Effectiveness of Superselective and Selective Neck Dissection for Advanced Nodal Metastases After Chemoradiation

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Objective: To determine the efficacy of selective and superselective neck dissection for patients with bulky or residual nodal metastasis treated with concomitant intra-arterial cisplatin and radiotherapy.

Design: Prospective study.

Setting: University of Tennessee, Memphis.

Patients: A total of 240 patients with stage III or IV head and neck squamous cell carcinoma.

Interventions: Treatment with cisplatin, 150 mg/m² intra-arterially, and sodium thiosulfate, 9 g/m² intravenously, weekly for 4 weeks; and radiotherapy, 2 Gy per fraction per day, 5 times weekly, for a total of 68 to 74 Gy over 6 to 7 weeks.

Main Outcome Measures: Regional control, distant metastases, and overall survival for patients undergoing radical or modified radical neck dissection (n=12), selective neck dissection (n=65), and superselective neck dissection (levels II-III only) (n=7).

Results: Among the total group of 240 patients, 106 neck dissections were performed on 84 patients who had bulky nodal disease. With a median follow-up of 38 months (range, 12-96 months), regional failure occurred in 11 (4.6%) of 240 patients: 2 (17%) of the 12 who had modified radical neck dissection, 3 (5%) of the 65 who had selective neck dissection, none of the 7 patients who had superselective neck dissection, and 6 (4%) of the 156 who had no neck dissection. The rates of overall survival and distant metastases were not significantly different among the 3 neck dissection subsets.

Conclusion: Selective and superselective neck dissection, which spare function and minimize morbidity, are viable therapeutic alternatives for patients with residual disease confined to 1 level after intra-arterial chemoradiation treatment, and possibly for other chemoradiation protocols.


During the past decade, chemoradiation has become a more common approach for treating head and neck cancer because of the growing body of evidence that it has higher efficacy than radiation alone. Our group has shown that advanced head and neck cancer treated with intra-arterial cisplatin chemotherapy and concurrent radiotherapy (RADPLAT) produced a complete response rate of 90.5% at the primary site and 70.7% in the regional lymph nodes. We have shown in patients treated with RADPLAT that the subsequent use of neck dissection in patients with bulky nodal disease (N2 and N3) resulted in an ultimate regional control rate of 91%. This supports other reports that there continues to be a need to perform an ancillary neck dissection for associated nodal metastases under certain circumstances and that the procedure is effective in helping to achieve regional disease control.

The paradigm shift to using chemoradiation over radiotherapy alone or primary surgery brings into question the need to perform the conventional types of neck dissection procedures. Because the majority of lymph node disease is likely to be sterilized by the potent combination of chemotherapy and radiotherapy, it may be feasible to use ancillary neck dissection procedures that are less extensive and result in less morbidity.

We hypothesize that most patients who have persistent nodal metastases after chemoradiation have limited positive disease that is confined to levels of high risk. We also believe that lymph nodes occupying neck levels that had no pretreatment evidence of disease involvement, and that remain clinically negative after che-
moradiation, rarely harbor occult metastases. Under this circumstance, it is unnecessary to remove such low-risk neck levels when performing neck dissection for patients with residual clinically positive disease confined to 2 or fewer neck levels. Such a neck dissection procedure is classified as a selective neck dissection (SND), although, in many situations, the term superselective neck dissection (SSND) would be more appropriate. This study was performed to test these hypotheses.

### METHODS

Between January 1, 1993, and December 31, 2000, 240 patients with advanced head and neck cancer (stages III and IV) were treated consecutively with the RADPLAT protocol at the University of Tennessee, Memphis. All patients were entered into an institutional review board–approved study, and their outcome data were collected prospectively. All patients had biopsy-proved squamous cell carcinoma. Sites of tumors were as follows: oropharynx, 106 patients; hypopharynx, 43 patients; larynx, 32 patients; oral cavity, 22 patients; and other sites, 17 patients. The median age was 57.7 years (age range, 26.0-85.8 years). The median duration of follow-up was 58 months (range, 12-96 months). The T and N stages are given in Table 1.

The RADPLAT protocol included 3 to 4 cycles of selective intra-arterial rapid infusions of high-dose cisplatin (150 mg/m²), which was delivered through a transfemoral micratheter. At the same time, sodium thiosulfate (9 g/m² intravenously) was given intravenously to neutralize the systemic effects of cisplatin. The chemotherapy was delivered once each week for 3 to 4 consecutive weeks. Concomitant radiotherapy (2 Gy per fraction daily, 5 treatments per week for 7 weeks) was administered beginning on day 1 of the treatment, to a total dose of 70 Gy.

Neck dissection was performed 2 months after treatment, initially for patients with bulky (N2-N3) nodal disease or for patients with residual neck mass on restaging imaging. Subsequently, neck dissections were performed only for patients who had clinical evidence of residual adenopathy regardless of the pretreatment N classification. The 10 patients who had evidence of residual disease in the primary site at the time of the restaging were not included in this analysis.

The extent of neck dissection was determined by posttreatment imaging. Three subgroups of patients were delineated by extent of neck dissection: radical or modified radical neck dissection (RND/MRND), SND, and SSND.

We evaluated the outcome of therapy in terms of regional control, rate of distant metastasis, and overall survival for the 3 different types of neck dissection surgery performed with RADPLAT therapy. The absence of residual tumor cells in pathological specimens (pathological complete response [pCR]) was also examined in relation to regional failure and overall survival.

The statistical analysis was done with JMP 4 for Windows (SAS Institute Inc, Cary, NC). Statistical analysis for all comparisons was done with the χ² method. Regional disease control at 3 years was estimated by the Kaplan-Meier method. The log-rank test was used to determine the significance of the differences between the estimates for each subset. A proportional hazards model was used to identify the variables with the greatest effect on overall survival.

Among the total group of 240 patients, nodal metastasis was observed in 171, including 130 with advanced N stage (N2 and N3). Among the 84 patients who underwent a total of 106 neck dissections (22 patients had bilateral neck dissections), the distribution of neck dissections by type was as follows: 12 patients (14%) had RND/MRND (14 procedures), 65 (77%) had SND (81 procedures), and 7 (8%) had SSND (dissection of levels II and III) (11 procedures). Type of surgery according to N stage is shown in Table 2.

Regional disease as the first site of failure was found in 11 patients (4.6% of the 240 patients), 2 of whom underwent MRND (17% of the patients in the MRND group), 3 of whom had SND (5% of the patients in the SND group), and 6 of whom did not undergo neck dissection (4%). None of the patients who underwent SSND had a regional failure. Regional control rates stratified by type of neck dissection are shown in Figure 1. The regional control rate of the whole group (n=240) was 89%. For each of the subgroups, the rate of regional disease control was as follows: 57% for RND/MRND, 91% for SND, and 100% for SSND. These differences were found to be statistically significant (P=.002) by the log-rank test.

The rates of distant metastases as the initial site of failure were as follows: RND/MRND, 25% (3 of 12 patients); SND, 22% (14/65); and SSND, 14% (1/7). The difference among the groups was not statistically significant.

At the time of analysis, 5 of 12 patients were alive in the RND/MRND group, 29 of 65 patients in the SND group, and 3 of 7 patients in the SSND group. However, overall survival was significantly different among the 3 subsets: RND/MRND had 25% 20-month survival, compared with 51% for SND and 46% for SSND (log-rank test, P=.04) (Figure 2).

### RESULTS

#### Table 1. T and N Staging of 240 Patients Treated With RADPLAT

<table>
<thead>
<tr>
<th>N Stage</th>
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<td>26</td>
<td>69</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>23</td>
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<td>41</td>
</tr>
<tr>
<td>2</td>
<td>6</td>
<td>36</td>
<td>57</td>
<td>99</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>11</td>
<td>8</td>
<td>31</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>113</td>
<td>106</td>
<td>240</td>
</tr>
</tbody>
</table>

Abbreviation: RADPLAT, intra-arterial cisplatin and concurrent radiotherapy.

#### Table 2. Distribution of Patients Based on Type of Neck Dissection and N Classification

<table>
<thead>
<tr>
<th>N Stage</th>
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<th>SND</th>
<th>SSND</th>
<th>Total</th>
</tr>
</thead>
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</tr>
<tr>
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<td>2</td>
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<tr>
<td>3</td>
<td>2</td>
<td>14</td>
<td>0</td>
<td>16</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>65</td>
<td>7</td>
<td>84</td>
</tr>
</tbody>
</table>

Abbreviations: RND/MRND, radical or modified radical neck dissection; SND, selective neck dissection; SSND, superselective neck dissection.
On pathological examination of neck dissection specimens, 50 patients (60%) had no residual disease (pCR) while 34 patients (40%) had residual tumor in the neck dissection specimens. There was a significant difference among the 3 groups in the rate of pCR. All patients who underwent SSND (7 patients) had pCR, compared with 58% (38 patients) of the SND group and 42% (5 patients) of the RND/MRND group ($\chi^2=8.84$, $P=.01$).

Thirty-four patients (40%) had pathological residual neck nodes. Among this group, the presence of residual nodal disease by number of neck levels was as follows: 41% (14 of 34 patients) had positive nodal disease confined to 1 level, 35% (12 of 34 patients) had positive nodal disease in 2 levels, and 24% (8 of 34 patients) had positive nodal disease in 3 or more neck levels.

Comparison of the regional rate of failure between patients who had no residual tumor cell (pCR) and those who did showed a significantly lower recurrence rate in those achieving pCR (8% vs 26%; Fisher exact test, $P=.03$). Comparison of the 5-year overall survival rate between patients with and without pCR in the neck showed an improved survival for the former group (39% vs 6%; log-rank test, $P<.001$) (Figure 3).

In a Cox proportional hazards model that included N classification, type of neck dissection, and residual tumor in the neck dissection specimen, the most significant variable to influence survival was residual cancer in the neck dissection specimen (risk ratio, 1.9; $P<.001$).

Salvage neck dissection is indicated for persistent nodal disease after chemoradiation. However, it remains controversial whether to perform a planned neck dissection for patients with bulky disease (N2-N3) who have a clinical complete response to chemoradiation. A few studies suggest that clinical assessment (including posttreatment imaging) after radiotherapy or chemoradiotherapy cannot ensure the absence of neck disease. Wang et al found that 31% of patients had pathological positive nodes following a complete clinical response.

Similarly, Brizel et al recommended planned neck dissection based on a 44% negative predictive value of a clinical complete response. Also, Velazquez et al found that the specificity of posttreatment computed tomographic scanning was only 24%. Roy et al found that 33% of patients had pathological positive nodes following chemoradiation, with negative computed tomographic scans. A negative positron emission tomographic scan indicates the absence of disease in only 14% of patients and therefore is unreliable for determining whether neck dissection should be omitted.

In contrast, Ojiri et al reported specific abnormal radiologic measures for predicting residual tumor in metastatic nodes in patients with head and neck tumor treated with radiotherapy. They concluded that it was feasible to make the decision to perform planned neck dissection by using such criteria.

Irrespective of the opposing opinions on when to perform a planned vs salvage neck dissection after chemoradiation, little attention has been given to the applicability of conservation neck dissection procedures in this setting. Head and neck surgeons are more inclined to remove persistent lymph node disease in this setting by us-
ing neck dissections that encompass all levels of lymph nodes with or without the nonlymphatic structures. This philosophy of erring on the side of removing more rather than less is likely based on concepts derived from managing nodal disease with primary surgery followed by adjuvant radiotherapy.

Neck dissection after chemoradiation for advanced head and neck cancer with associated bulky nodal disease is not without risks related to wound healing and chronic soft-tissue fibrosis. Dissection of all neck levels was reported to increase the incidence of spinal accessory nerve dysfunction and have a negative impact on quality of life.

The concurrent use of chemotherapy and radiotherapy is a potent combination that is likely to sterilize most of the metastatic lymph nodes in the neck. Therefore, in an attempt to treat residual adenopathy in the neck treated with chemoradiation, and to minimize the risk of postoperative complications, we examined the feasibility of limited neck dissection and its effect on the outcome of the patients with advanced head and neck tumors.

The rationale for SND when used as a primary treatment modality is based on the predictive patterns of lymphatic spread associated with carcinoma of the upper aerodigestive tract. However, with advanced neck disease and particularly for patients with nodes in multiple levels, the predictability becomes less certain. Thus, for the untreated neck, the risk of leaving behind nodal metastases is of concern when a selective neck dissection is performed as part of the initial treatment. The major difference for patients in the posttreatment setting is that the lymphatic drainage pathways are typically encompassed by the radiation fields. For clinically overt nodal disease after chemoradiation, neck dissection is essential. However, for clinically negative nodal disease in low-risk neck levels, one could argue that any occult nodal disease present before treatment within these zones would have been sterilized by the chemoradiation. Taking this concept one step further, one could argue that low-risk neck levels are most likely to be sterilized by chemoradiation despite the persistence of overt nodal metastases in adjacent high-risk levels after chemoradiation. Our earlier data and the more recent findings of Stenson et al appear to support this observation.

In the current study, 86% of the patients had a conservation neck dissection, the majority of whom had SND; 8% had SSND (removal of levels II and III only). In general, patients who had RND/MRND, in whom all 5 levels were removed, had multiple residual lymphadenopathy involving more than 2 levels. In contrast, patients who had residual disease confined to 2 levels involving the lymph node groups at greatest risk underwent SND. In the 7 patients who underwent SSND, the residual lymphadenopathy was confined to 1 level. Despite the limited dissection, the regional control rate was significantly higher in those subgroups compared with the patients who were treated with the more extensive RND/MRND (91% and 100% vs 57%, respectively). However, since the current study is not a randomized trial comparing SND and SSND with RND/MRND, we assume that the difference is related to patient selection, because patients with extended residual disease in the neck were treated with RND/MRND. The higher pCR in the SSND (100%) and SND (58%) subsets compared with the RND/MRND subset (42%) supports this selection bias. Similarly, the selection bias likely explains the higher 5-year overall survival rate in the patients who were treated with SND than the patients who had RND/MRND.

Among the total group of patients, the pCR rate was 60%; most of these had positive disease confined to 1 neck level. Only 23% of the 84 patients had positive metastases in more than 1 neck level, and this is the subgroup in which a more extensive neck dissection is needed. Our group has previously noted that the presence of pathologic nodal metastases in the neck dissection specimen is highly predictive of persistent disease in the primary site (26% vs 8%, respectively, patients without and with pCR). Others have also noted this correlation. In the current study, the 5-year overall survival rate was significantly higher for patients with a pCR (39%) than patients who had less than complete response (6%). The pathological response, based on examination of neck dissection specimens, was found to be the most significant independent variable predicting survival in the Cox proportional hazards model (P = .002). These findings are in agreement with previous reports.

The complication rate after neck dissection alone among patients who received RADPLAT has previously been reported. For patients who had a neck dissection performed as a clean procedure, the rate of acute wound complications is minimal.

In conclusion, it does not appear necessary to perform lymphadenectomy procedures that encompass all neck levels among patients with minimal residual lymphadenopathy after RADPLAT and possibly other regimens of concomitant chemoradiation. Preliminary experience with SSND suggests that it is an effective procedure for patients with residual adenopathy confined to 1 neck level after chemoradiation. Both SND and SSND offer patients a greater chance for preservation of function and less morbidity. Further prospective studies are needed by others using other concurrent chemoradiation protocols to confirm these observations.

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REFERENCES


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