ONCOLOGIC EFFECTIVENESS OF SELECTIVE NECK DISSECTION IN THE N0 IRRADIATED NECK

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Abstract: Background. The incidence and patterns of nodal spread in previously irradiated N0 necks are not well defined. Therefore, the safety and efficacy of selective neck dissection (SND) in this patient population is not well established. In a previous report from our institution, SND in irradiated patients with recurrent disease at the primary site but clinically negative necks resulted in excellent tumor control in the neck. The objective of this study is to validate our initial observations in a larger sample of patients with longer follow-up.

Methods. A retrospective chart analysis of patients previously treated with primary radiation therapy or chemoradiotherapy for squamous cell carcinoma (SCC) of the head and neck between January 1997 and June 2003 was performed. Patients with recurrent or persistent disease at the primary site or a second primary head and neck SCC, with no clinical or radiologic disease in the neck, who underwent surgical salvage with resection of the primary site along with a site-specific SND were analyzed. Patients who remained disease free at the primary site were analyzed for regional control after SND.

Results. Sixty-nine patients underwent a total of 96 site-specific SNDs. The mean age was 64.1 years (range, 39–91 years). There was histologically positive nodal disease in 17 of 69 patients (25%), and 22 of 96 necks (23%). Fifty-three patients had at least a 12-month follow-up. The mean follow-up was 23.3 months (range, 1–96 months). Of the patients with 1-year of follow-up, six patients died from recurrence at the primary site and nine died from distant metastasis. There were no cases of neck recurrence with the primary site controlled. All patients who had more than two positive nodes had recurrence either at the primary site or distant metastasis.

Conclusions. Our results confirm that the patterns of lymphatic spread are not affected by radiation. We conclude that SND is oncologically safe in the management of the N0 irradiated neck and that the finding of more than two positive nodes predicts a poor outcome. © 2005 Wiley Periodicals, Inc.

Keywords: selective neck dissection; N0 neck; radiation therapy; patterns of lymphatic spread

Selective neck dissection (SND) performed in patients with newly diagnosed, previously untreated squamous cell carcinoma (SCC) of the head and neck with a clinical N0 neck results in equal regional control rates as modified radical neck dissection.1–3 The safety and effectiveness of SND in patients who have N0 necks after radiotherapy failed at the primary site is not well established, in part because the pattern of nodal spread in a previously irradiated, undissected, N0 neck is not well defined. However, a more limited neck dissection may diminish morbidity in this patient population, particularly when bilateral neck dissections are performed.
It has been the practice of the senior author to perform a site-specific SND in patients who undergo primary site salvage surgery for recurrent, persistent, or second primary tumors who have had previous radiation or chemoradiation therapy and have clinically negative necks. Our institution previously reported that SND resulted in excellent tumor control in the neck in a small patient population. The objective of this study was to validate our initial findings in a larger sample of patients that (1) the patterns of nodal metastasis are unchanged after radiation therapy, (2) SND is oncologically safe and effective, and (3) the finding of two or more histologically positive nodes is a negative prognostic indicator for survival.

**MATERIALS AND METHODS**

**Design.** A retrospective chart analysis of patients previously treated with primary radiation therapy or chemoradiotherapy for SCC of the head and neck, seen at The Cleveland Clinic Head and Neck Institute between January 1997 and June 2003, was performed. The Cleveland Clinic Institutional Review Board approved the study. The inclusion criteria were as follows: (1) all patients had recurrent or persistent SCC at the primary site with clinical and radiographic N0 neck after radiation or chemoradiation therapy; (2) all patients underwent appropriate salvage surgery of the primary with site-specific SND; (3) all patients who remained disease free at the primary site were eligible for regional control analysis; and (4) all patients were analyzed for incidence and patterns of nodal spread in the neck.

**Patients.** Sixty-nine patients who met the inclusion criteria were included in the study. The patients’ charts were retrieved and the following information was recorded: age, sex, tumor site, surgical procedure and pathologic findings, interval between completion of radiation therapy and surgical salvage, status of the neck after salvage, documentation of primary site recurrence or distant metastasis after surgery, and length of follow-up. Pathologic analysis included documentation of the levels involved with nodal metastasis and the presence of extracapsular spread. Finally, recurrence at the primary site after surgical intervention disqualified the patient for further observation for long-term tumor control in the neck.

**Variables and Statistical Analysis.** The primary outcome variable was the proportion of patients with controlled neck disease with the primary site controlled after SND. In addition, the following observational variables were studied: incidence of occult nodal disease in the neck, incidence of extracapsular spread, number of positive nodes, recurrence at the primary site, and presence of distant metastasis. Data were summarized as frequency and percent for categorical variables and mean and range for continuous variables. The association between the two categorical variables was assessed by exact unconditional test. Kaplan-Meier survival analysis was used to get the overall survival estimates and compare the survival estimates among the patients with different positive nodes.

**RESULTS**

**Patients.** Sixty-nine patients with clinically negative necks underwent resection of a recurrent primary tumor, as well as a unilateral or bilateral SND, after primary radiation or chemoradiation therapy failure. None of the patients received additional planned treatment. The mean age was 64.1 years (range, 39–91 years). There were 60 men and nine women. The mean interval between completion of radiation and salvage surgery was 11.6 months (range, 3–82 months). The mean follow-up for the overall series was 23.3 months (range, 1–96 months). Fifty-three patients had at least a 12-month follow-up.

**Patterns of Lymphatic Spread.** A total of 96 site-specific SNDs were performed in these patients. There was histologically positive nodal disease in 17 (25%) of 69 patients and 22 (23%) of 96 necks. Fifty-two patients (75.4%) had no positive nodes, 10 patients (14.5%) had two or fewer positive nodes, and seven patients (10.1%) had more than two positive nodes. The specimens of three patients had evidence of extracapsular spread (17.6%). Fifty-five percent of supraglottic and 43% hypopharyngeal cancers had occult nodal disease in the neck, and 20% of patients with cancers of the oral cavity and oropharynx had pathologically positive lymph nodes, whereas only 12% of patients with glottic carcinomas had evidence of neck metastasis (Figure 1). Statistical analysis did not show a significant association between the presence of subclinical metastasis and the location of the primary tumor.
All nodal metastases were found in levels II to IV.

**Disease Control.** No patients had regional recurrence develop, either in the dissected field or undissected nodes, when the primary site was controlled. Forty-one patients (59.4%; 38 with ≥12-month follow-up) remained disease free after salvage surgery, 12 patients (17.4%; six with ≥12-month follow-up) had recurrence develop at the primary site, and 16 patients (23.2%; nine with ≥12-month follow-up) had distant metastasis develop. Of the 12 patients with primary site recurrence, one patient had regional failure as well. Given the small numbers, no statistical analysis was granted. The incidence of recurrence,
either at the primary site or distant metastasis, for patients with negative nodes was 13.5% and 21.2%, respectively, whereas for patients with two or fewer positive nodes was 20.0% and 10.0%, respectively. Overall, the incidence of recurrent disease in patients with two or fewer positive nodes was 33.9%. All patients who had more than two positive nodes had recurrence either at the primary site (42.9%) or distant metastasis (57.1%). Thus, the presence of more than two nodes with occult metastasis was a statistically significant predictor of cancer recurrence ($p = .001$, exact unconditional test). A Cox regression analysis was performed to compare the three groups (ie, no positive nodes, two or fewer nodes, and more than two positive nodes) on the survival rate adjusted for the interval period between radiation and recurrence. The interval was found to be nonsignificant ($p = .82$). In terms of patient outcomes by primary site in patients with a minimum of 12 months of follow-up, the data showed that overall patients with hypopharyngeal cancer were less likely to be salvaged by a surgical intervention after failed radiation ($p = .030$, Fisher’s exact test). Figure 2 summarizes the outcome by primary site of patients with at least a 12-month follow-up.

**Survival.** The overall 2-year and 5-year survival rates for the entire series were 65.7% and 59.7%, respectively (Figure 3). Survival estimates at 2 years were 74.7% for patients with 0 nodes, 57.1% for patients with two or fewer nodes, and 21.4% for patients with more than two nodes (Figure 4).

**DISCUSSION**

This study expands and confirms our findings in a preliminary study evaluating the safety and effectiveness of SND in patients with N0 necks undergoing surgical salvage after radiation or chemoradiation therapy. We demonstrate that (1) radiation therapy does not change the anticipated pattern of nodal metastasis; (2) SND is oncologically safe in the previously irradiated, clinically N0 neck; and (3) the presence of more than two positive nodes in this setting is a poor prognostic indicator.

The incidence and anatomic distribution of subclinical neck metastasis in our series was comparable to what has been reported in the literature in untreated N0 necks. Thus, we can conclude that radiation therapy does not change the anticipated pattern of nodal metastasis in patients who have recurrences after primary radiation therapy treatment. This patient population should be distinguished from patients who are undergoing radiation therapy in whom the lymphatic drainage may be acutely altered, as demonstrated by edema in the irradiated area. However, no studies have demonstrated permanent alterations in the patterns of lymphatic metastasis after therapeutic radiation doses. If
the patterns of lymphatic spread were significantly altered by radiation therapy in our patient population, one would expect no correlation between subclinical nodal involvement and tumor primary site. Our findings of no recurrences in the undissected levels and all metastasis in levels II to IV support this conclusion. In addition, the 25% incidence of micrometastasis found in our series is similar to the rate of occult positive nodes in untreated N0 necks.

Few studies in the literature address the appropriate neck dissection in a previously irradiated, clinically N0 neck. Some authors propose observation, whereas others advocate using a modified radical neck dissection because of the possibility of altered lymphatic spread. Wax and Touma reported subclinical cervical metastasis in 17% of patients with N0 laryngeal carcinoma who had primary site recurrence after radiotherapy. In their study, however, it was unclear as to which patients had received radiation therapy to the neck. Nevertheless, the authors concluded that these patients should be managed with a lateral neck dissection because its morbidity is minimal while it provides excellent control of the neck. Thus, this study provides support for a less extensive neck dissection. In our preliminary study, we demonstrated that SND provided excellent control of neck disease in previously irradiated patients who had a recurrence of the primary site with an N0 neck. This study confirms that SND is oncologically safe and effective in this setting as evidenced by no neck recurrences either in the dissected levels or undissected levels I and/or V when the primary site was controlled. Although the minimum follow-up was 1 year, none of the patients in our earlier report had late neck metastasis develop with more than 2 years of follow-up. We do not expect a significant number of neck recurrences with longer follow-up. This compares favorably with the 95% disease control in unirradiated, N0 necks.

This study also confirms our previous finding that the presence of more than two positive nodes is a poor prognostic indicator for survival. Hosal et al found that patients with previously untreated necks who were found to have more than two metastatic lymph nodes had a higher incidence of recurrent disease than the patients with carcinoma limited to one or two nodes. These findings are similar to what we observed in our patient series. Also, these authors reported a 24% incidence of extracapsular spread, which compares to our 17.6%. Other authors, however, have reported higher incidences of extracapsular spread in patients with occult neck metastasis in previously untreated necks, suggesting that radiation may have a mitigating effect on lymphatic spread.

In conclusion, SND is a viable alternative to a modified radical neck dissection in the management of a clinically N0, undissected, previously irradiated neck. Our findings confirm the observations made in our preliminary study that the patterns of lymphatic spread are not affected by radiation and that the finding of more than two positive nodes predicts a poor outcome. Thus, SND is oncologically safe and effective in the management of this patient population.

REFERENCES
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