Transoral Laser Surgery for Pharyngeal and Pharyngolaryngeal Carcinomas

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Objective: To assess early oncological and functional outcomes after transoral laser surgery in patients with pharyngeal or pharyngolaryngeal squamous cell carcinoma.

Design: Inception cohort, with a median follow-up of 24 months.

Setting: Tertiary university center.

Patients: Fifty-five consecutive patients with pharyngeal or pharyngolaryngeal squamous cell carcinoma (T1, 24 patients; T2, 28 patients; and T3, 3 patients) were included. Patients had to be eligible for open functional surgery, and exposure in suspension micropharyngoscopy had to be possible.

Interventions: The pharynx and larynx were exposed with a bivalved laryngopharyngoscope, and the resection of the tumor was performed with a carbon dioxide laser coupled to a microscope. Neck dissection was performed in 43 patients. It was not attempted in the other 12 patients for the following reasons: N0 neck and severe comorbidities (n=6), microinvasive cancer (n=3), patient’s refusal (n=1), inoperable N3 disease (n=1), and rapid local recurrence (n=1). Eighteen patients (33%) received adjuvant radiotherapy: 12 for neck disease and 6 for positive resection margins.

Main Outcome Measures: Local control and overall survival at the median follow-up visit. Evaluation of complications, pain, and rehabilitation of swallowing capacity.

Results: At a median follow-up of 24 months, the local control rate was 90%, and the overall survival rate was 78%. There were 16 early postoperative complications: recurrent aspiration pneumonia (n=7); laryngeal obstruction, which required tracheotomy (n=3); severe postoperative hemorrhage (n=2); and cervical emphysema, which resolved spontaneously (n=4). Feeding tubes were necessary in 37 patients. They were removed after a median period of 7 days. The median pain score was 4 of 10 during the first postoperative week and 0 of 10 after 4 weeks. The median hospital stay was 13 days (15 days for patients with neck dissection).

Conclusions: Transoral laser surgery for pharyngeal and pharyngolaryngeal squamous cell carcinoma is a safe and acceptable therapeutic modality in selected cases. Good local control and avoidance of tracheotomy can be expected in most cases. Oral food intake is immediate, but feeding tubes are required to avoid weight loss during the postoperative period. Frequent early problems include transient postoperative bronchoinhalations and pain.

Arch Otolaryngol Head Neck Surg. 2007;133:139-144

Pharyngeal squamous cell carcinoma has a poor oncological prognosis even when it is treated with combined surgery and postoperative irradiation. Although neoadjuvant chemotherapy does not improve survival, its local response can be used as a selection criterion for combined chemoradiotherapy protocols. Despite a good organ preservation rate, concomitant chemoradiotherapy with curative intent is associated with important early and late morbidities. Long-term swallowing dysfunction is not rare, and adapted nutrition or a feeding tube is often required, impairing social life. Although functional open surgery for selected pharyngeal or pharyngolaryngeal tumors has oncological outcomes that are similar to those of more destructive surgical procedures, it requires a temporary tracheotomy and the use of a nasogastric tube for several weeks, as well as a relatively long hospital stay. For these reasons, new, less invasive techniques such as transoral...
laser surgery (TOLS) are warranted. Transoral laser surgery has become a standard treatment option for early glottic cancer, with local control similar to that of radiotherapy. When the effects on posttreatment vocal function are considered, however, a preference for radiotherapy has clearly dominated the literature, although a recent publication of excellent vocal results after TOLS for small tumors challenges this position. Nevertheless, the application of TOLS for more advanced laryngeal, epilaryngeal, and piriform sinus squamous cell carcinomas remains controversial, and experience is limited. To date, the oncological results of TOLS are encouraging and seem to be equal to those of open functional surgery in properly selected cases. Several advantages have been reported in comparison to open functional surgery: tracheotomy can be avoided in most cases; feeding tubes are not systematically required; the risk of aspiration pneumonia is reduced; and the hospital stay is shorter. Also, TOLS, in contrast to open surgery, better spares sensory pharyngeal nerve branches and thus improves the capability of protecting the airway during swallowing. Therefore, TOLS might extend the indications of functional surgery to selected elderly patients. The high incidence of occult metastases justifies elective neck dissection, which is performed 3 weeks after TOLS in most cases, to diminish the risk of postoperative pharyngocutaneous fistulas.

Our study was designed to verify the functional advantages of TOLS and to confirm the sound rationale of its oncological results. Special emphasis was given to the importance of the surgeon’s and pathologist’s assessment of the resection margins and their implication on local control.

### METHODS

Between September 1999 and August 2004, a total of 55 patients (20 women and 35 men; median age, 60 years; age range, 46 to 87 years) with pharyngeal or pharyngolaryngeal histologically confirmed squamous cell carcinomas were treated with TOLS at University Hospital, Lausanne, Switzerland. The T classification and tumor location are summarized in the Table. Fifteen patients (27%) had stage I disease; 12 patients (22%), stage II disease; 11 patients (20%), stage III disease; and 17 patients (31%), stage IV disease. Inclusion criteria were eligibility for functional open surgery and adequate exposure of the lesion in suspension micropharyngoscopy.

After endoscopic exposure in suspension micropharyngoscopy, the lesion was stained with toluidine blue for precise delineation of the tumor’s margins. Small tumors were removed in 1 piece, whereas larger tumors required piecemeal resections. In cases involving a large tumor, the resection began with a section through the tumor for visualization of its depth of infiltration. Under microscopic guidance, the depth of infiltration is easily recognizable because, unlike healthy tissue, the transmural section does not spread apart. Special emphasis is given to the surgeon’s microscopic evaluation of the resection margins because pathologic examination of the tumor margins is made difficult by laser-induced artifacts (carbonization) and piecemeal resections. No systematic frozen section was used in the present study. However, the resected specimen was oriented on a flat surface, with the location of the true margins identified for the pathologist. Fifteen patients (29%) underwent a second TOLS for positive resection margins. Neck dissection was performed in 43 patients. This second surgery was delayed in 37 patients (86%) with lateral tumor extension in the pharynx to minimize the risk of postoperative pharyngocutaneous fistulas and significant edema. Neck dissection was not performed in 12 patients for the following reasons: 6 patients had clinical N0 stage and severe comorbidities; 3 patients had clinical N0 stage and microinvasive disease; 1 patient had inoperable N3 stage disease; 1 patient had inoperable rapid local recurrence; and 1 patient with a clinical N0 neck refused the procedure. One patient with inoperable N3 stage disease did not respond to radiotherapy; the other 11 patients without neck dissection did not receive radiotherapy. Six patients had a primary tracheotomy at the time of the bilateral neck dissection. Eighteen patients (38%) underwent adjuvant radiotherapy: 12 for neck disease (more than 2 positive nodes or extracapsular spread) and 6 for positive resection margins.

Twenty-one patients (38%) with positive or doubtful resection margins received follow-up endoscopy (within 1 to 4 months after the initial TOLS) with biopsy (n=6) or a second resection (n=15). Pain (using an analog scale), bronchoinhalation, and nutritional status were prospectively followed up in 32 patients.

According to the surgeon’s judgment during the operation, resection margins were free of tumor in 48 (87%) of 55 patients. Histologic examination confirmed free margins in only 17 patients (31%) and doubtful (<2 mm) or positive resection margins in 33 patients (60%). In 5 patients, histologic evaluation of the resection margins was not possible owing to piecemeal resections. Twenty-one patients (38%) with positive or doubtful margins underwent control endoscopy either with biopsy or with a second transoral resection. In this group, results of the new histologic assessment were positive in only 4 patients (19%): 2 had a successful new transoral resection; 1 had a total laryngectomy; and 1 with a second primary tumor in the esophagus was not fit for major open surgery and underwent palliative treatment. Eventually, histologically free margins were obtained in 36 patients (66%). In 6 patients with positive or dubious margins, adjuvant radiotherapy was given. The result of the final surgical control of histologic margins did not have any significant influence on overall survival (75% vs 79%) or even on local control (88% vs 91%) after 2 years (Figure 1 and Figure 2).

Two patients had a local recurrence: one was treated with a second TOLS and the other with curative radiotherapy. Six other patients had a recurrence in the neck,
positive or doubtful resection margins (both groups together). There was no significant difference between the patients with histologically negative margins and those with invasive disease only. (n=52, patients with invasive disease only). There was no significant difference between the patients with histologically negative margins and those with positive or doubtful resection margins (P=.84). Combined indicates patients with negative resection margins and patients with positive resection margins (both groups together).

Figure 1. Overall survival according to the Kaplan-Meier method (n=52, patients with invasive disease only). There was no significant difference between the patients with histologically negative margins and those with positive or doubtful resection margins (P=.25).

Figure 2. Local disease control according to the Kaplan-Meier method (n=52, patients with invasive disease only). There was no significant difference between the patients with histologically negative margins and those with positive or doubtful resection margins (P=.38). Combined indicates patients with negative resection margins and patients with positive resection margins (both groups together).

Figure 3. Disease-free survival (n=52, patients with invasive disease only). An event was defined as local or regional recurrence, distant metastasis, and second primary tumor. There was no significant difference between the patients with histologically negative margin and those with positive or doubtful resection margins (P=.88). Combined indicates patients with negative resection margins and patients with positive resection margins (both groups together).

and 1 patient presented with distant metastasis after 6 months. Eleven patients, 4 of whom underwent postoperative radiotherapy, presented with second primary tumors: 4 in the esophagus and 7 in the oral cavity or pharynx (2 of them in the postoperatively irradiated field). Six of the latter 7 tumors were treated with a second TOLS. The 3 patients with microinvasive disease were excluded before survival and local control were calculated, because they had a different prognosis than those with invasive disease (the local control rate and the overall survival rate were 100% in this group of 3 patients). Among the N0-classified patients who did not undergo neck dissection, there were no recurrences in the neck. With a median follow-up of 24 months, the local control rate was 90% and the overall survival rate was 78% (Figure 1 and Figure 2). The locoregional control rate was 72%. Oncological event-free survival time was calculated as the time until development of a local recurrence, regional recurrence, distant metastasis, or a second primary tumor. It was 59% at 24 months, reflecting the high incidence of second metachronous primary tumors (Figure 3). There were 16 early postoperative complications (29%): 7 patients (13%) presented with a recurrent aspiration pneumonia; 3 patients (5%) required a secondary tracheotomy for laryngeal obstruction due to edema; 2 patients (4%) needed a second general anesthesia for hemorrhage (endoscopic coagulation) of severe postoperative bleeding; and 4 patients (7%) presented with cervical emphysema that resolved spontaneously.

Tracheotomy closure was possible in a median of 7 days (range, 4-41 days), but the 3 patients who underwent a secondary tracheotomy for obstruction had to retain it for a median period of 40 days (range, 4-41 days). The total median hospitalization stay (including a possible second hospitalization stay for neck dissection) was 13 days (range, 1-88 days) for all patients and 15 days (range, 4-88 days) for patients with neck dissection. Pain was a major factor during the first week, with a median score of 4 of 10 on the analog pain scale (range, 0-7 of 10), and regressed after 4 weeks to a median of 0 of 10 (range, 0-2 of 10). Despite early swallowing rehabilitation that was started on postoperative day 1 (range, 0-13) in most patients, 37 patients (67%) required additional alimentation through a feeding tube. Feeding tubes were removed after a median period of 7 days (range, 0-679 days). Patients who underwent radiotherapy required significantly longer median use of their feeding tube (24 days vs 4 days) (P=.03) (Figure 4). After 4 weeks, 16 (50%) of the 32 patients who were prospectively followed up had a normal diet, 13 patients (41%) had an adapted diet (mixed/liquid), and 3 patients (9%) were totally dependent on their feeding tube. After 8 weeks, 25 patients (78%) had a normal diet (Figure 5). Bronchoaspira-
Combined indicates patients with and without radiotherapy (both groups together).

**Table**: Comparison of feeding tube usage and diet intake between patients with and without radiotherapy.

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**COMMENT**

This study revealed an early complication rate of 29% for TOLS of pharyngeal and pharyngolaryngeal carcinomas. If minor complications that resolved spontaneously are excluded, then the rate is reduced to 22%, which is comparable to the rates reported in the literature. If minor complications that resolved spontaneously are excluded, then the rate is reduced to 22%, which is comparable to the rates reported in the literature. Our study confirms early oral realimentation in most patients. In a series of 158 patients who were operated on with open surgery in our institution, swallowing rehabilitation could be started only after a median time of 2 weeks, and the feeding tube was used for a median time of 18 days. With TOLS, additional feeding tubes were necessary in 67% of the patients (vs 100% of the patients in open surgery) and remained in place for a shorter period (7 days vs 18 days). Weight loss is avoided during the postoperative period until the patients recover sufficient oral intake. In a series reported by Oeken et al,11 percutaneous endoscopic gastrostomy was necessary in 10 of 14 patients with supraglottic carcinoma. The percutaneous endoscopic gastrostomy tube was removed in most patients after 2 to 9 months. Oeken and colleagues advocate an easier swallowing training without a nasogastric feeding tube. In our group, feeding tubes were necessary during a relatively short period for most patients; therefore, we recommend percutaneous endoscopic gastrostomy only for patients with severe swallowing dysfunction. The relatively high rate of aspiration pneumonia that was encountered may be attributable to the age composition of the group: 9 patients (18%) were older than 70 years. Elderly persons are known to have more swallowing difficulties after functional open surgery. For this reason, we strongly suggest selecting patients with a careful evaluation of their learning capabilities before surgery to assess whether the postoperative swallowing training will be successful. In our group, only one 77-year-old patient needed a total laryngectomy for functional reasons. Few studies have compared open surgery with TOLS. Cabanillas et al19 retrospectively compared the functional outcome of 52 patients treated with TOLS or functional open surgery. The temporary tracheotomy rate was lower and the period of time with nutrition through feeding tubes was shorter in the TOLS group. The incidence of complications, the hospital stay, and the swallowing capacity were not different. In our series, the hospital stay seems relatively short, with a median time of 13 days, compared with the median hospital stay of 33 days in a previous report describing patients operated on by open surgery.17

Pain is a major complaint during the first 2 postoperative weeks, especially during swallowing, but it subsides after approximately 1 month. The delayed healing of the resected area takes longer than the healing of a primary suture performed during open surgery and is the primary reason for the postoperative pain. A second major disadvantage of the technique is the difficulty of obtaining good endoscopic exposure in suspension micropharyngoscopy in some cases, especially for piriform sinus cancer. Bad exposure can increase the risk of positive tumor margins. Precisely evaluating the resection margin may be difficult because of laser-induced artifacts and piecemeal resections. The surgeon’s judgment of the resection margin under the microscope during the intervention does not seem to be sufficiently accurate. In doubtful cases, a new endoscopic evaluation with biopsies or additional laser resection should be performed 1 to 4 months after the initial resection. The orientation of the resected tumor, with clear indication of the true resection margins, helps identify the location of doubtful margins for reoperation. The latter should be performed before complete reepithelialization has occurred in order...
to identify the resected area and its margins clearly. Mucosal frozen sections may be helpful in assessing the surgical margins. However, deep-frozen sections of the musculature in the resected area can be difficult to obtain, especially in the piriform sinus. The status of the final histologic resection margins did not influence local control and overall survival in our series, most likely because of the additional resections and biopsies that were performed during the control endoscopy and because of the radiotherapy that was administered to 6 of our patients with positive or doubtful margins. These results confirm those reported by McMahon et al,21 who found no significant influence of resection margins on local control, disease-specific survival, or overall survival after laser resections were performed in the oral cavity and oropharynx. The possibility of obtaining adequate surgical margins with TOLS has been confirmed by the relatively low rate of local recurrence: 10% in this study. In a series of 129 patients with hypopharyngeal carcinomas, Steiner et al23 reported 6.1% and 6.3% local recurrence rates for stage I/II and III/IV disease, respectively. Thus, piecemeal tumor resection, which does not follow the traditional oncological principles, does not jeopardize local control. On the contrary, it is well known that lymph node metastases govern the overall oncological prognosis for these tumors. The prevalence of neck metastases at initial presentation was 53% in our study. With a 2-year regional control of 72%, the postponement of the neck dissection to 3 weeks does not compromise control of carcinoma of the neck. This has been confirmed by other investigators.9,10 Second primary tumors are also known to worsen the prognosis. Second primary malignancies were diagnosed in 11 patients (20%) in our series. This relatively high rate corresponds to a well-established epidemiologic fact in western Switzerland. Of the 7 cases located in the oral cavity and the pharynx, 6 were successfully treated with a new transoral laser approach. The high incidence of second primary cancers warrants a close follow-up with abrasive pharyngoesophageal cytology that allows diagnosis at an early stage in most cases.22 The possibility of repeating the resection over time offers an important advantage in patients with metachronous second primary cancers. Also, avoiding radiotherapy in early stages of the disease allows this therapeutic modality to be reserved for more advanced metachronous cancers in the future, should it be needed. Prophylactic radiotherapy to avoid early second primary tumors is not justified and would be ill advised considering the possibility of a second minimally invasive treatment.

The preliminary oncological results seem to be similar to those obtained by an open approach, but long-term confirmation is required. Makeiiff et al23 reported a local recurrence rate of 19.5% in a series of laryngeal rim and piriform sinus tumors treated by open surgery. Two patients died of complications, and the 5-year survival rate was 60%. In a series of 31 patients with T1/T2 piriform sinus cancer treated by open surgery, Chevalier et al24 reported a local control rate of 98%, but the survival rate was relatively low (only 52% at 3 years and 47% at 5 years). Patients are usually highly selected in studies of TOLS, which may partially explain the discrepancies of the results reported in the literature, when compared with other treatment modalities.

CONCLUSIONS

Considering the poor prognosis of pharyngeal and hypopharyngeal malignancies of the otorhinolaryngeal tumors, preservation of function through various therapeutic modalities has become a major concern for a head and neck team. Within this scope, open functional surgery has proved over the years to be as efficient as more radical surgery. Currently, TOLS represents a new surgical approach that tends to reduce the morbidity of treatments without compromising the oncological results. Compared with open surgery, locoregional control is effectively similar, and the functional results are even better, with less morbidity. The benefit is attributable primarily to the avoidance of a temporary tracheotomy and to the use of a feeding tube for a limited period of time in most of the patients. However, this technique is indicated only for a highly selected group of patients. In the future, further studies should also compare the oncological and functional results and morbidity of each organ-preservation treatment to select the optimal therapeutic approach for each situation.