SELECTIVE NECK DISSECTION FOLLOWING ADJUVANT THERAPY FOR ADVANCED HEAD AND NECK CANCER

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Abstract: Background. In the past, surgeons believed that in order to eradicate regional disease, a radical or modified radical neck dissection was necessary. An evolution in surgical principles and the popularization of primary chemoradiation has raised the questions regarding the role of neck dissection and the extent of neck dissection following therapy. The aim of this study was to determine the efficacy of selective neck dissection (SND) for patients with N2 or N3 disease following treatment with primary radiation therapy or chemoradiation.

Methods. A retrospective review of 58 patients with stage III or IV head and neck squamous cell carcinoma was conducted. The primary sites included base of tongue (n = 15), hypopharynx (n = 12), tonsil (n = 16), larynx (n = 11), and unknown primary (n = 4). Definitive treatment consisted of either concomitant chemoradiation (67.2%) or external beam radiation therapy (32.8%). In the monotherapy group, all patients received a total curative dose of 66 to 72 Gy in once-daily fractions of 180 to 200 cGy. The combined chemoradiation group received a similar radiation schedule and a 4-day continuous infusion of cisplatin (20 mg/m²/day) and 5-fluorouracil (1000 mg/m²/day). A planned SND of levels II to IV was performed on all the patients 3 to 6 weeks after completion of definitive medical therapy.

Results. Seventy neck dissections were performed on 58 patients with advanced neck disease following radiation or chemoradiation. The median time of follow-up was 34 months (range, 9–71 months) following the neck dissection. Pathologically, 22.4% (13/58) of the patients had viable tumor cells identified in the neck dissection specimen. Seventy-two percent of the patients are currently alive, and 28% died as a result of distant disease, local or regional recurrence, or other causes. Of patients who died from distant disease, 11% had pathological evidence of residual tumor cells identified in the neck dissection specimen. Of patients who died from local or regional disease, 50% had pathological evidence of residual tumor cells identified in the neck dissection specimen.

Conclusion. The rate of regional recurrence following SND is similar to reported rates following modified/radical neck dissection. This suggests that SND provides an appropriate surgical option for advanced neck disease in select patients following adjuvant therapy. ©2008 Wiley Periodicals, Inc. Head Neck 31: 183–188, 2009

Keywords: selective neck dissection; postchemoradiation neck dissection; postradiation neck dissection; head and neck cancer

It has been estimated that about 500,000 cases of head and neck cancer are diagnosed each year worldwide and the majority of patients present with advanced disease. In patients with N2 and N3 disease, regional recurrence is a common reason for treatment failure. In recent years, combined chemoradiation has become more commonly used for patients with advanced-stage disease. Multiple groups have demonstrated that combined chemoradiation improves overall survival
and locoregional control when compared with radiation alone. Even more recently, induction chemotherapy in addition to concomitant chemoradiation has been shown to further improve the pathologic response seen in neck dissection specimens over that of chemoradiation alone.

Concurrent with these advances in medical therapy there has been a gradual shift in the philosophy of surgical management of advanced head and neck cancer. In the past, surgeons strongly believed that in order to eradicate regional disease, a radical dissection of lymphatic as well as nonlymphatic structures was necessary. Recently, the surgical principles have evolved focusing on the regional lymphatics which have clinical evidence of gross disease or a high probability of occult disease, while sparing uninvolved nonlymphatic structures. Prior studies have demonstrated the efficacy of the selective neck dissection (SND) in patients with clinically positive neck disease. Recently, there has been an emergence of data which suggest that there is a role for SND in patients with locoregionally advanced disease after primary treatment with radiation or chemoradiation.

The purpose of this study was to determine the efficacy of SND after primary radiation or chemoradiation in patients with advanced squamous cell carcinoma of the upper aerodigestive tract (N2, N3). We hypothesized that a well-planned SND is adequate at controlling neck disease after primary radiation or chemoradiation, while reducing the surgical morbidity associated with more extensive neck dissections.

**PATIENTS AND METHODS**

A retrospective analysis was performed on outcomes in patients with advanced cervical nodal metastases who received primary radiation therapy or chemoradiation followed by a staged SND. The Mount Sinai Head and Neck Cancer Database was queried for patients with advanced head and neck cancer of the upper aerodigestive tract (N2, N3) who were treated between August 1, 2000, and October 31, 2005. Patients were excluded from the study if they had evidence of deep muscle invasion or distant metastasis based on PET/CT, or total body CT with liver function studies. All patients were treated with either preoperative external beam radiation or concomitant chemoradiation and a planned postoperative SND. Only patients with histologically confirmed squamous cell carcinoma of the head and neck were included in the study.

Patients in this series were analyzed for the site of primary disease, TNM stage, the efficacy of SND in terms of locoregional recurrence, overall survival, and the pathological status of the lymph nodes following planned neck dissection. To estimate survival rates for patients with different levels of nodal disease (N2 vs N3) and treatment (combined chemoradiation vs radiation alone), the Kaplan–Meier method was used with the aid of XLSTAT software (Addinsoft). The survival rates were then compared using the log rank test, with the level of statistical significance set to \( p < .05 \). The protocol for this study was reviewed and approved by the Institutional Review Board of Mount Sinai Hospital, New York, NY.

**RESULTS**

Fifty-eight patients with advanced head and neck cancer were included in this study. The study population included 49 men (85%) and 9 women (15%). The median age was 64 years (range, 39–89 years). Primary sites of the tumor included base of tongue (15/58, 26%), hypopharynx (12/58, 21%), tonsil (16/58, 28%), larynx (11/58, 19%), and unknown primary (4/58, 6%). All patients had neck metastasis and were with either stage III or IV disease. Patients were staged prior to radiation or chemoradiation as N2a (31/58, 53%), N2b (10/58, 17%), N2c (12/58, 22%), or N3 (5/58, 8%).

Definitive treatment consisted of either concomitant chemoradiation (36/58, 62.1%) or external beam radiation therapy (22/58, 37.9%). In the monotherapy group, all patients received a total curative dose of 66 to 72 Gy in once-daily fractions of 180 to 200 cGy. The chemoradiation group received a similar radiation schedule and a 4-day continuous infusion of cisplatin (20 mg/m²/day) and 5-fluorouracil (1000 mg/m²/day). The infusions were given on the first and fourth weeks of radiotherapy. A planned SND encompassing levels II to IV was performed on all the patients 3 to 6 weeks after completion of definitive medical therapy. CT scans of the neck were not routinely obtained prior to the staged neck dissection.

Fifty-eight patients were included in the study; however, the analysis was done on a total of 70 SNDs to incorporate the 12 patients with bilateral disease. Following neck dissection, the median time of follow-up was 34 months (range, 9–71 months). At the time of analysis, 72% (42/58) of...
the patients were alive and 28% (16/58) of the patients had expired. Causes of death included distant disease (15.5%, 9/58), regional recurrence (5.2%, 3/58), local recurrence (1.7%, 1/58), or other causes such as cerebrovascular accident, myocardial infarction, or another malignancy (5.2%, 3/58). The overall survival and disease-specific survival at 34 months was 84.1% and 86.7%, respectively. In patients treated with radiation alone, the local, regional, and distant control rates were 100%, 95.5%, and 72.3%, respectively. In patients treated with combined chemoradiation, the local, regional, and distant control rates were 97.2%, 94.4%, and 91.7%, respectively. The overall control rate in patients treated with radiation alone and chemoradiation was 68.2% and 83.3%, respectively. Of patients who died from distant disease, 1 patient had viable tumor cells identified in the planned neck dissection specimen based on histological analysis (Table 1). There was no correlation between the cause of death and primary site, method of therapy, stage, or the presence of viable disease in the neck dissection. Of patients who died from local or regional disease, 2 patients (50%) had viable tumor cells identified in the planned neck dissection specimen and there was no correlation between the cause of death and primary site, method of therapy, stage, or the presence of viable disease in the neck dissection.

On pathological examination of the planned neck dissection specimens, 22.4% (13/58) of the patients had evidence of residual tumor. Five patients with viable disease in the neck dissection specimen had been treated with XRT alone, whereas the remaining 8 had been treated with combined chemoradiation.

Kaplan–Maier analysis was used to estimate survival rates in terms of treatment and nodal stage (Figures 1 and 2). The mean survival time of patients receiving combined chemoradiation (36/58, 62.1%) was 60 months (95% CI = 53–68), whereas that for patients receiving only radiation (22/58, 37.9%) was 46 months (95% CI = 39–53). When the treatment groups were compared using the log rank test, the difference in survival rates was not statistically significant (p = .06).

In terms of nodal stage, the mean survival time of patients with N2 nodal disease (n = 42)

### Table 1. Patients who died from distant metastasis.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Stage</th>
<th>Viable disease</th>
<th>Treatment</th>
<th>Primary site</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>T2N2</td>
<td>No</td>
<td>XRT</td>
<td>Hypopharynx</td>
</tr>
<tr>
<td>2</td>
<td>T3N2</td>
<td>No</td>
<td>CXRT</td>
<td>Larynx</td>
</tr>
<tr>
<td>3</td>
<td>T2N2</td>
<td>Yes</td>
<td>XRT</td>
<td>Tonsil</td>
</tr>
<tr>
<td>4</td>
<td>T3N2</td>
<td>No</td>
<td>CXRT</td>
<td>BOT</td>
</tr>
<tr>
<td>5</td>
<td>T2N2</td>
<td>No</td>
<td>XRT</td>
<td>BOT</td>
</tr>
<tr>
<td>6</td>
<td>T2N2</td>
<td>No</td>
<td>CXRT</td>
<td>Tonsil</td>
</tr>
<tr>
<td>7</td>
<td>T2N2</td>
<td>No</td>
<td>CXRT</td>
<td>BOT</td>
</tr>
<tr>
<td>8</td>
<td>T2N2</td>
<td>No</td>
<td>CXRT</td>
<td>Tonsil</td>
</tr>
</tbody>
</table>

Note: This table demonstrates that only 1 patient with viable disease at the time of neck dissection progressed to develop distant metastasis.
receiving combined chemoradiation (24/42, 57.1%) was 64 months (95% CI = 54–73), whereas that for patients receiving only radiation (18/42, 42.9%) was 47 months (95% CI = 39–54). The difference in survival rates was not statistically significant (p = .06). Regarding patients with N3 nodal disease (n = 16), the mean survival time of those receiving combined chemoradiation (13/16, 81%) was 49 months (95% CI = 40–59), whereas that for patients receiving only radiation (3/16, 19%) was 33 months. Again, the difference in survival rates was not statistically significant (p = .14).

DISCUSSION

In addition to chemotherapy and radiation, cervical lymphadenectomy has been a critical component in the treatment of regional metastasis in head and neck squamous cell carcinoma. Combined chemoradiation is often successful at eradicating low-volume nodal disease. However, the role of the neck dissection as a planned procedure for high-volume disease (N2, N3) has become controversial. In patients with bulky nodal disease, many experts advocate neck dissection as a salvage procedure in the event of a partial clinical response to chemoradiation.11–16 Proponents of this approach argue that patients with a complete clinical response have excellent locoregional control and should not be exposed to the surgical morbidity associated with a neck dissection. However, other investigators advocate performing a planned neck dissection regardless of clinical response, arguing that a complete clinical response to chemoradiation does not necessarily imply the absence of residual nodal disease, and that the morbidity of a future recurrence in the neck merits a planned dissection for all patients with advanced disease.17–21 Additionally, it has been shown that patients who present with a recurrence in the neck commonly present with unresectable disease and the patients that do have a resectable recurrence eventually go on to develop locoregional and distant disease.

The use of physical exam and imaging to determine which patients may benefit from a neck dissection represents another area of controversy. Some have suggested that a thorough examination is adequate, whereas others have advocated either CT or co-registered PET/CT scan to provide insight into which patients harbor disease following combined therapy. Tan et al22 compared neck examination, CT, and PET/CT to clinically evaluate for residual neck disease after definitive chemoradiotherapy. In this study, planned neck dissection was performed in 33 necks and was positive for residual neck node disease in 5 necks. A delayed neck dissection was performed in 5 necks and was positive in 3 necks. Tan et al found that the positive predictive value was low for all 3 methods of assessment and that the addition of PET did not significantly improve the negative predictive value or positive predictive value of CT and the clinical examination. Gourin et al found similar limitations with PET/CT and in a smaller study involving 17 patients found that PET/CT was not sufficiently specific or sensitive to reliably predict the need for posttreatment neck dissection. Finally, a review of the literature related to this topic by Pellitteri et al23 states that although PET/CT hold promise for predicting patients who would benefit from neck dissection following combined therapy for advanced disease, such techniques remain unproven. Therefore, until such time when we are able to reliably predict which patients will benefit from a neck dissection, it is important to limit the morbidity without compromising the regional control or disease-specific survival.

In the past, the radical and modified radical neck dissections were the gold standard for management of advanced neck disease following radiation therapy. The prevailing belief was that patients with advanced disease who underwent radiation therapy required extensive removal of all lymph node basins and nonlymphatic structures to effectively prevent locoregional recurrence. It is clear that this aggressive approach can often render patients dysfunctional from sacrifice of the nonlymphatic structures.1 Additionally, patients who have undergone external beam radiation have extensive fibrosis of the neck, problems with wound healing, and spinal accessory nerve dysfunction much more commonly after a neck dissection. Furthermore, studies have shown that radical neck dissections are correlated with worse quality-of-life scores.24

Support for conservative neck dissection comes from studies showing that head and neck cancer exhibits predictable patterns of lymph node metastasis.10,25–27 In a series of 25 patients with planned postradiotherapy neck dissections for advanced head and neck cancer, Boyd et al26 showed that only 1 patient had tumor outside of levels II to IV, concluding that an SND may have been appropriate in these patients. Robbins et al13,28 have argued that chemoradiation would
sterilize occult nodal disease in the lower-risk lymph node levels and posttreatment SND could then target residual disease in high-risk lymph node levels. In fact, in a series of 56 patients with advanced head and neck cancer, Stenson et al showed that although SND excised a lower quantity of nodes than radical dissections, the pathological nodal yield was not significantly different. This seems to further bolster the concept that when an SND appropriately targets high-risk levels, it has comparable efficacy to modified and radical neck dissection in controlling neck disease. This efficacy, combined with reduced surgical morbidity, makes SND a viable and attractive option for patients with advanced head and neck cancer after primary radiation or chemoradiation.

At Mount Sinai Hospital, our management plan usually includes a postradiation or postchemoradiation SND for patients with bulky nodal disease (N2, N3) regardless of the clinical response to medical therapy. Our data as well as that of others have shown that the incidence of pathological viable disease is 25% to 40%; therefore, we feel that this justifies the use of staged neck dissection at the completion of medical treatment. This study demonstrates pathological evidence of viable tumor in 22.4% (13/58) of patients after undergoing primary radiation or chemoradiation. We believe that this percentage of persistent viable tumor following treatment supports the need to perform staged SNDs in patients after completion of their radiation or chemoradiation.

Our findings suggest that the use of SND in patients with bulky nodal disease is oncologically appropriate and that performing SND after adjuvant therapy does not adversely affect the regional or distant control when compared with historical controls. The failure to provide a control group of patients treated with radical or modified radical neck dissection represents a shortcoming of the study. Instead, we have referred to historical controls to compare local, regional, and distant control rates. Sewall et al examined the incidence of regional and distant control as well as overall survival in patients treated with staged SNDs and compared these outcomes with patients who had comprehensive neck dissections. They found that regional control, distant control, and overall survival were unchanged whether the patient underwent an SND or a comprehensive neck dissection. In another study by Narayan et al, regional and distant control after radiation therapy and a modified radical or radical neck dissection approximated 83%. Additionally, Gupta and Agarwal showed that regional and distant control after chemoradiation and a radical or modified radical neck dissection approximated 88%. In this study of SNDs after adjuvant therapy with radiation or chemoradiation, the local, regional, and distant control rates were comparable to that of historical controls. It is our contention that performing SND after primary medical treatment results in similar locoregional and distant control rates as the classic radical and modified radical neck dissections.

Our study group represents a heterogeneous group of patients treated with either radiation therapy or combined chemoradiation. We have chosen to include both groups because there is no significant difference between the groups with regard to outcome. In terms of survival rates, this study shows no statistically significant difference between the mean survival of patients receiving combined chemoradiation (60 months) or only radiation (46 months, \( p = .06 \)). When the patients are compared in terms of nodal disease, N2 patients who received combined chemoradiation (64 months) did not survive significantly longer than those who received only radiation (47 months, \( p = .06 \)). N3 patients also did not survive significantly longer whether they received combined chemoradiation or radiation (\( p = .14 \)), although the number of patients with N3 disease receiving only radiation in this study was exceptionally low (\( n = 3 \)). The study size represents a shortcoming of the study and future studies would need to enroll more patients with advanced disease to more accurately discern any differences in survival. However, this study addresses a question that has not been fully addressed, namely, is SND appropriate for patients with advanced disease following adjuvant therapy?

**CONCLUSION**

A staged SND represents an alternative to the classic radical or modified radical neck dissections for the management of N2, and possibly N3 disease after primary medical treatment.

**REFERENCES**


