Transoral Lateral Oropharyngectomy for Squamous Cell Carcinoma of the Tonsillar Region

II. An Analysis of the Incidence, Related Variables, and Consequences of Local Recurrence

Olivier Laccourreye, MD; Stéphane Hans, MD; Madeleine Ménard, MD; Dominique Garcia, MD; Daniel Brasnu, MD; F. Christopher Holsinger, MD

**Objectives:** To determine the incidence of local and regional failure, distant metastasis, and overall survival following transoral lateral oropharyngectomy (TLO) and to determine factors associated with local recurrence.

**Design:** Retrospective case series throughout 20 years; mean follow-up of 10 years.

**Setting:** Academic center.

**Patients:** A total of 166 previously untreated patients with squamous cell carcinoma of the tonsil.

**Interventions:** A total of 131 (81.9%) of the 166 patients received preoperative induction chemotherapy. Fifty-one patients (30.7%) underwent postoperative radiation therapy.

**Main Outcome Measures:** Local and regional recurrence, distant metastasis, second primary tumors, and survival.

**Results:** The 1- and 5-year Kaplan-Meier local control estimates were 91.2% and 82.1%, respectively. The 1- and 5-year Kaplan-Meier local control estimates were 98.3% and 89.0% for T1, 88.9% and 81.7% for T2, and 78.9% and 62.7% for T3 lesions, respectively \((P = .02)\). In univariate analysis, 7 variables were significantly associated with an increased risk of local failure: increasing T classification; positive margins of resection; poor clinical response to induction chemotherapy; tumor spread to the posterior pillar, posterior pharyngeal wall, and contralateral soft palate; and invasion of the junction between the tonsil and soft palate. In a logistic regression model, spread to the posterior pillar was the only variable statistically associated with local failure \((P = .02)\). The 1-, 3-, and 5-year Kaplan-Meier survival estimates were 87.9%, 67.2%, and 57.7%, respectively. The Kaplan-Meier survival estimate was significantly reduced \((P = .009)\) in patients with local failure.

**Conclusions:** Selected tonsillar squamous cell carcinoma can be managed with TLO with local control comparable to radiotherapy. Patient selection is critical and TLO is best suited for patients with anterior T1 to T2 squamous cell carcinoma of the tonsil, without posterior anatomic spread.


---

*IN 1951, PIERRE-CHARLES HUET¹ described an innovative transoral surgical resection of the oropharynx, sparing mandibular continuity, for a patient with recurrent T3 squamous cell carcinoma (SCC) of the tonsil following radiotherapy. Since this initial report, the technique has been advocated as an option for selected invasive SCC of the tonsil in the French otolaryngology literature²,³ and in the 1983 annual Proceedings of the Société Française d’Oto-Rhino-Laryngologie et de Pathologie Cervico-Faciale.⁴ In a companion article,⁵ we describe the technique, postoperative management, and long-term functional results of transoral lateral oropharyngectomy (TLO), a novel surgical technique based on Huet’s report. The current retrospective study of patients with moderately to well-differentiated invasive SCC of the tonsillar region was designed to determine the rate of local control and factors associated with local failure following TLO.*

See also page 583

**METHODS**

From 1978 to 1998, the TLO technique⁵ was performed on 191 patients with selected well-
Patients had tumoral spread to the nasopharynx, mandible, or side the tonsil and/or tonsillar fossa are given in patients. The incidence and patterns of anatomic spread out-motion in 16. Normal motion was present in the remaining 146 involved site. The tonsil was fixed in 4 patients and had reduced and its motion was compared with the contralateral noninvasive, moderately to well-differentiated SCC of the tonsillar re-

Table 1. Demographic Profile of Patients

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Patients, No. (%) (N = 166)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>140 (84.3)</td>
</tr>
<tr>
<td>Female</td>
<td>26 (15.7)</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>57</td>
</tr>
<tr>
<td>Median</td>
<td>56</td>
</tr>
<tr>
<td>Range</td>
<td>30-80</td>
</tr>
<tr>
<td>Charlson comorbidity scale score6</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>74 (44.6)</td>
</tr>
<tr>
<td>1</td>
<td>40 (24.1)</td>
</tr>
<tr>
<td>2</td>
<td>27 (16.3)</td>
</tr>
<tr>
<td>3-5</td>
<td>21 (12.7)</td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (2.4)</td>
</tr>
<tr>
<td>Tobacco intake, packs per year</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>25 (15.1)</td>
</tr>
<tr>
<td>1-20</td>
<td>23 (13.9)</td>
</tr>
<tr>
<td>21-40</td>
<td>59 (35.5)</td>
</tr>
<tr>
<td>41-60</td>
<td>39 (23.5)</td>
</tr>
<tr>
<td>61-80</td>
<td>9 (5.4)</td>
</tr>
<tr>
<td>&gt;80</td>
<td>10 (6.0)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Alcohol intake</td>
<td></td>
</tr>
<tr>
<td>0-L glass of wine per meal</td>
<td>25</td>
</tr>
<tr>
<td>1-L of wine per day</td>
<td>66</td>
</tr>
<tr>
<td>1-2-L of wine per day</td>
<td>43</td>
</tr>
<tr>
<td>&gt;2-L of wine per day</td>
<td>26</td>
</tr>
<tr>
<td>Unknown</td>
<td>6</td>
</tr>
</tbody>
</table>

Tobacco intake, packs per year

| Alcohol intake                   |                             |
| 0-L glass of wine per meal       | 25                          |
| 1-L of wine per day              | 66                          |
| 1-2-L of wine per day            | 43                          |
| >2-L of wine per day             | 26                          |
| Unknown                          | 6                           |

Table 2. TNM Classification and Staging

<table>
<thead>
<tr>
<th>Node Category</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>30</td>
<td>46</td>
<td>9</td>
<td>85</td>
</tr>
<tr>
<td>N1</td>
<td>18</td>
<td>21</td>
<td>5</td>
<td>44</td>
</tr>
<tr>
<td>N2</td>
<td>10</td>
<td>16</td>
<td>5</td>
<td>31</td>
</tr>
<tr>
<td>N3</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>60</td>
<td>87</td>
<td>19</td>
<td></td>
</tr>
</tbody>
</table>

Table 3. Anatomic Sites Involved by Tumor Spread

<table>
<thead>
<tr>
<th>Anatomic Subsite</th>
<th>Patients, No. (%) (N = 166)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Junction between tonsil and soft palate</td>
<td>63 (38.0)</td>
</tr>
<tr>
<td>Ipsilateral soft palate</td>
<td>52 (31.3)</td>
</tr>
<tr>
<td>Anterior pillar</td>
<td>47 (28.3)</td>
</tr>
<tr>
<td>Posterior pillar</td>
<td>41 (24.7)</td>
</tr>
<tr>
<td>Junction with oral tongue</td>
<td>29 (17.5)</td>
</tr>
<tr>
<td>Internal surface of mandible</td>
<td>17 (10.2)</td>
</tr>
<tr>
<td>Uvula</td>
<td>16 (9.6)</td>
</tr>
<tr>
<td>Subtonsillar region</td>
<td>14 (8.4)</td>
</tr>
<tr>
<td>Contralateral soft palate</td>
<td>9 (5.4)</td>
</tr>
<tr>
<td>Glossosulcaneous fold</td>
<td>9 (5.4)</td>
</tr>
<tr>
<td>Intermaxillary region</td>
<td>6 (3.6)</td>
</tr>
<tr>
<td>Posterior pharyngeal wall</td>
<td>5 (3.0)</td>
</tr>
<tr>
<td>Posterior floor of mouth</td>
<td>4 (2.4)</td>
</tr>
<tr>
<td>Oral (mobile) tongue</td>
<td>2 (1.2)</td>
</tr>
<tr>
<td>Mucosa overlying maxillary tuberosity</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Hard palate</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Fold between lateral floor of mouth and tongue</td>
<td>0</td>
</tr>
<tr>
<td>Gingiva</td>
<td>0</td>
</tr>
<tr>
<td>Mandibular or maxillary bone</td>
<td>0</td>
</tr>
<tr>
<td>Torus tubarius</td>
<td>0</td>
</tr>
</tbody>
</table>

According to the technique described in our companion article and practiced at our institution, the oncologic con-

The TNM classification of these patients’ tumors is presented in Table 2, according to the 1997 American Joint Com-

The TLO classification of these patients’ tumors is presented in Table 2, according to the 1997 American Joint Com-

Adjunctive surgical treatment performed with the TLO included an ipsilateral cervical lymph node dissection in 131 pa-

Preoperatively, 136 patients (81.9%) underwent induction chemotherapy. The current regimen was based on cisplatin (25 mg/m² daily) and fluorouracil (1 g/m² daily) delivered as daily continuous intravenous dosages. Platinum and fluorouracil were administered with a portable chemotherapy delivery system that provided a continuous infusion of the drugs for 24 hours. Anti-

©2005 American Medical Association. All rights reserved.
Figure 1. The impact of local control on nodal recurrence. The upper line (solid circles) represents patients with local control, whereas the lower line (open diamonds) represents those patients with local failure.

during the treatment. The course duration was 4 days. Induction chemotherapy was administered with a hiatus of 2 to 3 weeks between courses. This interval was determined solely by toxic effects, and dosages were adjusted to tolerance. Clinical examination, blood cell counts, and chemical analyses performed 15 days after each course allowed for analysis of the cumulative toxic effects according to the Eastern Cooperative Oncology Group criteria. The median number of cycles before definitive surgical resection was 3 (range, 1-11). Early in the study, 5 to 6 courses were used before surgery, but currently 2 to 3 courses are used before TLO. A workup with a complete head and neck examination, direct laryngoscopy, and computed tomography of the neck (since the late 1980s) performed by the last course allowed analysis of the clinical response to neoadjuvant chemotherapy.

The clinical responses of the primary tumor after the chemotherapy regimen were graded as complete response in 32 patients (38.2%), partial response of more than 90% in 21 patients, partial response of more than 50% but less than 90% in 35 patients, and no change in 25 patients. Four patients experienced the growth of tumor despite chemotherapy. The clinical response to the induction chemotherapy regimen led to a modification in the definitive local treatment option in 16 patients (11.7%). In other words, patients who were initially considered not amenable to this surgery, because of the extensive tumor burden at the primary site, became surgical candidates after induction chemotherapy.

Each patient’s surgical pathologic findings were reviewed. Margins of resection were positive, close, and negative in 13 patients (7.8%), 8 patients (4.8%), and 142 patients (85.5%), respectively. Two patients (1.2%) had evidence of dysplasia at the margin of resection. Among the 137 patients who received induction chemotherapy, the pathologic analysis of the specimen revealed no residual tumor (complete histologic regression) in 41 patients (30.5%), invasive SCC in 85 patients (62.5%), in situ carcinoma in 6 patients (4.4%), dysplasia in 4 patients (2.9%), and unknown in 1 patient (0.7%). Furthermore, there was a statistical correlation between complete clinical response and histologic regression in patients who received an induction chemotherapy regimen ($\chi^2$ test; $P = .01$).

For all 131 patients undergoing neck dissection, including 116 with and 15 without chemotherapy, histologic evidence of metastasis existed in 67 patients (51.1%). Extracapsular spread was identified in 40 patients (30.5%), fibrosis but no viable tumor in 8 patients (6.1%), and no disease in 52 patients (39.7%). Among the 85 patients with disease classified clinically as N0, 51 underwent a neck dissection and 8 (15.7%) had histologic evidence of regional spread.

Postoperative radiation therapy was performed in 51 patients (30.7%) in our series. Indications for postoperative radiation therapy varied over time: positive margins of resection in 13 patients; close margins, 1 patient; lymphovascular invasion, 4 patients; perineural invasion, 1 patient; and multiple nodal metastasis or extracapsular spread, 29 patients. The average dose delivered was 60 Gy to the oropharynx (median dose, 60 Gy; range, 45-75 Gy) and 55 Gy to the neck (median dose, 55 Gy; range, 0-70 Gy).

Follow-up data were collected at periodic visits to our department. Follow-up time was the time from the first appointment in our department for index SCC of the tonsil until the date of last contact or death. Except for a single patient who was lost to follow-up at 3 months, median follow-up time was 10 years (range, 33 months to 18 years). An IBM computer (Armonk, NY) with StatView and SAS statistical software (SAS Institute Inc, Cary, NC) was used for storing and calculating statistical data. This report was designed to (1) determine the rate (overall and Kaplan-Meier) of local control following TLO; (2) search for potential statistical relationships with the following variables: age, sex, tobacco intake, alcohol intake, site of origin of the tumor (tonsil, anterior pillar, or posterior pillar), other sites involved by tumor, T stage, motion of the tonsil, clinical response to induction chemotherapy, complete histologic response, margins of resection, and postoperative radiation therapy to the remaining oropharynx (yes vs no and dosage); and (3) determine the impact of local recurrence on regional recurrence, the development of distant metastasis, and survival. Survival, local control, regional control, and distant metastasis estimated were calculated using the Kaplan-Meier product-limit method with the log-rank (Mantel-Cox) test method for statistical comparison. The nonparametric Mann-Whitney U test and the $\chi^2$ test were used for quantitative and qualitative variable analysis, respectively. If there were 5 or fewer patients in a group, the 2-tailed Fisher exact test was used. Multivariate analysis was performed by iterative logistical regression modeling. Statistical significance was set at the $P = .05$ level.

### LOCAL CONTROL AND FACTORS ASSOCIATED WITH LOCAL RECURRENCE

The 1-, 3-, and 5-year Kaplan-Meier local control estimates were 91.2%, 82.1%, and 82.1%, respectively. Overall, in our series, 27 patients (16.3%) experienced local failure. Local recurrence was not observed after the 28th postoperative month. When grouped by T classification, 1-, 3-, and 5-year Kaplan-Meier estimates of local control were 98.3%, 89.0%, and 89.0% for T1, 88.9%, 81.7%, and 81.7% for T2, and 78.9%, 62.7%, and 62.7% for T3 lesions (Figure 1; $P = .02$). By univariate analysis, as depicted in Table 4, 7 variables were significantly associated with an increased risk of local failure. Those variables included increasing T classification, positive margins of resection, poor clinical response to induction chemotherapy, and the following sites involved by the tumor: posterior pillar, posterior pharyngeal wall, contralateral soft palate, and invasion of the junction between the tonsil and soft palate. For the 16 patients whose surgical approach was changed from a transmandibular approach to the TLO after chemotherapy, no significant difference occurred in rates of local recurrence ($\chi^2$ test; $P = .35$). In a logistic regression model, spread beyond the
posterior pillar was independently associated with local failure (relative risk, 1.9; 95% confidence interval, 1.28-16.27; \( P = .02 \)). Although not statistically significant, complete clinical response to chemotherapy was marginally associated with local control in this model (\( P = .06 \)).

**CONSEQUENCES OF LOCAL RECURRENTCE**

Local recurrence had a significant impact on the nodal failure (\( P < .001 \)) (Figure 2) but not on the development of distant metastasis (\( P = .23 \)). The rates of nodal control for patients with local recurrence were 85.0%, 56.9%, and 42.9% at 1, 3, and 5 years, respectively, compared with 91.6%, 86.7%, and 86.7% at 1, 3, and 5 years for patients with local control.

**Table 4. Factors Associated With Local Recurrence**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Local Recurrence, %</th>
<th>Yes</th>
<th>No</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>NA NA NA</td>
<td>.45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>Female 28.5 71.5</td>
<td>.31</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Male 16.8 83.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tobacco use, packs per year</td>
<td>16.0 84.0</td>
<td>.96</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>13.6 86.4</td>
<td>.45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Site of origin</td>
<td>16.3 83.7</td>
<td>.76</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tonsil or tonsillar fossa</td>
<td>14.5 85.5</td>
<td>.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior pillar</td>
<td>23.1 76.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posterior pillar</td>
<td>0 100</td>
<td>.003</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T classification</td>
<td>T1 11 89</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>T2 19.1 81.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>T3 58 42</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motion of the tonsil</td>
<td>Normal 16 84</td>
<td>.43</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Abnormal 25 75</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Fixed 0 100</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical response</td>
<td>Progression 75.0 25.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No response (&lt;50%) 21.7 78.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Partial response &gt;50% 28.6 71.4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Partial response &gt;90% 9.5 90.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Complete clinical response 5.8 94.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histologic response</td>
<td>Squamous cell carcinoma 21.4 78.6</td>
<td>.15</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dysplasia 20.0 80.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>In situ carcinoma 0.0 100.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Complete histologic response 4.9 95.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Margins of resection</td>
<td>Negative 12.7 87.3</td>
<td>.003</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Close 25.0 75.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Positive 53.8 46.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dysplasia 0.0 100.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative RT to the oropharynx</td>
<td>Yes 17 83</td>
<td>.82</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No 16 84</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dosage trend</td>
<td>NA NA NA</td>
<td>.91</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(continued)

Salvage treatment for local recurrence was as follows: 9 underwent combined surgery and postoperative radiation therapy, 7 underwent surgery alone, and 2 received only radiotherapy. Nine patients received no further treatment. Thirteen (48%) of these patients with local failure were successfully salvaged. Twelve patients experienced concurrent local and regional failure, whereas a single patient developed local, regional, and distant disease.

The 1-, 3-, and 5-year Kaplan-Meier survival estimates were 87.9%, 67.2%, and 57.7%, respectively, for the whole series. The 1-, 3-, and 5-year Kaplan-Meier survival estimates were 89.1%, 73.2%, and 62.4%, respectively, in pa-
In patients with moderately to well-differentiated invasive SCC of the tonsillar region, the conservative treatment modality currently used worldwide is radiation therapy. \cite{Larson1983, Galati2002} Local control for these patients treated with radiation therapy varies widely by T classification, as depicted in Table 5, with a weighted average local control estimate of 87.5% for tumors classified as T1, 77.8% for tumors classified as T2, and 54.7% for tumors classified as T3. Among the published reports, the best results in terms of local control with radiation therapy alone were reported by Gwozdz et al,\cite{Gwozdz2005} using the innovative concomitant boost technique, which resulted in a 100%, 96%, and 76% local control rate for tumors classified as T1, T2, and T3, respectively. However, in this series,\cite{Gwozdz2005} all patients developed grade 4 mucositis, and 5 patients developed persistent chronic grade 3 ulcerations. Ten patients required hospitalization during or following radiation therapy, and 6 patients developed late complications (chronic dysphagia in 5 and mandibular osteosarcoma in the radiated field in 1).

As early as 1983, Larson et al,\cite{Larson1983} in a 10-year retrospective review of radiotherapy in cancer of the oral cavity and oropharynx, noted that half of patients with cancer of the tonsil had grade 4 sequelae (including mandibular osteoradionecrosis for some). This study also found that the dose of radiation was the main factor that appeared to have a correlation with adverse effects. Although new radiotherapy technologies, such as intensity-modulated radiation therapy, may cause fewer adverse effects, this study and others confirm that the radiation therapy for SCC of the tonsillar fossa is not without certain morbidity, especially in terms of longer-term xerostomia and dysphagia.

In a companion article,\cite{Watkinson2005} we reported the functional results achieved with a conservative surgical alternative to radiation therapy. Called the TLO, this operation appears to be extremely safe, with a low incidence of postoperative complications.\cite{Watkinson2005} This TLO approach uses a transoral approach to resect the whole tonsillar region (tonsillar fossa, anterior pillar, and posterior pillar) together with the underlying constrictor muscles.

Huet first described this technique in 1951. In his case report, Huet successfully treated a patient with a recurrent moderately to well-differentiated invasive T3 NO M0 SCC of the tonsil following radiation and achieved local control with 3 years of follow-up. Since this initial case report, a few reports mentioned this technique in the French otolaryngology literature,\cite{Watkinson2005, Huet1951} and this technique was mentioned as an option for selected invasive SCC of the tonsil in the 1983 annual textbook of the French Society of Otorhinolaryngology Head and Neck Surgery.\cite{Watkinson2005} However, to our knowledge, no report with a large series of patients with lengthy follow-up has documented rates of survival and local control following TLO.

In our department, the following clinical features are considered major contraindications for the TLO approach in patients with moderately to well-differentiated invasive SCC of the tonsillar region: trismus, fixation of the tonsil to the lateral oropharyngeal wall, and mandibular invasion. Each of these 3 features suggests infiltration of the tumor into the parapharyngeal space (ie, along the surgical plane of dissection). Also, invasion of the nasopharynx, glossopharyngeal fold, base of tongue, vallecula, pharyngoepiglottic fold, and/or pyriform sinus and poor exposure due to individual patient anatomic or dental considerations are considered major oncologic contraindications. For these patients, proper visualization and resection of the tumor cannot be guaranteed through the TLO approach alone. Therefore, most patients with T1 to T2 lesions and few patients with selected T3 lesions are included in the current retrospective series (Table 2). Of interest, it would appear that N staging does not preclude the use of the TLO procedure, since in our series, 51 (30.7%) of the 166 patients had an advanced stage (III-IV) tumor.

The TLO is substantially different than a radical tonsillectomy. A complete resection of the tonsil is performed with large and wide resection of the adjacent muscle and mucosa. The TLO must be distinguished from the previously reported transoral approaches to resect tonsillar carcinoma. Galati et al\cite{Galati2002} relied on “the superior constrictor as the deep margin (if it is not involved) and a 1- to 2-cm circumferential margin of normal-appearing mucosa.” Watkinson et al\cite{Watkinson2005} reported a piecemeal resection “carried out along with a cuff of pharyngeal musculature and the excision extended to include parts of the soft palate, lateral pharyngeal wall or tongue base as appropriate.” Because the TLO approach allows for en bloc resection of both mucosa and muscle through a noninvaded parapharyngeal space, we believe that this technique is oncologically superior to the surgical conservative approaches previously described.
For all patients (T1-T3 tumors) in our surgical series, the 1- and 5-year Kaplan-Meier estimates of local control were 91.2% and 82.1%, respectively. When grouped by T classification, the 1- and 5-year Kaplan-Meier estimates of local control were 98.3% and 89.0% for T1, 88.9% and 81.7% for T2, and 78.9% and 62.7% for T3 lesions, respectively (Figure 1; \( P = .02 \)). Preoperative induction chemotherapy had been administered in 137 patients (81.9%), whereas 51 (30.7%) received postoperative radiotherapy.

In comparison, the local control in 89% of our patients with T1 lesions at 5 years is better than the weighted average of 87% but firmly between the results from the largest and most recent studies: 83% from the University of Florida\(^1^8\) and 94% achieved at M. D. Anderson Cancer Center\(^1^3\) and Vancouver Cancer Center\(^1^7\), using conventional fractionation. Similarly, local control for T2 lesions of 87.5% at 5 years is also better than the weighted average of 77.5% and again between 78% from the University of Virginia\(^1^4\) and 81% from the University of Florida’s most recent series.\(^1^6\)

Seven variables were significantly associated with an increased risk for local failure in our series by univariate analysis (Table 4). These variables included increasing T classification, positive margins of resection, poor clinical response to induction chemotherapy, and the following sites involved by the tumor: posterior pillar, posterior pharyngeal wall, contralateral soft palate, and invasion of the junction between the tonsil and soft palate. In a logistic regression model, spread to the posterior pillar was independently associated with local failure (\( P = .02 \)). Although this was not statistically significant, patients with a complete clinical response to chemotherapy (\( P = .06 \)) also had marginally associated improved local control in this model. Neither the postoperative radiation therapy nor the dosage locally administered postoperatively appeared to play a significant statistical role in the logistic regression model. At first glance it might be tempting to conclude that the use of induction chemotherapy, surgery, and postoperative radiation therapy in the current series was overtreatment; however, 52 patients (38.2%) had a complete clinical response or more than a 90% reduction of the tumor volume following the induction chemotherapy regimen, and 35 patients (25.7%) had more than a 50% reduction in the tumor volume after the induction chemotherapy regimen.

The clinical response to the induction chemotherapy regimen led to a modification in the definitive treatment option in 16 (11.7%) of 136 patients. These patients were considered initially not to be amenable to TLO due to extensive tumor at the primary site. Following induction chemotherapy, the remobilization of the tonsil permitted the use of the TLO in lieu of an initially planned transmandibular composite (“jaw-neck”) resection in 4 patients. Although intriguing, this observation requires further evaluation, since no direct comparison or con-

<table>
<thead>
<tr>
<th>Source, ( y ) (Institution)</th>
<th>No. of Patients</th>
<th>Radiotherapy Dosage, Gy</th>
<th>Local Control, %</th>
<th>Posttreatment, ( y )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garrett et al,(^1^1) 1983 (Princess Margaret, Toronto, Ontario)</td>
<td></td>
<td>50-66</td>
<td>87</td>
<td>5</td>
</tr>
<tr>
<td>T1</td>
<td>47</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>161</td>
<td></td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>164</td>
<td></td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Lusinchi et al,(^1^2) 1989 (Gustave-Roussy, Villejuif, France)</td>
<td></td>
<td>71</td>
<td>88</td>
<td>2</td>
</tr>
<tr>
<td>T1</td>
<td>48</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>145</td>
<td></td>
<td>79</td>
<td></td>
</tr>
<tr>
<td>Wong et al,(^1^3) 1989 (M. D. Anderson, Houston, Tex)</td>
<td></td>
<td>64</td>
<td>94</td>
<td>5</td>
</tr>
<tr>
<td>T1</td>
<td>23</td>
<td>76.8</td>
<td>87</td>
<td>5</td>
</tr>
<tr>
<td>T2</td>
<td>59</td>
<td></td>
<td>79</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>67</td>
<td></td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>Moose et al,(^1^4) 1995 (University of Virginia, Charlottesville)</td>
<td></td>
<td>61-63</td>
<td>83</td>
<td>5</td>
</tr>
<tr>
<td>T1</td>
<td>30</td>
<td></td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>23</td>
<td></td>
<td>25.7</td>
<td></td>
</tr>
<tr>
<td>Felt et al,(^1^5) 1996 (University of Florida, Gainesville)</td>
<td></td>
<td>Concomitant boost, 69-72</td>
<td>100</td>
<td>5</td>
</tr>
<tr>
<td>T1</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>27</td>
<td></td>
<td>96.3</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>33</td>
<td></td>
<td>75.8</td>
<td></td>
</tr>
<tr>
<td>Jackson et al,(^1^7) 1999 (Vancouver Cancer Center, Vancouver, British Columbia)</td>
<td></td>
<td>50-66</td>
<td>94</td>
<td>5</td>
</tr>
<tr>
<td>T1</td>
<td>36</td>
<td></td>
<td>79</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>80</td>
<td></td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>53</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mendenhall et al,(^1^8) 2000 (University of Florida)</td>
<td></td>
<td>65.6 (mean range, 47-80 )</td>
<td>83</td>
<td>5</td>
</tr>
<tr>
<td>T1</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>156</td>
<td></td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>126</td>
<td></td>
<td>74</td>
<td></td>
</tr>
</tbody>
</table>

©2005 American Medical Association. All rights reserved.
trol group was possible in this retrospective review. Finally, pathologic analysis of the specimen revealed no residual tumor (complete histologic regression) in 41 patients (30.1%).

The idea of induction chemotherapy for oropharyngeal carcinoma is not new. Vokes et al.22 reported an intensive regimen with induction chemotherapy that consisted of carboplatin (area under the curve = 2.25) and paclitaxel (135 mg/m²) administered weekly for 6 doses followed by concomitant chemoradiation. Eighty-seven percent of patients achieved a tumor response to the induction therapy with a complete response in 35%. There were no deaths. Overall 3-year progression-free survival was 80%, and less than 10% of patients have been observed to have distant tumor recurrence. Shin et al.23 have reported promising phase 2 results in patients with locally advanced SCC of the head and neck, using a paclitaxel-based induction chemotherapy regimen and achieving similar response rates (81% overall, with complete response in 31% of patients).

Although induction chemotherapy has been shown to decrease the incidence of distant metastasis, indicating activity against systemic micrometastatic disease,25-27 its impact on local control has never been conclusively demonstrated. We present data herein to suggest that response to chemotherapy was correlated with local control. Since the study is a retrospective, nonrandomized review of a single institution’s experience, the clinical benefit of the induction chemotherapy protocol in this setting cannot be determined and thus requires further evaluation.

Finally, postoperative radiation therapy was not used systematically in this series. Only 30.7% of patients received external beam therapy, with average doses of 60 and 55 Gy delivered to the oropharynx and the ipsilateral aspect of the neck, respectively. The main indication for postoperative radiation therapy in our series was positive margins of resection and the pathologic nodal status of the neck after the completion of an associated dissection of the ipsilateral aspect of the neck (multiple nodes, extracapsular spread of disease, and lymphovascular invasion). Since patients with head and neck cancer28,29 are at high risk of second primary tumors, the use of radiotherapy, although effective, eliminates the opportunity to use this modality for larger, more aggressive, or more morbid metachronous lesions. When a surgical approach to head and neck cancer can be used with minimal morbidity and equal oncologic efficacy, the use of definitive chemoradiation can be reserved for subsequent disease.

Local recurrence following TLO has a significant impact on overall survival: 1-year and 5-year Kaplan-Meier survival estimates were 89.1% and 62.4%, respectively, in patients without local recurrence and 81.5% and 33.3%, respectively, in patients with local recurrence (Figure 1; P = .009). Local recurrence also had a significant impact on the nodal failure (Figure 2; P < .001) but not on the development of distant metastasis. The rates of nodal failure for patients with local recurrence were 85.0%, 56.9%, and 42.9% at 1, 3, and 5 years, respectively, compared with 91.6%, 86.7%, and 86.7% at 1, 3, and 5 years, respectively, for patients with local control.

Nevertheless, more patients in our series died of metachronous primary tumors and intercurrent disease (23% and 27%, respectively) than from distant metastasis, nodal recurrence, or local recurrence (14.6%, 9.4%, and 14.6%, respectively). The Kaplan-Meier survival estimates at 1 and 5 years were 87.9% and 57.7%, respectively, keeping with other published reports. For instance, Gwozdz et al.26 reported a 60% overall 5-year survival, despite high local control rates. In a thorough review of the literature by Parsons et al.,30 which provided benchmarks of evidence-based counseling of patients with SCC of the oropharynx, overall 5-year survival was 43% for patients with tonsillar carcinoma.

The current retrospective series suggests that appropriately selected invasive SCC of the tonsillar region can be managed with induction chemotherapy and TLO with local control highly comparable to radiotherapy. Patient selection is critical, and TLO is best suited for patients with anterior T1 to T2 SCC of the tonsil, without posterior anatomic spread. This approach avoids the late complications related to the use of radiation therapy or chemoradiation and reserves these therapeutic options for the subsequent management of metachronous primary tumors. As such, this technique should be integrated into the conservative armamentarium of the head and neck surgeon.

In this retrospective series, the impact of induction chemotherapy on oncologic outcomes remains uncertain. A total of 30.1% of patients treated with a platinum-based regimen experienced a complete histologic response. Although the role of induction chemotherapy in intermediate-stage larynx cancer has been reported,31,32 the long-term durability of clinical responses to cisplatin and fluorouracil in tonsillar carcinoma has not to our knowledge been previously described. It is possible that selective surgery alone would achieve the same results. Therefore, further study is warranted to determine both the efficacy of the TLO alone and the significance of induction chemotherapy in this patient population.
Acknowledgment: We are grateful to the following surgeons for allowing us to use their medical and operative records: Paul André, MD, Phillippe Bessede, MD, Patrice Beutter, MD, Bernard Bicacbe, MD, Serge Bobin, MD, Michel Bodard, MD, Daniel Brasnou, MD, Régis Cauchois, MD, Eric Chabardes, MD, Alain Fabre, MD, Dominique Fernandez, MD, Stéphane Hans, MD, François Janot, MD, Véronique Jouffre, MD, Jean Lacau St. Guily, MD, Henri Laccourreye, MD, Ollivier Laccourreye, MD, Madeleine Ménard, MD, Philippe Naudo, MD, Pascal Pichancourt, MD, and Pierre Tison, MD.

REFERENCES


