage III (28.6%), and stage IV (50%).

All patients were operated on under general anesthesia and extubated immediately after laser surgery. One patient needed a preoperative tracheotomy because of the impossibility of oro/nasotracheal intubation. Postoperative prophylactic tracheotomy was performed in one patient. Nine patients (32.1%) did not need a nasogastric feeding tube in the postoperative period. The feeding tube was kept in place in the remaining patients for a mean of 15.27 ± 27.3 days (range, 2–100 days).

Six patients (21.4%) had complications related to tumor resection, which were major in three (10.7%) and minor in another three cases (10.7%). In two patients (7.1%), postoperative bleeding occurred, and endoscopic coagulation under general anesthesia was required in both. One patient was initially seen with local infection with a cutaneous fistula, which healed spontaneously. Occasional coughing during oral intake was a common symptom during the first months after surgery and improved over time. Postoperative aspiration pneumonia occurred in three patients (10.7%), in the immediate postoperative period in one and a few months later in two. Delayed pneumonias were treated with conventional antibiotic therapy in an outpatient regimen. Aspiration symptoms were correlated with tumor extension (p = .001) but not with age (p = .2). No fatal complications were seen in our sample.

Twenty-one patients (75%) underwent unilateral neck dissection (radical in seven and modified in 14). In the remaining seven patients (25%), a bilateral neck dissection was performed (bilat-

### Table 1. Characteristics of the patients according to T and N classification.

<table>
<thead>
<tr>
<th>T classification</th>
<th>N0</th>
<th>N1</th>
<th>N2b</th>
<th>N2c</th>
<th>Total no. patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td>2 (7.1)</td>
</tr>
<tr>
<td>T2</td>
<td>6</td>
<td>4</td>
<td>6</td>
<td></td>
<td>16 (57.1)</td>
</tr>
<tr>
<td>T3</td>
<td>2</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>9 (32.1)</td>
</tr>
<tr>
<td>T4</td>
<td></td>
<td></td>
<td>1</td>
<td></td>
<td>1 (3.6)</td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>6</td>
<td>12</td>
<td>2</td>
<td>28 (100)</td>
</tr>
</tbody>
</table>

Note. —, no patients were included in that group.

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![Figure 1. Disease-specific survival rate according to stage.](www.interscience.wiley.com)
eral modified in four and radical plus modified in
three). Additional postoperative radiotherapy to
the neck was administered in 12 patients (42.9%).
Four patients (14.3%) received postoperative ra-
diation to the neck and the primary site. Two of
them had radionecrosis, one healed with conserva-
tive treatment, and the other died of massive hem-
orrhage with no evidence of tumor at the necropsy.
The mean follow-up period was 40.5 ±
12.2 months (range, 16–56 months). Fourteen
deaths were registered (50%). Nine patients
(32.1%) died from HC or complications resulting
from the treatment. Five patients (17.8%) died
from other diseases. Fourteen patients were alive
without evidence of tumor at the time the study
was finished. The 4-year overall and disease-
specific survival rates were 43.4% and 59.4%,
respectively. Figure 1 shows the disease-specific
survival rate according to the stage of the disease.

Five patients had treatment fail locally, with
a probability of initial local control of 77.2%.
However, in two of them, additional laser resec-
tion was performed with curative intention, and
both are alive with no evidence of disease 15 and
7 months after treatment. Thus, the final local
control after salvage laser surgery was 87.1%. Of
the remaining three patients, one was treated
with total pharyngolaryngectomy, and two more
patients were considered palliative because of
additional distant disease. The patient who had

| Table 2. Demographic data, clinical characteristics, and follow-up of the patients with local relapse. |
|---|---|---|---|---|---|
| Age, y | Sex | pTNM | Time to relapse, mo | Site of relapse | Treatment | Follow-up |
| 50 | F | pT2N2bR+M0 | 15 | Local | CO2 laser | Alive without evidence of disease |
| 61 | M | pT2N1R–M0 | 19 | Local | CO2 laser | Alive without evidence of disease |
| 43 | M | pT3N0M0 | 4 | Locoregional | Pharyngolaryngectomy plus neck dissection | Died from tumor |
| 46 | M | pT3N2cR+M0 | 12 | Locoregional and distant | Palliative | Died from tumor |
| 53 | M | pT3N2bR+M0 | 6 | Locoregional and distant | Palliative | Died from tumor |

Abbreviations: F, female; M, male; y, years; pTNM, TNM classification after treatment.
total pharyngolaryngectomy had local and distant metastasis 8 months later and died. Figure 2 shows the probability of local control according to T classification. The characteristics and treatment of patients with local failure are expressed in Table 2.

All 14 patients without evidence of disease during the follow-up period had the larynx preserved. In 11 (78.5%), the larynx was completely functional. Three patients (21.5%) are gastros-tomy dependent. The need for postoperative gastrostomy correlated significantly with T classifications \( (p = .006) \) but not with age \( (p = .61) \). However, only four patients were older than 65 years in our sample. Table 3 expresses the percentage of organ and function preservation.

No significant differences in survival rates between laser surgery and historical patients treated with neoadjuvant chemotherapy before radical radiation or surgery were seen in our study \( (p = .41) \), but laser surgery was able to preserve 78% of the functional larynx compared with 8% in the historical group \( (p = .000) \).

**DISCUSSION**

Our preliminary results, obtained with transoral CO₂ laser microsurgery, show that selected patients with HC can be treated with CO₂ laser, with a high percentage of larynx preservation. After 4 years of follow-up, the overall and disease-specific survival rates were 43.4% and 59.4%, respectively, with almost 80% of patients with a functional larynx preserved. Furthermore, compared with the historical patients treated with neoadjuvant chemotherapy, laser surgery showed a better preservation outcome without a compromise in survival.

These results are in accordance with previous studies with the CO₂ laser. Eckel et al. reported a 92% organ preservation rate in a sample of patients with T1 and T2 squamous cell carcinoma (SCC) hypopharyngeal tumors treated by the transoral approach. The 5-year overall and disease-specific survival rates were 61.1% and 75.9%, respectively. Rudert and Hoft. reported 100% organ preservation with 5-year overall and disease-free survival of 62% and 82%, and Mori et al. reported 16 patients with T1–T2 disease treated with laser debulking before radiation, with a 5-year local control rate, disease-specific survival rate, and larynx preservation of 87.1%, 87.5%, and 93.8%, respectively. Compared with these studies, our results show lower preservation rates, probably because we included almost 40% of patients with locally advanced tumors (10 of 28), and radical radiotherapy to the primary site was not used in most of our patients. The largest study of selected patients with both small and locally advanced tumors treated with laser was published by Steiner et al., with overall survival rates of 71% for stages I and II and 47% for stages III and IV. In this study, 18% of patients with stage I–II and 81% of patients with stage III–IV received additional postoperative radiation to the neck and the primary site. In our study, the survival rates were slightly lower, perhaps because of the smaller number of patients postoperatively irradiated (57%) or perhaps as a reflection of their great experience with transoral surgery.

Our results are also consistent with previous reports achieved by external conservative surgery. Chevalier et al. reported 49 patients treated with supraglottic hemilaryngopharyngectomy plus radiation, with a 5-year survival rate of 78% in T1 and 38% in T2. Lacourreye et al. reported a 56% 5-year survival rate in 34 patients with T2 disease treated with supraccricoid hemilaryngopharyngectomy. Compared with external approaches, we were able to extend the indications for surgery, avoid the tracheotomy in most
of the patients, and even avoid the feeding tube in some of them.

A point of concern in our sample was the high incidence (25%) of distant metastasis. All of these patients had an advanced stage of disease at the initial surgery, with more than one node involved in six of them and a high percentage (57.1%) of extranodal spread. Three patients had distant metastasis without evidence of local or neck recurrence. This percentage of distant metastasis is higher than that previously seen at our institution with neoadjuvant chemotherapy\(^\text{10}\) and than that published by Steiner et al\(^\text{24}\) but is similar to the results by Rudert and Holt.\(^\text{20}\) The systemic benefits of chemotherapy administered to our historical patients could explain these differences, but not the difference from the Steiner group. Manipulation of the tumor has been hypothesized to promote spread of cancer. In this case, larger tumors should be at higher risk. We analyzed the characteristics of the tumors included in our study (one T1, three T2, and three T3), but no relationship was seen between T classification or tumor volume and distant disease. Distant metastasis only correlated with nodal involvement and advanced stages. Further studies are needed to clarify this point.

Transoral laser surgery is considered a minimally aggressive procedure compared with the external approach, with a low percentage of complications and more rapid recovery.\(^\text{31}\)

Steiner et al\(^\text{24}\) reported a reduced preoperative morbidity, with no fatal complications. In our study, the morbidity related to treatment was a little bit higher, but most patients did not need tracheotomy or gastrostomy during the postoperative period. We experienced a 7% rate of postoperative bleeding, which was managed by endoscopic coagulation. Occasional coughing during oral intake may be expected up to 50% of patients. In most of them, this is temporary and improves over time, but in a few patients, it may lead to aspiration pneumonia, and patients should be advised, especially those with larger resections. No deaths related to treatment were registered in our sample.

Another potential advantage of the CO\(_2\) laser is that it allows a good endoscopic follow-up of the remaining larynx because of the absence of edema. It makes it easy to identify local relapses and second neoplasms. In fact, two local failures (40%) were small and could be salvaged with the CO\(_2\) laser. However, we should note that in large resections the piriform sinus tends to be obliterated after surgery. In these cases, additional CT or MRI is routinely necessary for the follow-up. We are now trying to reduce the percentage of oblitative scarring by reconstructing the medial wall, when possible, with mucosa from the piriform sinus.

An interesting point of the use of the transoral approach with CO\(_2\) laser is that it has increased the possibility for partial surgery (tumors arising in both the lateral or medial surfaces of the hypopharynx can be treated, even in older patients). Organ preservation with transoral CO\(_2\) laser depends on anatomic characteristics and tumor extension and is independent of tumor chemosensitivity. Thus, patients not suitable for laser surgery may still be included in an organ preservation strategy with neoadjuvant or concurrent chemoradiation. Moreover, the use of laser surgery as a first-line treatment in patients with HC allows us to reserve radiotherapy to treat a second primary tumor if it appears. This possibility should be seriously considered, because the mean age of our patients was 56.6 ± 7.32, the prevalence of second primary tumors in head and neck carcinomas ranges between 6.3% and 22%,\(^\text{3,24,27,32–34}\) and the estimated risk is between 4% and 8.5% per year, most frequently in the upper aerodigestive tract.\(^\text{35,36}\)

The transoral approach has reduced postoperative morbidity compared with external approaches and has increased the indications for this type of surgery in the elderly. We previously reported\(^\text{25}\) that older patients, those with locally advanced tumors, and those with supraglottic and hypopharyngeal locations had a higher risk of postoperative aspiration. In this study, age was not an exclusion criterion and did not correlate with aspiration symptoms or the need for postoperative gastrostomy. However, this issue should be considered with caution, because only four patients were older than 65 and none of them were older than 70.

In summary, transoral CO\(_2\) laser microsurgery should be considered a surgical alternative to treat selected hypopharyngeal carcinomas, with a high larynx preservation rate and an easy recovery compared with external approaches. Major complications are low but may occur, and centers should be prepared to deal with them. Follow-up seems to be easy compared with other treatment modalities, and the use of postoperative radiotherapy exclusively to the neck allows us to use radiation if a second neoplasm appears. Further studies are necessary to clarify the re-
REFERENCES


