ROLE OF NECK DISSECTION FOLLOWING CONCURRENT CHEMORADIATION FOR ADVANCED HEAD AND NECK CARCINOMA

Véronique-Isabelle Forest, MD, MSc,1 Phuc Félix Nguyen-Tan, MD,2 Jean-Claude Tabet, MD,1 Marie-Jo Olivier, MD,1 Daniel Larochelle, MD,1 Bernard Fortin, MD, MSc,2 Michel Gélinas, MD,2 Denis Soulières, MD,3 Danielle Charpentier, MD,3 Louis Guertin, MD1

1 Department of Otolaryngology—Head and Neck Surgery, Centre Hospitalier Universitaire de l’Université de Montréal, Pavillon B—Hôpital Notre-Dame, 1560, Sherbrooke East, Montreal, PQ, Canada H2L 4M1.
E-mail: guertinorl@videotron.ca
2 Department of Radiotherapy, Centre Hospitalier Universitaire de l’Université de Montréal, Pavillon B—Hôpital Notre-Dame, 1560, Sherbrooke East, Montreal, PQ, Canada H2L 4M1
3 Department of Hematology and Oncology, Centre Hospitalier Universitaire de l’Université de Montréal, Pavillon B—Hôpital Notre-Dame, 1560, Sherbrooke East, Montreal, PQ, Canada H2L 4M1

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Abstract: Background. Our primary objective was to determine the role of neck dissection following concomitant chemoradiation (CRT) for advanced stage III–IV head and neck squamous cell carcinoma (HNSCC).

Methods. One hundred eighty-four patients with HNSCC treated with CRT were included. One hundred twenty-three patients reached a regional complete response (CR) after CRT and no neck dissection was performed. Forty-five patients among the 58 who reached a regional partial response (PR) underwent a neck dissection.

Results. Overall, regional CR rate after CRT was 68%. Patients who reached a regional CR (no neck dissection) had an overall neck recurrence rate of 5%. Patients with regional PR who underwent a neck dissection had a 7% neck recurrence rate.

Conclusions. Patients with regional CR not followed by a neck dissection have a low rate of neck recurrence. Systematic neck dissection is not mandatory for patients with nodes less than 6 cm reaching a regional CR. For patients with nodes larger than 6 cm, no firm recommendation can be given because of the small number of patients in this series. If the regional response is incomplete, cervical dissection is warranted. © 2006 Wiley Periodicals, Inc. Head Neck 28: 1099–1105, 2006

Keywords: neck dissection; neck management; concurrent chemoradiation; lymph nodes; squamous cell carcinoma; regional recurrence

Treatment options for advanced head and neck squamous cell carcinoma (HNSCC) have evolved in recent years. Multimodal treatment regimens such as concomitant chemoradiation (CRT) have achieved higher locoregional control and survival rates compared with radiotherapy alone. CRT also offers the potential advantage of organ preservation and function.1–7 Hence, CRT has become a recognized therapeutic option for advanced HNSCC.

It is well known that patients with HNSCC with regional metastasis at diagnosis carry a
worse prognosis than patients having clinically/radiologically negative neck nodes. Moreover, locoregional recurrence represents a dominant form of initial failure for advanced HNSCC after CRT. Regional recurrence posttreatment has a poor rate of surgical salvage and consequently a bad outcome. Therefore, management of the neck following CRT is of utmost importance in the overall control of the disease.

It is well accepted that patients with a partial regional response after chemoradiation should undergo neck dissection. However, for patients with a complete regional response following treatment, especially N2 or N3, some controversies remain. Posttreatment systematic neck dissection for these patients, regardless of regional response to treatment, is the recommended practice in many centers. Others consider that planned neck dissection for all patients with nodes greater than 3 cm at diagnosis is not mandatory to secure neck control, especially when patients achieve a complete regional response. The upholders of this strategy consider that the concept of systematic neck dissection exposes many patients to unnecessary morbidity.

In our institution, the decision to perform a neck dissection following concurrent chemoradiation is not made a priori. We tend to consider that this decision should be made according to the evaluation of the regional response after treatment and the diameter of the largest node at diagnosis. In a retrospective study of all cases of patients with stage III–IV squamous cell carcinoma of the head and neck treated with CRT, we investigated the regional response to treatment and the regional control on follow-up of the patients having achieved a complete local response and no local recurrence. The patients at risk of regional recurrence were identified and the validity of posttreatment neck dissection was examined.

**MATERIALS AND METHODS**

Three hundred twenty-five patients were treated with concurrent platinum-based chemotherapy and standard fractionation radiotherapy (RT) at Notre-Dame Hospital (Montreal, Canada) between July 1998 and April 2004 for stage III–IV HNSCC. Patients included in this study all had HNSCC and presented with neck metastasis. They also achieved a CR at the primary site after CRT. The exclusion criteria were a follow-up of less than 6 months; a primary of the nasopharynx, the salivary glands, the paranasal sinuses, or the orbit; a local or regional surgery before treatment; persistent or recurrent disease at the primary site; and the presence of distant metastasis before treatment.

**Clinical Data.** One hundred eighty-four patients were eligible. There were 140 men and 44 women, with a median age at diagnosis of 57 years (range, 31–78). The median follow-up was 36 months. Only 5 patients had less than 1 year of follow-up; 4 of them died within 1 year from the end of CRT of unrelated causes and 1 was lost on follow-up. The distribution of the primary sites was 134 oropharynx, 24 larynx, 11 hypopharynx, 4 oral cavity, and 11 unknown primary. All the data were reported according to the 1998 American Joint Committee on Cancer (AJCC) classification (Table 1).

The lymph nodes were clinically and radiologically measured for every patient at diagnosis and were classified according to their largest diameter into 3 subgroups: nodes ≤3 cm, nodes 3.1 to 6 cm, and nodes >6 cm.

**Concurrent Chemoradiation.** All patients underwent concurrent platinum-based chemotherapy and
standard fractionation RT. Every patient received standard fractionation RT of 2 Gy per day, 5 fractions a week for 7 weeks for a total dose of 70 Gy. Four patients received a concomitant boost of 72 Gy in 42 fractions over 6 weeks. The mean RT dose was 70 Gy (68–72 Gy).

Regional Response Evaluation. The neck response was evaluated 6 to 8 weeks following the end of treatment with a physical examination and a CT scan of the neck for all patients. Occasionally, an MRI of the neck was done as an adjunct. All CT scans and MR images were read by the neuroradiologists of our institution. The regional response was considered complete (CR) if there was no evidence of residual disease in the neck. If any residual tissue corresponding to the initial neck disease was noted on CT scans or MR images, the node must have a volume reduction of 90% or greater and/or be smaller than 1 cm and be oval-shaped with smooth borders and it must have no imaging evidence of extracapsular spread, no necrotic or enhancing area (a fatty central area is a normal feature).19,20 If 1 of these criteria was not met, it was classified as a regional PR.

Neck Dissection. A neck dissection was performed 6 to 12 weeks (range, 6–26 weeks) following the end of treatment for the patients with a regional PR, if they were eligible and accepted the surgery. Three patients with a complete regional response had a neck dissection after treatment to meet the research protocol requirements in which they were already enrolled.

The type of neck dissection performed was decided by the surgeon according to the initial cancer and the intraoperative findings.

Statistical Analysis. SAS version 8.2 was used to compute the different data (Statistical Analysis System, Cary, NC). Fisher tests were used to try to demonstrate predictors of CR or positive pathological analysis. Regional control rates were estimated using the Kaplan–Meier method.

RESULTS

Regional Response Following CRT. Among the 184 patients included in this study, 68% reached a regional CR 6 to 8 weeks following the completion of CRT. Eighty-three percent of nodes 3 cm or less, 66% of nodes from 3.1 to 6 cm and 43% of nodes greater than 6 cm had a regional CR (Tables 2 and 3).

Neck Dissection. One hundred twenty-six patients had a regional CR following CRT. No neck dissection was systematically planned for them, except for 3 patients who were already enrolled in a research protocol that required a neck dissection regardless of the response. Fifty-eight patients had a regional PR following CRT; 45 of them underwent a neck dissection. Thirteen patients did not have a neck dissection because they were not operable or refused the surgery (9 patients) or because the residual nodes completely regressed by the time the surgery was scheduled (4 patients). Overall, 48 neck dissections were performed post-CRT (Figure 1).

Regional Control According to Regional Response Post-CRT. Among the 123 patients who reached a regional CR and did not undergo neck dissection, only 5% (6 patients) had regional recurrence on follow-up (Table 4). One of them had T2N2a disease of the oropharynx with the largest node measuring 6 cm. This patient had apparent regional recurrence and underwent ipsilateral neck dissection. The surgical specimen was positive on pathologic analysis. There was no evidence of disease after 29 months of follow-up. The other 5 patients had regional recurrences within 2.5 years of the end of treatment, except for 1 patient who presented a neck recurrence 3 years after the end of CRT. These patients were either not salvageable by neck dissection or developed distant metastasis. Four of them ultimately died of their disease.

Table 2. Regional response post-CRT according to N classification.

<table>
<thead>
<tr>
<th>N classification</th>
<th>Regional CR, no. (%)</th>
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<tbody>
<tr>
<td>N1</td>
<td>20/24 (83)</td>
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<tr>
<td>N2a</td>
<td>31/41 (76)</td>
</tr>
<tr>
<td>N2b</td>
<td>26/42 (62)</td>
</tr>
<tr>
<td>N2c</td>
<td>37/49 (76)</td>
</tr>
<tr>
<td>N3</td>
<td>12/28 (43)</td>
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</table>

Abbreviations: CRT, concomitant chemoradiation; CR, complete response.

Table 3. Regional response post-CRT according to nodal size at diagnosis.

<table>
<thead>
<tr>
<th>Nodal size at diagnosis</th>
<th>Regional CR, no. (%)</th>
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<tbody>
<tr>
<td>&lt;3 cm</td>
<td>54/65 (83)</td>
</tr>
<tr>
<td>3.1–6 cm</td>
<td>60/91 (66)</td>
</tr>
<tr>
<td>&gt;6 cm</td>
<td>12/28 (43)</td>
</tr>
</tbody>
</table>

Abbreviations: CRT, concomitant chemoradiation; CR, complete response.
recurrences at last follow-up (7%) (Figure 2). These patients initially had a T3N2c of the larynx, a T4N2b of the oropharynx, and a TxN3 of an unknown primary with the largest node measuring 2, 5, and 10 cm respectively. All the surgical specimens of neck dissection were positive for squamous cell carcinoma on pathologic analysis. Three patients died of their disease despite salvage neck dissection.

Even if they had achieved a regional CR following CRT, 3 patients on research protocol did undergo a neck dissection. Two of them initially had squamous cell carcinoma of the oropharynx, T2N2a and T4N2a, with nodes of 4.5 and 5 cm, respectively. Both surgical specimens were negative on pathology. The other patient had a T4N3 lesion of the oropharynx with a node of 7.5 cm. The pathology result of the specimen of the neck dissection was positive. All 3 of these patients were free of regional disease at last follow-up and are still alive.

Regional Control According to Nodal Size at Diagnosis. The regional response rate according to the largest diameter at diagnosis was analyzed. Each of the first 2 groups, nodes 3 cm or less and 3.1 to 6 cm, had 9% with evidence of regional disease at their last visit. Eighteen percent of patients with nodes larger than 6 cm had presence of regional disease at last follow-up (Table 4). These rates include all patients of each subgroup including those with a regional PR who were inoperable or refused to undergo a neck dissection following CRT. These analyses were repeated without patients with persistent neck disease (regional PR with no neck dissection).

Hence, for the group of patients with nodes 3 cm or less, 2 of the 54 patients (4%) who reached a regional CR (no neck dissection) had actual regional failure at last follow-up. One patient among the 8 who had regional PR with a neck dissection performed had evidence of neck disease at last follow-up.

Among the group of patients with nodes 3.1 to 6 cm, 4 patients of 58 had a regional recurrence. One of them was salvaged surgically and is alive after 30 months of follow-up. The other 3 patients died of regional progression or distant metastasis. Only 5% of patients (3 of 58) who achieved regional CR without neck dissection had evidence of regional disease at last follow-up. One patient (4%) with regional PR and a neck dissection presented with a regional recurrence at his last visit.

<table>
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<th>Table 4. Regional recurrence according to regional response post-CRT and nodal size at diagnosis.</th>
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<tr>
<td><strong>Regional recurrence</strong></td>
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<tr>
<td><strong>Nodal size at diagnosis</strong></td>
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<tr>
<td>Population (% regional recurrence) CR–ND (% regional recurrence) PR + ND (% regional recurrence)</td>
</tr>
<tr>
<td>&lt;3 cm  6/65 (9)  2/54 (4)  1/8 (13)</td>
</tr>
<tr>
<td>3.1–6 cm  8/91 (9)  4/58 (7)  1/25 (4)</td>
</tr>
<tr>
<td>&gt;6 cm  5/28 (18)  1/11 (9)  1/12 (8)</td>
</tr>
</tbody>
</table>

Abbreviations: CRT, concomitant chemoradiation; CR–ND, complete response without neck dissection; PR, partial response, PR + ND, partial response with neck dissection.
patients with nodes larger than 6 cm and a regional CR who were not operated on in the neck had a neck recurrence rate at last follow-up of 9% (1 of 11 patients). Patients with regional PR followed by neck dissection had an 8% rate (1 of 12 patients). In the 12 patients who underwent neck dissection, 3 surgical specimens were positive for squamous cell carcinoma (25%).

Pathology. In the 3 patients with a regional CR and a neck dissection following treatment, 1 surgical specimen was positive on pathologic analysis (node of 7.5 cm at diagnosis). This patient is still alive without evidence of regional disease. In the 45 patients with a regional PR who underwent neck dissection following CRT, 60% (27 specimens) were negative on pathology. These 27 patients were free of regional disease at their last visit, but 2 of them died on follow-up (distant metastasis and pneumonia, respectively). Eighteen patients (40%) had a positive neck dissection specimen. Fifteen patients had their neck secured and were free of regional disease at last follow-up; 3 of them ultimately died (distant metastasis, hepatic encephalitis, and carotid blow-out). Despite neck dissection, 3 patients had progression of their regional disease and died of their disease.

No correlation could be established between the pathology results and the diameter of the largest node at diagnosis.

DISCUSSION

The overall regional control rate after CRT was 68%, which is comparable to data already published.10,21,22 When a regional CR following concurrent chemoradiation is reached, the overall risk of regional recurrence is very low (5%). Proponents of close observation of regional complete responders obtained similar results.22,23 Even studies using radiotherapy alone, with no neck dissection if regional CR post-CRT was reached, achieved similar results.24–26

In this study, the neck control rate was excellent with close observation of the regional CR after treatment for patients who had nodes 3 cm or less at diagnosis. Mendenhall et al27 observed that regional control rate was the same for patients treated with radiotherapy alone and radiotherapy with subsequent planned neck dissection for this subgroup.

Management of nodes from 3.1 to 6 cm following therapy is much debated. The decision to perform a neck dissection relies on the accurate and reliable evaluation of the status of the neck after completion of the treatment. This group of patients, when achieving a regional CR, had a low risk of neck recurrence. Only 5% had evidence of regional disease at last visit. Hence, for the group of patients with nodes 3 cm or less, we do not think that systematic neck dissection is necessary when a regional CR is reached.

However, for patients with nodes larger than 6 cm, CR to concurrent chemoradiation was less frequent than in the other subgroups coinciding with a poorer prognosis, as already shown by Ahmed et al and Chan et al.17,28 Overall, the risk of regional recurrence on follow-up is higher than for nodes less than 6 cm (18 vs. 9%). Looking only at the patients with regional CR who did not have a neck dissection, the occurrence of neck failure was 9%. Even without systematic neck dissection, these patients had a low rate of regional recurrence on follow-up.

Ahmed et al17 evaluated the outcome of N3 disease following concomitant CRT. They observed 23 N3 patients who were rendered free of disease after CRT. No neck dissection was performed on patients who reached a regional CR following treatment. No regional recurrence was noted on follow-up. One patient had a recurrence at the primary site and 11 patients had recurrence at distant sites. Our results concur with those of Ahmed et al. This calls into question systematic neck dissection for the N3 patients who reach a regional CR following CRT. Up to now, no data have shown significant benefits on regional recurrence, disease-free survival, and overall survival rates. In our institution, we tend to endorse the position of Ahmed et al: close observation of the N3 patients.
who reach a regional CR after CRT. However, since the number of patients in that subgroup is relatively small, further longitudinal studies need to be conducted before definitive conclusions.

Neck dissection is associated with potentially very morbid complications. The rate of surgical complications reported in the literature ranges from 26% to 61%, such as healing complications requiring surgical intervention for ultimate closure and non–wound healing complications, including tracheotomy, cranial nerve transection or paresis (X–XII), and permanent hypocalcemia.29–31 These rates are much higher than the risk of a possible regional failure. As already mentioned, the risk of regional recurrence was low (5%) in this study. Mendenhall et al32 withheld neck dissection if the risk of neck recurrence for a patient with regional clinical and radiological CR following treatment was thought to be 5% or less.

Finally, at the moment, whether to perform a neck dissection or not is almost a matter of opinion. In our institution, we consider that systematically submitting every patient to a surgery associated with significant morbidity and even mortality to salvage the 5% at risk of regional recurrence is not indicated. Our results suggest that patients with nodes 6 cm and less at diagnosis who reach regional CR should only be closely observed with frequent follow-up and a baseline CT scan. This is in agreement with the findings of Argiris et al, who demonstrated that neck dissection had no significant impact on the outcome of N2 patients treated with concomitant chemoradiation who achieved a regional CR.33 Similarly, for the patients with nodes larger than 6 cm who reach a regional CR after CRT, our results suggest that close observation would be an appropriate therapeutic option. This supports the view of Corry et al: “Unnecessary neck dissection is unnecessarily morbid and cannot be condoned on the basis that they are safe and effective.”

In patients with a regional PR following treatment, we showed that neck dissection reduces the risk of subsequent neck failure to a rate near the 1 patient who achieved a regional CR after CRT. This is particularly accurate if the pathologic results were negative. In fact, none of these patients had regional recurrence on follow-up. The regional PR who had pathologically positive nodal disease in the neck dissection specimen had a higher risk of regional failure and consequently, a poorer outcome. This correlates the results of other studies.34 No correlation was established between the pathologic analysis and the diameter of the largest node at diagnosis. This correlates with the results of other studies.35,36

CONCLUSION
Our results demonstrate that patients reaching a regional CR following concomitant chemoradiation, regardless of the size of the nodal disease at diagnosis, have a low rate of regional recurrence. Patients with nodes 6 cm or less and a regional CR post-CRT have little benefit from neck dissection. Close observation of these patients is our practice. For patients with nodes more than 6 cm and a regional CR, a firm recommendation cannot be made since the number of patients in this subgroup was relatively small. On the other hand, patients who achieve a regional PR posttreatment must have a neck dissection whenever possible. Patients with a regional PR, who following a neck dissection have a positive pathologic specimen, have the worst prognosis. More aggressive therapeutic options, such as targeted therapy, must be explored for these patients.

REFERENCES
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