Otolaryngology–Head and Neck Surgery (2009) 141, 474-477

ORIGINAL RESEARCH–HEAD AND NECK SURGERY

Planned neck dissection following primary chemoradiation for advanced-stage head and neck cancer

Peter R. Sabatini, MD, and **Yadranko Ducic, MD,** Dallas and Fort Worth, TX

No sponsorships or competing interests have been disclosed for this article.

ABSTRACT

OBJECTIVES: To determine the prevalence of residual cancer in planned neck dissection specimens for advanced-stage squamous cell carcinoma following chemoradiation.

STUDY DESIGN: A case series.

SETTING: A single-surgeon community-based head and neck practice.

SUBJECTS AND METHODS: Twenty-six patients were identified during 2000 to 2007. All patients were treated with external beam radiation; the average dose to the neck was 60 Gy (range 50-72 Gy). Concurrent chemotherapy was given with cisplatin and 5-fluorouracil. Patients presenting with greater than N2 cervical disease and at least one node greater than 3 cm were considered advanced. Post-chemoradiation physical examinations were performed by the primary surgeon and oncologist. Absence of physical evidence of disease was deemed a complete clinical response.

RESULTS: Fourteen of 21 (67%; 95% confidence interval [CI], 0.449-0.854) patients were found to have carcinoma in their neck specimens. Seven patients were noted to have a clinically complete response, and two of seven (29%; 95% CI, 0.053-0.659) patients with a clinically complete response were found to have carcinoma in their neck specimens. Fourteen patients were noted to have an incomplete response to therapy. Two of these 14 (14%; 95% CI, 0.026-0.419) patients had negative pathology in their neck dissection specimens. Three patients had local recurrence and succumbed to their disease.

CONCLUSION: Planned neck dissection in the setting of advanced neck disease following chemoradiation should remain an important consideration when counseling patients presenting with advanced cervical metastasis from squamous cell head and neck cancer.

Treatment of patients with advanced locoregional head and neck cancer continues to challenge head and neck surgeons and oncologists. Preservation of important functions such as speech and swallowing has become paramount when deciding the best primary treatment plan for an individual patient. Organ-sparing techniques have recently become an equivalent initial option to traditional extirpative surgery for patients with advanced head and neck cancer. Among these options, primary radiation, chemoradiation, and transoral laser microsurgery are the most common. This article will review those patients with advanced head and neck squamous cell carcinoma (HNSCC) treated with neoadjuvant concurrent chemoradiation and a planned neck dissection by the senior author.

Treatment of advanced local metastasis to the neck has continued to fuel debate.[1] Traditionally, patients presenting with advanced local neck metastasis would undergo planned neck dissections four to 12 weeks after receiving primary radiation or chemoradiation, under the rationale that such advanced local disease is difficult to eradicate without surgery. This approach is done despite the fact that some patients have no physical or radiographic evidence of residual disease. Recent studies[2,3] have looked at the utility of fluorodeoxyglucose-positron emission tomography (FDG-PET) and PET/CT as a means of surveillance to challenge this dogma and cite excellent negative predictive values. Other investigators[4] have found this strategy to be less useful. Proponents of the planned neck dissection report that accurate post-therapy clinical and radiologic surveillance is difficult at best and that viable tumor can be demonstrated despite a clinically complete response. In addition, assuming a selective nodal dissection, many argue that the morbidity of surgery is minimal if done during the four- to 12-week planned post-therapy period and that salvage surgery performed outside of this window increases morbidity and lessens survival.

Observing patients with advanced neck disease who demonstrate a complete clinical response is complicated because salvage surgery becomes increasingly morbid outside of the four- to 12-week window.[5] The idea of a four- to 12-week surgical window is based on the observed physiological changes that occur before four weeks (acute radiation injury) and after 12 weeks (chronic radiation injury) of radiation.[6] Currently, FDG-PET scanning is recommended no earlier than 12 weeks after chemoradiation for determi-

Received January 11, 2009; revised June 8, 2009; accepted June 30, 2009.

0194-5998/$36.00
doi:10.1016/j.otohns.2009.06.749

nation of active residual cancer or metastasis. Physicians who use this strategy accept that patients will be outside the window ideal for planned neck dissection. The observation argument counters that patients with a complete response can be predicted not to recur if they have a negative PET scan at 12 weeks post-chemoradiation and that the potential morbidity of a neck dissection can be avoided for the majority of patients in this category.

This retrospective study represents a review of the senior author's experience performing planned neck dissection at four to 12 weeks post-chemoradiation for all patients presenting with advanced (N2-3) local metastasis. We wanted to determine the prevalence of cancer present in our specimens. In addition, we were also curious to determine the percentage of patients with a clinically complete response who had carcinoma in their pathology specimen, as well as those who had a partial clinical response and pathologically negative specimen.

METHODS

Institutional review board approval was obtained to review the charts of all patients who underwent a planned neck dissection within 12 weeks of concurrent chemoradiotherapy. Patients were excluded if their neck disease at presentation was less than N2. In addition, only patients with nodal disease greater than 3 cm were included. Patients staged N2b for multiple enlarged nodes not exceeding 3 cm also were not included in the analysis because these patients are observed in our practice if they have a clinically complete response to therapy. All patients who underwent a neck dissection more than 12 weeks from the time of completion of their chemoradiation were considered to have salvage neck dissections and were excluded. Table 1 lists the patient and tumor characteristics. Twenty-six patients were identified during 2000 to 2007. Five patients were excluded because of incomplete information regarding their post-therapy clinical response. The remaining 21 patients were included in the cohort. There were three female patients and 18 male patients. The average age was 59 years. The site of the primary was as follows: 13 oropharynx, two hypopharynx, two larynx, three unknown primary, and one auricle. All patients were treated with external beam radiation; the median dose to the neck was 70 Gy (range 50-72 Gy). Concurrent chemotherapy was given with cisplatin and 5-fluorouracil (5-FU). For the purposes of this report, patients presenting with greater than N2 cervical disease and at least one node greater than 3 cm were considered advanced (all stage IV). All neck dissections were modified radical neck dissections unless a radical neck dissection was dictated by the disease, and they were performed an average of six weeks post-chemoradiotherapy (range 4-10 weeks). Post-chemoradiation physical examinations were performed by the senior author, a medical oncologist, and a radiation oncologist. Absence of physical evidence of disease was deemed a complete clinical response. Post-therapy CT scans were not routinely obtained because neck dissections were planned as dictated by the presenting disease, not the response to treatment. All of the neck specimens were examined by routine hematoxylin-eosin staining.

Table 1
Patient and tumor characteristics

Average age (yrs) (range)	59 (43-85)
Sex	
Male	18
Female	3
Average time from CRT to surgery (wk) (range)	6 (4-10)
Average length of follow-up (mo) (range)	27 (1-59)
T stage	
T1	3
T2	5
T3	7
T4	3
Tx	3
N stage	
N2	11
N3	10
Subsite	
Oropharynx	13
Hypopharynx	2
Larynx	2
Unknown	3
Auricle	1

CRT, chemoradiation therapy.

RESULTS

Fourteen of 21 (67%; 95% confidence interval [CI], 0.449-0.854) patients were found to have carcinoma in their neck specimens. Seven patients were noted to have a clinically complete response, and two of seven (29%; 95% CI, 0.053-0.659) patients with a clinically complete response were found to have carcinoma in their neck specimens. Fourteen patients were noted to have an incomplete response to therapy. Two of these 14 (14%; 95% CI, 0.026-0.419) patients had negative pathology in their neck dissection specimens. Three patients had local recurrence and succumbed to their disease. One of the three presented with local and distant metastatic disease eight months after neck dissection. One patient had a single lung metastasis discovered 10 months after neck dissection and was salvaged with a pulmonary wedge resection. One patient developed a second primary lung cancer seven months after neck dissection. There were no rehospitalizations for surgical complications (ie, no fistulas or infections requiring intravenous antibiotics). Two patients returned to the clinic with seromas that were drained in the clinic. Morbidity was 10 percent overall (2/21).

DISCUSSION

There is little argument that a patient with advanced neck disease at presentation who demonstrates a less than complete response to chemoradiation should be considered for a neck dissection. The controversy of planned neck dissection with advanced HNSCC after chemoradiation is centered on patients with advanced neck disease (N2 by size or greater) who seemingly respond completely or almost completely to chemoradiation. Clinical examination and traditional radiographic studies (CT, MRI, and ultrasound) performed after high-dose radiation therapy is unreliable, and others[7,8] have demonstrated poor correlation when evaluating for residual disease. Some authors who advocate surveillance for patients with a clinically complete response depend on the use of imaging studies that use biological uptake of FDG. FDG-PET (with or without CT) is relied on to determine the activity of the primary, regional, and distant sites.

In a recent comprehensive review of the history of planned neck dissection after concurrent chemoradiotherapy for advanced-stage HNSCC, Pelliteri et al[1] concluded that patients with extensive neck disease (N2-3) who demonstrated a complete response should undergo PET/CT 12 weeks after treatment followed by a planned neck dissection. In this way, correlation of imaging results and pathological node status can be performed to determine the accuracy of this modality of surveillance. Our approach to neck dissections being performed at a planned interval is in agreement with this statement.

Some investigators have sought to find means of evaluating patients earlier in the post-chemoradiation course to determine which patients are likely to recur. Gourin et al[4] reviewed a group of 17 patients with advanced-stage neck disease (N2-3) who were evaluated with PET/CT within eight to 10 weeks after chemoradiation and underwent a planned neck dissection. They used a standard uptake value (SUV) of 1.7 to 3.8 to determine a positive scan. Eleven (64.7%) patients had a positive scan, of which two (18.2%) had carcinoma present in their specimen. Of the six patients with negative scans, carcinoma was present in three (50%) of their specimens. Sensitivity and specificity of PET/CT in predicting occult nodal disease was 40 percent and 25 percent, respectively, using these parameters. Brkovich et al[2] found similarly disappointing results using FDG-PET before 12 weeks; however, they found a negative predictive value of 91.7 percent. These studies demonstrate the difficulty of determining whether a patient has residual cancer before the 12-week post-therapy with FDG-PET.

Brizel et al[7] looked at a subset of patients with N2-3 disease who underwent hyperfractionated radiotherapy and concurrent cisplatin/5-FU chemotherapy to determine the negative predictive value of a clinically complete response, positive predictive value of a less than clinically complete response, and overall accuracy of clinical response. These values were 74 percent, 44 percent, and 60 percent, respectively. In addition, the 4-year disease-free survival rate was 75 percent for N2-3 patients who had a clinically complete response and had undergone a neck dissection versus 53 percent for patients who had a clinically complete response but did not undergo a neck dissection ($P = 0.08$). The four-year overall survival rate was 77 percent versus 50 percent, respectively, for these two groups of patients ($P = 0.04$).

Sewall et al[9] reviewed their experience with planned post–radiation/chemoradiation therapy neck dissection and discovered an overall 28 percent incidence of residual disease. Planned neck dissection was performed on average 9.3 weeks after therapy. Of 107 neck dissections, only four were performed on patients with less than N2 disease. These investigators did not evaluate a clinical response to therapy. Owing to the high overall incidence of residual cancer in their series, they currently perform planned selective neck dissections on all pretreatment N2-3 disease following chemoradiation. Morbidity from the neck dissection was 10 percent. Nouraei et al,[10] who published a series of 41 patients who underwent planned neck dissections at eight weeks, had a 20 percent rate of significant complications. We experienced a low level of morbidity of 10 percent in our series.

Yao et al[11] demonstrated that FDG-PET may be a reliable surveillance modality for patients who achieve a good clinical response to concurrent intensity-modulated radiochemotherapy. They routinely perform FDG-PET at 12 weeks post-therapy, citing an increased false-negative rate before this time period. They used a cutoff SUV value of greater than 3.0 to constitute a positive result in an effort to reduce the number of false positives. In their series of 13 patients with N2 or greater disease at presentation and a negative PET scan after definitive chemoradiation, they experienced no regional recurrences (100% negative predictive value). This group performed FDG-PET at variable time periods after treatment, the average being 14 weeks post-chemoradiation.

In light of current information and in agreement with our findings, a planned neck dissection performed four to 12 weeks following primary chemoradiation is supported by available literature for optimizing patient outcomes, even with a clinically complete response. Surgical morbidity of a planned neck dissection is low. It seems that PET/CT surveillance may be an alternative option for those patients who demonstrate a clinically complete response and are concerned about the surgical risk incurred with a neck dissection. It remains to be demonstrated that a positive PET scan can predict pathologically viable cancer following chemoradiation before 12 weeks. Owing to the retrospective nature of our study, it is difficult to make conclusions about our results. The wide confidence intervals in our article are due to the limited number of patients enrolled. We believe that until a method of surveillance is developed that predicts which patients with a complete response are truly free of residual disease, it is better to err on the side of a planned neck dissection. The percentage of patients with a clinically complete response that wind up demonstrating viable tumor in

their specimens is high enough to warrant consideration of planned neck dissections on all patients presenting with advanced neck disease following concurrent chemoradiation.

AUTHOR INFORMATION

From the Department of Otolaryngology–Head and Neck Surgery, University of Texas Southwestern Medical Center, Dallas, TX; and Otolaryngology and Facial Plastic Surgery Associates, Fort Worth, TX.

Corresponding author: Y. Ducic, MD, 923 Pennsylvania Ave, Ste 100, Fort Worth, TX 76104.

E-mail address: yducic@sbcglobal.net.

AUTHOR CONTRIBUTIONS

Peter R. Sabatini, data gathering, writing; **Yadranko Ducic,** source for patients, study design, writing.

DISCLOSURES

Competing interests: None.

Sponsorships: None.

REFERENCES

1. Pellitteri PK, Ferlito A, Rinaldo A, et al. Planned neck dissection following chemoradiotherapy for advanced head and neck cancer: is it necessary for all? Head Neck 2006;28:166–75.
2. Brkovich VS, Miller FR, Karnad AB, et al. The role of positron emission tomography scans in the management of the N-positive neck in head and neck squamous cell carcinoma after chemoradiotherapy. Laryngoscope 2006;116:855–8.
3. Yao M, Smith RB, Graham MM, et al. The role of FDG PET in management of neck metastasis from head-and-neck cancer after definitive radiation treatment. Int J Radiat Oncol Biol Phys 2005; 63:991–9.
4. Gourin CG, Williams HT, Seabolt WN, et al. Utility of positron emission tomography-computed tomography in identification of residual nodal disease after chemoradiation for advanced head and neck cancer. Laryngoscope 2006;116:705–10.
5. Stenson KM, Haraf DJ, Pelzer H, et al. The role of cervical lymphadenectomy after aggressive concomitant chemoradiotherapy: the feasibility of selective neck dissection. Arch Otolaryngol Head Neck Surg 2000;126:950–6.
6. Grabenbauer GG, Rodel C, Ernst-Stecken A, et al. Neck dissection following radiochemotherapy of advanced head and neck cancer—for selected cases only? Radiother Oncol 2003;66:57–63.
7. Brizel DM, Prosnitz RG, Hunter S, et al. Necessity for adjuvant neck dissection in setting of concurrent chemoradiation for advanced head-and-neck cancer. Int J Radiat Oncol Biol Phys 2004; 58:1418–23.
8. McHam SA, Adelstein DJ, Rybicki LA, et al. Who merits a neck dissection after definitive chemoradiotherapy for N2-N3 squamous cell head and neck cancer? Head Neck 2003;25:791–8.
9. Sewall GK, Palazzi-Churas KL, Richards GM, et al. Planned postradiotherapy neck dissection: Rationale and clinical outcomes. Laryngoscope 2007;117:121–8.
10. Nouraei SA, Upile T, Al-Yaghchi C, et al. Role of planned postchemoradiotherapy selective neck dissection in the multimodality management of head and neck cancer. Laryngoscope 2008;118:797–803.
11. Yao M, Luo P, Hoffman HT, et al. Pathology and FDG PET correlation of residual lymph nodes in head and neck cancer after radiation treatment. Am J Clin Oncol 2007;30:264–70.