Recurrence Rates After Selective Neck Dissection in the N0 Irradiated Neck

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Objectives: To define patterns of subclinical metastases in irradiated N0 necks with recurrent or persistent primary site disease and to determine the regional control rate when selective neck dissection (SND) is used in this setting.

Patients and Intervention: Individuals included were previously treated for head and neck squamous cell carcinoma with primary radiation therapy or chemoradiotherapy. All had recurrent or persistent disease at the primary site, with no clinical or radiographic evidence of nodal disease. The patients underwent surgical treatment of the primary site along with site-specific SND and were required to undergo at least 1 year of follow-up. Subsequent recurrence at the primary site disqualified the patient from further evaluation.

Main Outcome Measure: Regional tumor control.

Results: Forty-three patients meeting the inclusion criteria underwent 59 SNDs (levels dissected: I-IV [n = 22], II-IV [n = 34], and I-III [n = 3]). Sixteen specimens were positive for nodal disease. The charts of 26 patients, who underwent a total of 35 SNDs, were available for review after 1 year (none of the patients involved died of disease in the neck). There were no neck recurrences (mean follow-up, 25 months; median, 21 months). All patients with more than 2 occult nodal metastases experienced primary site recurrence or distant metastases.

Conclusions: In this small cohort, SND in previously irradiated patients with recurrent primary disease but clinically negative necks has resulted in excellent tumor control in the neck. The usual patterns of nodal spread do not appear to be significantly altered with primary site recurrence after radiation therapy. The presence of more than 2 positive nodes in the neck specimen correlates with poor prognosis.

PATIENTS AND METHODS

A retrospective chart review was performed from January 1997 to May 2000 at the Department of Otolaryngology and Communicative Disorders, The Cleveland Clinic Foundation. Forty-three individuals who met the inclusion criteria had been previously treated for head and neck squamous cell carcinoma with daily or twice-daily radiation therapy or with chemoradiation therapy (concurrent irradiation with 3 courses of fluorouracil and cisplatin). Radiation doses to neck fields ranged from 5000 to 6400 rads (standard practice at our institution) to treat at-risk clinically negative necks with 5200-5400 rads and clinically positive necks with 6200-6400 rads coned to 7000-7200 rads over clinically positive nodes. The stages of neck disease before primary therapy were as follows: N0 (n=37), N1 (n=5), and N2c (n=1). All patients had either recurrent or persistent disease at the primary site (33 patients) or a metastatic second primary tumor (8 patients). The patients had no clinical or radiographic evidence of nodal disease and underwent surgical treatment of the primary lesion along with site-specific SND. All patients with previously N-positive necks were assessed with both high-contrast computed tomography and clinical examination. Fifty-nine SNDs were performed (levels dissected: 1-IV [n=22], II-IV [n=34], and I-III [n=3]). Individuals who received a “planned” salvage neck dissection after radiotherapy or chemoradiation therapy were excluded from this study.

A chart review of the cases in which these criteria were met documented initial tumor site and stage, the location of active primary site disease, and the elapsed interval between the completion of radiation therapy and surgical salvage. Surgical procedures, perioperative complications, and pathologic findings were reviewed. Pathologic analysis included documentation of number and anatomical location of occult nodal metastases, as well as the presence of nodal extracapsular spread.

The patients were required to have at least 1 year of follow-up examinations for evaluation of regional control after SND. Recurrence at the primary site after surgical intervention disqualified the patient from further observation for long-term tumor control in the neck. In addition to documentation of the status of the neck, primary site control and metastatic disease were recorded.

RESULTS

Forty-three patients underwent resection of their recurrent primary site tumors accompanied by unilateral or bilateral elective SND. The nodal levels that were dissected depended on the primary tumor location. The mean interval between the completion of radiotherapy and salvage surgery was 13 months, with a median interval of 7 months. In addition to 59 SNDs, surgical procedures included 26 total and 5 partial laryngectomies as well as 3 regional and 16 free-flap reconstructions. Twelve patients (28%) and 16 SND specimens (28%) harbored occult nodal disease. Two specimens (17%) had pathologic evidence of extracapsular tumor spread. The neck dissection specimens contained 0 positive nodes in 47 patients, 1 positive node in 5 patients, 2 positive nodes in 1 patient, and 3 positive nodes in 2 patients. Four patients had more than 3 positive nodes; 4, 5, 6, and 7 tumor-containing lymph nodes were each present in 1 patient. The frequency of cervical metastases nodes was not higher in the 6 individuals whose disease was initially staged either N1 or N2 (1 of 6 patients, or 17%).

Regional metastatic rates varied with primary site, with supraglottic and hypopharyngeal cancers spreading most readily to the neck (Table 1). Despite advanced primary site lesions requiring 15 total laryngectomies and 2 supraglottic laryngectomies in 17 patients, glottic cancers metastasized to the neck in only 2 of 24 specimens. All nodal metastases were found in levels II-IV. Seven specimens revealed tumor in levels III and IV, without involving level II. Supraglottic, advanced glottic, and hypopharyngeal lesions metastasized to both sides of the neck.

Surgical complications included 2 pharyngocutaneous fistulas, 2 hematomas, and 2 infections. One patient suffered from exposed bone as a result of partial flap breakdown, and another experienced actinomycosis of the mandible after a mandibulotomy was performed for surgical access. There were no perioperative deaths.

Seventeen patients were not followed up for a full year. Five patients died of uncontrolled local disease, 5 of distant metastatic disease, and 3 of unrelated causes. There was an insufficient time interval after surgery in 2 cases, and 2 patients were unavailable for follow-up. No patients died of disease in the neck.

Twenty-six patients who underwent 35 SNDs completed more than 1 year of follow-up. The mean follow-up period was 25 months, and the median was 21 months. Of these 26 patients, 3 had a recurrence at the primary site and 6 developed distant metastatic disease. No patients had a recurrence in the neck (Table 2).

Patient survival correlated with the number of occult cervical metastases. Despite small patient numbers, a statistically significant difference in survival was seen between those patients with more than 2 positive lymph nodes and those with 2 or fewer regional metastases (P= .006, Fisher exact test comparison). All patients in the group with 2 or more positive nodes died of either primary site recurrence or distant metastatic disease. Twelve (38%) of 32 patients without evidence of tumor in SND specimens suffered similar outcomes. Disease recurrence in 1 (17%) of 6 patients with 1 or 2 nodal metastases was not significantly different from those with no pathologic findings (P=.64).

COMMENT

The most important findings of this study are as follows:
- Selective neck dissection provides excellent regional control in the previously irradiated, clinically N0 neck.
The incidence and patterns of subclinical neck metastases are not significantly altered after radiation therapy. The finding of more than 2 occult positive nodes correlates with poor prognosis.

The utility of SND has been demonstrated in various clinical settings. Its use in the elective management of the previously untreated, clinically N0 neck is supported by many authors. In such a setting, site-specific neck dissections can result in regional control and patient survival rates comparable to those of more extensive neck dissections. In addition, SND has been effective for surgical salvage after radiation therapy or chemoradiotherapy. Stenson et al using planned SND after chemoradiotherapy for N2 to N3 disease, demonstrated low neck recurrence rates (1 of 69 patients and 1 of 52 patients, respectively) and low complication rates. They concluded that SND, rather than a more extensive neck procedure, was therapeutically appropriate in this setting. Boyd et al, reviewing salvage neck dissection after radiotherapy alone, also endorsed the use of SND.

Despite many clinical studies of elective SND, its oncologic efficacy in the previously irradiated N0 neck with recurrent or persistent primary site disease is not well established. As a result, few authors have recommended its use in this setting. Goodwin and Chandler reviewed the pathologic findings in elective radical neck dissections in 22 patients who had received prior neck irradiation for N0 or N1 disease. Four (18%) of 22 specimens demonstrated neck metastases and 9 of 12 patients were without evidence of disease at 2 years. Nodal echelons involved, site and status of primary disease, and neck control rates were not addressed. Because of the low yield of subclinical disease and increased morbidity associated with radical neck dissection after radiation therapy, the authors recommended observation over elective neck dissection.

In our study, 26 patients underwent 36 site-specific SNDs and experienced no neck recurrences (mean follow-up, 25 months). This finding supports the ongoing use of SND to manage clinically negative necks in this specific patient population.

Table 1. Subclinical Metastases by Primary Site

<table>
<thead>
<tr>
<th>Anatomical Site</th>
<th>No. of Patients</th>
<th>No. (%) of Patients With Positive Nodal Disease</th>
<th>No. of SNDs</th>
<th>No. (%) of Positive SNDs</th>
<th>Levels Involved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral cavity</td>
<td>8</td>
<td>2 (25)</td>
<td>9</td>
<td>2 (22)</td>
<td>II, III</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>7</td>
<td>0</td>
<td>8</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>4</td>
<td>2 (50)</td>
<td>5</td>
<td>3 (60)†</td>
<td>III, IV</td>
</tr>
<tr>
<td>Supraglottis</td>
<td>7</td>
<td>6 (86)</td>
<td>13</td>
<td>9 (69)</td>
<td>II, IV, VI</td>
</tr>
<tr>
<td>Glottis</td>
<td>17</td>
<td>2 (12)</td>
<td>24</td>
<td>2 (8)</td>
<td>II, IV, VI</td>
</tr>
<tr>
<td>Total</td>
<td>43</td>
<td>12 (27)</td>
<td>59</td>
<td>16 (28)†</td>
<td>II-IV, VI</td>
</tr>
</tbody>
</table>

*SND indicates selective neck dissection; ellipses, not applicable.
†One patient in the hypopharyngeal group had ipsilateral modified radical neck dissection with occult metastasis (overall incidence unchanged, 28%).

Table 2. Patient Outcomes by Primary Site

<table>
<thead>
<tr>
<th>Anatomical Site</th>
<th>No. of Patients</th>
<th>No. of SNDs</th>
<th>Death From Primary Recurrence</th>
<th>Death From Distant Metastasis</th>
<th>Neck Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral cavity</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Oropharynx</td>
<td>3</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Hypopharynx</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Supraglottis</td>
<td>5</td>
<td>9</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Glottis</td>
<td>12</td>
<td>16</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
<td>35</td>
<td>4</td>
<td>6</td>
<td>0</td>
</tr>
</tbody>
</table>

*Mean follow-up, 25 months (median, 21 months). SND indicates selective neck dissection.

Table 3. Outcomes Based on Number of Occult-Positive Nodes

<table>
<thead>
<tr>
<th>No. of Positive Nodes</th>
<th>No. of Patients</th>
<th>Death From Uncontrolled Primary Tumor</th>
<th>Death From Distant Metastasis</th>
<th>No Disease at 1-yr Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>31</td>
<td>4</td>
<td>8</td>
<td>19*</td>
</tr>
<tr>
<td>≤2</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>6*</td>
</tr>
<tr>
<td>&gt;2</td>
<td>6</td>
<td>3</td>
<td>3</td>
<td>0*</td>
</tr>
</tbody>
</table>

*Pairwise Fisher exact test: 0 vs ≤2, P = .64; 0 vs >2, P = .007; and ≤2 vs <2, P = .02.

- The incidence and patterns of subclinical neck metastases are not significantly altered after radiation therapy.
- The finding of more than 2 occult positive nodes correlates with poor prognosis.

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The incidence and patterns of occult regional tumor spread in previously irradiated necks have not been well defined. While the short-term disturbance of lymphatic flow is clearly demonstrated by the edema that has been observed at the primary site in many patients who
undergo irradiation of the head and neck, to our knowledge no studies to date have demonstrated permanent alterations in the patterns of lymphatic metastases after therapeutic radiation doses. Despite previous radiotherapy, the patients in our study experienced a frequency and an anatomical distribution of occult neck metastases similar to those reported in previous articles on untreated N0 necks. The 28% incidence of subclinical neck tumor is similar to the generally reported rate of 30% in the nonirradiated neck and supports the use of elective neck dissection in the specific patient population in this study. The nodal levels involved as a function of primary site closely resemble the results of Shah,17 the absence of neck failures in undissected, previously irradiated levels excludes occult regional metastases beyond the range of the SNDs performed.

The most important factor in the prognosis of squamous carcinomas of the head and neck is the status of the cervical lymph nodes.2,8,15 The presence of clinical neck metastases decreases overall survival by at least half, and the number of positive nodes relates to the frequency of distant metastases.20 In nonirradiated N0 necks, Alvi and Johnson21 found that occult cervical metastases also carried grave prognostic significance, with disease recurrence occurring in 60% of patients with histologically positive nodes, compared with 18% of those with negative nodes. Viani et al.22,23 reporting on glottic and oropharyngeal recurrence after radiotherapy, analyzed the specimens from neck dissections that were performed for clinically positive disease. In these cases, regional lymphatic metastases corresponded with a dismal survival rate: 16% for glottic cancer and 19% for oropharyngeal cancer. However, the authors reported that neither the number of positive lymphatic metastases nor the presence of extracapsular spread affected patient outcomes.

Occult neck metastases in the previously irradiated neck appear to carry different prognostic significance. In contrast to Alvi and Johnson’s21 findings in nonirradiated necks, the presence of 1 or 2 subclinical neck metastases did not result in a significantly worse outcome than did pathologically negative necks (P = .64). However, all patients with more than 2 histologically positive nodes had disease recurrence. Although patient numbers are small, the difference in survival was statistically significant (Table 3).

Alvi and Johnson21 observed a 49% incidence of extracapsular tumor spread in occult neck metastases. The results in our patient population differ considerably, with only 2 (17%) of 12 patients having extracapsular spread. This contrast may indicate a possible mitigating effect of radiation-induced lymphatic changes and, if so, may suggest an increased likelihood of regional control in these patients with nodal foci removed by elective neck dissection. This possibility may be reflected in the similar outcomes observed between patients with 2 or fewer occult metastases and those with clinically negative necks.

Selective neck dissection in previously irradiated patients with recurrent primary disease but clinically negative necks results in excellent regional tumor control. The usual patterns of nodal spread are not significantly altered with primary site recurrence after radiation therapy. The presence of more than 2 positive nodes in the neck specimen correlates with poor prognosis. The findings and conclusions of this study must be tempered by its small patient numbers, mean follow-up of 25 months, and varied primary sites of recurrent disease. Despite these limitations, we believe that these preliminary data justify continued study of SND in this setting.

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REFERENCES