Salvage Surgery After Failure of Nonsurgical Therapy for Carcinoma of the Larynx and Hypopharynx

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Background: For larynx preservation, radiotherapy is gaining popularity for primary treatment of laryngeal and hypopharyngeal cancer, reserving surgery for salvage.

Objective: To analyze the outcome of salvage surgery after failure of primary radiotherapy.

Design: Nine-year retrospective outcome analysis.

Setting: University referral center.

Patients: Fifty-four patients with squamous cell carcinoma of the larynx (n=39) or hypopharynx (n=15).

Results: For laryngeal cancer, mean interval from radiation to detection of recurrence was 14.5 months (range, 2-66 months). Twenty-three patients (59%) presented with a more advanced tumor stage after radiation than at the initial evaluation. Total laryngectomy was needed in 36 patients (92%). Disease-specific 5-year survival rate was 63%. Survival of patients with small recurrent tumors was statistically significantly better than those with advanced tumors (P=.004). For hypopharyngeal cancer, mean interval from radiation to detection of the recurrence was 10.6 months (range, 3-40 months). Total laryngopharyngectomy was needed in 8 of 9 patients with local recurrence; neck dissection, in 6 patients with regional recurrence. Disease-specific 5-year survival rate was only 20%. Recurrent tumor and node stages did not influence the outcome. Patients with regional recurrences did no better than those with local ones.

Conclusions: Salvage surgery in laryngeal cancer achieves good results, especially for small recurrences. Because of tumor progression, larynx preservation is seldom possible at the time of salvage. Salvage surgery in hypopharyngeal cancer shows poor survival regardless of tumor stage and despite radical surgical procedures, and can be recommended only for carefully selected patients.


RESULTS

SCC OF THE LARYNX

Of 109 patients with an SCC of the larynx undergoing primary radiation therapy, a local recurrence developed in 44 (40%), and 39 of these patients (37 male; mean age, 62.6 years) underwent salvage surgery. The initial tumors were located in the glottis in 66 patients (61%) and in advanced laryngeal and hypopharyngeal tumors because of the larynx preservation. Although organ preservation by means of combined chemotherapy and radiotherapy is gaining more and more popularity, few studies have addressed the clinical course of patients undergoing salvage surgery after radiation therapy failure. The aim of our study was to review the results of surgical salvage after radiation therapy failure in SCC of the larynx and hypopharynx and to determine its indications for the future.
PATIENTS AND METHODS

From January 1, 1990, through December 31, 1998, a total of 165 previously untreated patients with an SCC of the larynx or hypopharynx underwent full-course radiation therapy and chemotherapy for large or advanced tumors at the University Hospital Zurich, Zurich, Switzerland. Pretreatment workup routinely included panendoscopy and computed tomographic scans. Only patients with potentially resectable initial tumors were entered into the study. Radiotherapy was always administered in a curative intent. Patients treated in a palliative regimen were excluded. All patients underwent planning computed tomography before the onset of the radiation therapy, and the fields were calculated using a computer-guided system. Small (T1 and T2) glottic tumors were radiated in a narrow-field technique including only the larynx. The daily fraction ranged from 1.8 to 2.0 Gy, the weekly dose was 12 Gy, and the total dose ranged from 70 to 72 Gy. Large (T3 and T4) glottic, all supraglottic, and all hypopharyngeal carcinomas were radiated with single doses of 1.2-1.8, or 2.0 Gy; a weekly dose of 12 Gy; and a total dose ranging from 70 to 74 Gy for the primary site. In the adjuvant situation, 50 Gy of radiotherapy was administered to the cervical lymph nodes bilaterally, and involved nodes received a boost up to a total dose of 66 to 70 Gy. All large tumors were additionally treated with a concomitant chemotherapy with cisplatin in week 1 and 5 of the radiotherapy. Posttreatment survey consisted of 6 weekly clinical controls followed by endoscopy in any case of suspicion of recurrence. Surgical salvage after radiation therapy failure had to be performed in 54 patients (33%) with locoregional recurrence. These patients represent the database of this study. The mean follow-up after salvage surgery was 32.9 months (range, 3-95 months) for the patients with laryngeal cancer and 18.8 months (range, 0-91 months) for the patients with hypopharyngeal cancer. According to the literature, successful salvage surgery was defined as no evidence of disease (NED) for 2 years postoperatively.

Table 1. Clinical Stages of Initial Laryngeal Tumors*

<table>
<thead>
<tr>
<th>Tumor Stage</th>
<th>cN0</th>
<th>cN1</th>
<th>cN2</th>
</tr>
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<tbody>
<tr>
<td>cT1</td>
<td>13</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>cT2</td>
<td>14</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>cT3</td>
<td>7</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>cT4</td>
<td>0</td>
<td>0</td>
<td>1</td>
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</tbody>
</table>

*Staging system is described in Sobin and Wittekind. Data are given as number of patients (n = 39).

Table 2. Recurrent Stages Laryngeal Tumors*

<table>
<thead>
<tr>
<th>Tumor Stage</th>
<th>rN0</th>
<th>rN1</th>
<th>rN2</th>
</tr>
</thead>
<tbody>
<tr>
<td>rT1</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>rT2</td>
<td>9</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>rT3</td>
<td>11</td>
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<td>1</td>
</tr>
<tr>
<td>rT4</td>
<td>15</td>
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<td>1</td>
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*Staging System is described in Sobin and Wittekind. Data are given as number of patients (n = 39).

The mean disease-specific 5-year survival rate after salvage surgery for all 39 patients was 63% (Figure 1). No statistically significant difference in survival between patients with initial glottic and supraglottic carcinomas was found. A tendency toward a better outcome of small initial (cT1 and cT2) vs advanced initial (cT3 and cT4) tumors was found (Figure 2), although this difference was statistically not significant (P = .05). There was a statistically significant (P = .004) better survival for the group of patients with low recurrent tumor stages (rT1 and rT2) than for those with advanced stages (rT3 and rT4) (Figure 3). Successful salvage surgery (NED >2 years) was achieved in 21 patients (54%).

The overall mortality rate was 49%, with 9 patients (23%) dying of local recurrences, 3 (8%) of lymph node recurrences, 3 (8%) of second primary cancers, 2 (5%) of distant metastasis, and 2 (5%) of other non–tumor-related diseases.

SCC OF THE HYPOPHARYNX

Of 56 patients undergoing primary radiation therapy for an SCC of the hypopharynx, a locoregional recurrence developed in 33 (59%), but only 15 (13 male and 2 female; mean age, 57.4 years) underwent salvage surgery. All initial primary tumors involved the piriform sinus, and there were no tumors involving only the posterior pharyngeal wall or the postcricoid area. The other patients were not treated further or were referred to palliative chemotherapy because of tumors that were no longer surgically resectable due to tumor progression during and/or after radiotherapy.

The initial TNM stages (Table 3) disclosed 13 patients (87%) already presenting with advanced disease (cT3-cT4 and cN2-cN3).
Nine patients (60%) experienced a local recurrence in the hypopharynx and 6 patients (40%), a regional lymph node relapse. The mean interval from radiation to detection of the recurrence was 10.6 months (range, 3-40 months).

The surgical salvage procedure included total laryngopharyngectomy in 8 patients and partial laryngopharyngectomy in 1 patient. These procedures were always combined with a neck dissection of the levels II to IV on the side of the primary tumor. Six patients underwent salvage by means of neck dissection alone.

The pharyngeal defect was reconstructed using a myocutaneous pectoralis major flap in 4 patients, a free jejunal graft in 4 patients, and a gastric pull-up procedure in 1 patient.

Postoperative complications were seen in 6 patients (40%), consisting of carotid ruptures after carotid reconstruction in 2 patients (causing 1 death), pharyngocutaneous fistula in 1 patient, stomal stenosis in 2 patients, and peripheral deep venous thrombosis in 1 patient.

The mean disease-specific 5-year survival rate after salvage surgery for all 15 patients was 20% (Figure 4).

There was no significant difference ($P = .40$) between the groups of patients with initial cN0 or cN1 and initial cN2 or cN3 disease (Figure 5). Interestingly, patients with lymph node recurrence did no better than those with local hypopharyngeal recurrence.

Successful salvage surgery (NED >2 years) was possible in only 2 patients (13%). The overall mortality rate was 87%, with 5 patients (33%) dying of local recurrences; 5 patients (33%), lymph node recurrences; 1 patient (6%), second primary cancer; and 2 patients (13%), other non–tumor-related diseases.
The treatment of laryngeal and hypopharyngeal cancer by means of primary radiotherapy with the preservation of the functional integrity of the laryngopharyngeal complex is gaining more and more popularity. This concept implies that surgery may be required for salvage after radiation therapy fails. Although it is of paramount importance to obtain information on the outcome of these patients, few studies provide detailed data. This study does not focus on the indication for radiotherapy or the reasons for its failure. The aim of our study was to evaluate the outcome of our patients after salvage surgery.

In our group of patients undergoing salvage surgery after radiation therapy failure in laryngeal SCC, a 5-year disease-specific survival rate of 63% was achieved. This result appears favorable in comparison with that of Parsons et al2 or McLaughlin et al,3 who report 5-year survival rates of 30% and 41%, respectively. In contrast, Champell and Goepfert4 and Nibu et al5 published 5-year survival rates of 64% and 86%, respectively, but only T1 and T2 disease were included in their studies. In agreement with other authors,6 survival in our series was influenced mainly by the recurrent and not the initial tumor stage. Although there was a considerably large subgroup of patients with small initial tumors that could not be controlled by radiotherapy, partial laryngectomy as a salvage procedure was seldom possible because of tumor progression ending in more advanced recurrent tumor stages. This fact has been underlined by previous studies7,8 and should always be mentioned to the patients before radiotherapy.

The morbidity of salvage laryngectomy in our series was acceptable, with a rather low rate of pharyngocutaneous fistulas compared with that of the literature,7,9,10 although the radiation dose ranged from 70 to 74 Gy.

Despite the performance of a neck dissection in addition to salvage laryngectomy, and although histologically free margins were achieved in all patients, the main cause of death was locoregional recurrence. It seems that the growth pattern of the cancer changes during radiotherapy to a more dissolute one,11 and in some cases even radical surgical procedures fail to eliminate all tumor cells.3,7,12,13

Our group of patients with hypopharyngeal carcinoma presented in very advanced initial tumor stages. Although all of them could have been treated surgically, primary radiotherapy was chosen to prevent the sacrifice of the larynx. As in laryngeal cancer, the recurrent tumor stages were shown to be even more advanced, excluding the possibility of surgical salvage in most patients. Those patients who still were candidates for salvage surgery showed a very poor outcome (5-year survival rate, 20%), despite radical surgery with removal of the complete laryngopharyngeal complex in almost all patients. The main cause of death was locoregional recurrence. These results agree strongly with those of previous studies by Davidson et al8 and Jones,14 who reported 5-year survival rates of 18% and 23%, respectively.

**CONCLUSIONS**

In laryngeal and hypopharyngeal cancer, most recurrent tumors after failure of radiotherapy appear in more advanced stages than at the initial evaluation. This tumor progression prevents partial laryngectomy in almost all cases of laryngeal carcinoma and any salvage surgery in many cases of hypopharyngeal carcinoma. Patients have to know that they cannot expect salvage by means

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**COMMENT**

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of surgery in any case of radiation failure, and that sal-
vage surgery means loss of the larynx.

In our experience, salvage surgery in laryngeal SCC
achieves good survival with a low morbidity rate and
therefore can be recommended. Salvage surgery in hy-
popharyngeal SCC has a very low success rate and should
only be performed in carefully selected cases.

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