The Use of Clinical Criteria Alone in the Management of the Clinically Negative Neck Among Patients With Squamous Cell Carcinoma of the Oral Cavity and Oropharynx

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Background: Management of the clinically negative neck among patients with oral and oropharyngeal squamous cell carcinoma at the Royal Prince Alfred Hospital, Sydney, Australia has been based on the site and stage of the primary cancer, the likely incidence of microscopic nodal involvement, the treatment modality used for the primary cancer, and whether the neck will be entered during resection or reconstruction. This report analyzes the results of treatment when patients are allocated to either treatment or observation of the neck based on these clinical factors.

Methods: This is a prospectively documented series of 162 consecutively treated patients with squamous cell carcinoma of the oral cavity and oropharynx and clinically negative necks, treated by 1 surgeon (C.J.O.). There were 128 oral cavity and 34 oropharyngeal cancers clinically staged at T1 for 62 patients, T2 for 61, T3 for 16, and T4 for 23 patients. Management of the neck consisted of elective neck dissection (END) in 96 patients (12 bilateral), elective radiotherapy in 8, and observation in 58. Neck treatment correlated with the T stage in a statistically significant way. Forty-six patients underwent postoperative radiotherapy, which was directed to the neck in 22 patients because of pathological findings following neck dissection. Free-flap reconstruction was used in 90 patients.

Results: Metastatic squamous cell carcinoma was identified in 32 of 108 neck dissections (30%). There was 1 positive node in 15 necks, 2 positive nodes in 11 necks, and 3 or more positive nodes in 6 necks. Extracapsular spread was present in 8 of 32 positive END specimens (25%). Regional control rates in the neck at 3 years were 94% for END, 100% for elective radiotherapy, and 98% for patients initially observed and then treated by therapeutic neck dissection. Death with uncontrolled disease in the neck occurred in 4 of 96 patients (4%) after END and 1 of 58 patients (2%) after neck observation. Overall disease-specific survival was 83%, comprising an 86% rate for patients with pathologically negative necks and 68% if pathologically positive. Disease-specific survival was 86% at 3 years for patients having END, 67% following radiotherapy, and 94% for the observation group.

Conclusions: Elective neck dissection was performed in most patients, and occult metastatic disease was found in nearly 30% of neck dissections. Observation was most frequently used for patients with early stage disease, and subsequent development of neck metastases was uncommon (9%) in this group. Selective treatment of the clinically negative neck based on the primary tumor site and stage led to a high rate of regional disease control in this series.

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Head and neck oncologists continue to debate the appropriate management of the clinically negative neck among patients with mucosal squamous cell carcinoma (SCC) of the upper aerodigestive tract. Various therapeutic approaches are available, but the quality of data supporting any particular strategy is quite variable. Clinicians are therefore guided as much by personal philosophy and local custom as by scientific evidence.

Broadly, there are 3 management options. The first is observation, reserving therapeutic neck dissection for only those patients who subsequently develop metastatic disease in the neck. The second option involves staging and reserving definitive treatment for those who are found to have subclinical disease in the neck. Staging may involve computed tomography (CT), ultrasound-guided fine-needle aspiration biopsy, or a “staging” neck dissection. In the latter case, a selective neck dissection is usually appropriate, but it is a controversial issue whether this surgery is a staging or a therapeutic procedure. The third option is to electively treat the neck using either neck dissection, radiotherapy, or both.

In reality, all of these strategies may be appropriate, depending on the clinical...
PATIENTS AND METHODS

Since 1988, all clinicopathological data concerning patients treated in the Department of Head and Neck Surgery, Royal Prince Alfred Hospital, Sydney, Australia, have been prospectively entered into a comprehensive database. To date, over 3500 patients have been registered. For the present study, all patients with clinically negative necks and SCC of the oral cavity or oropharynx, treated by 1 of us (C.J.O.) between January 1988 and March 1997, were identified. Patients who were previously treated, those with clinical metastatic disease in the neck and/or those with more than 1 primary cancer, and/or those followed up for less than 2 years were excluded.

A total of 162 patients met the criteria for inclusion and make up the study group. There were 109 men and 53 women, with a median age of 62 years (range, 30-86 years). Median follow-up time was 38 months (minimum, 18 months). The primary tumor sites are listed in Table 1, with the oral tongue and the floor of the mouth most frequently involved. The clinical T stages before treatment were: T1 in 62 patients, T2 in 61, T3 in 16, and T4 in 23 patients.

Management of the neck was based on the site and stage of the primary cancer, and an attempt was made to use 1 treatment modality for the primary cancer and the neck. The principal indicator for elective neck treatment, surgery, or radiotherapy was a risk of metastatic disease of 20% or more. If the risk of metastatic disease to the neck was low, a policy of observation was followed, which involved regular clinical follow-up, usually at 6-week intervals for the first 2 years. All patients treated with definitive radiotherapy to the primary site had at least partial neck irradiation. The extent of elective neck surgery varied over the course of the study period. For patients with oropharyngeal cancers, modified radical dissection was initially used, that is, a comprehensive dissection of all 5 neck levels preserving the internal jugular vein and spinal accessory nerve but sacrificing the sternomastoid muscle. Selective dissection of levels I through IV was later used for oropharyngeal cancers and remains our preferred END in this patient group. For oral cavity cancers selective dissection of levels I through IV was used initially but, because none of the early patients had disease at level IV, only levels I through III (supraomohyoid dissection) were dissected subsequently, and this remains our preferred neck dissection method for patients with oral cavity cancer and N0 necks.

When pathological examination of the neck dissection specimens revealed multiple involved nodes or extracapsular spread, postoperative radiotherapy to the neck was given. Histologically negative necks were not irradiated; however, postoperative radiotherapy was frequently used for the primary site based on the following criteria: advanced stage at presentation (T3 or T4), positive or close surgical margins, perineural spread, and/or an irregular pattern of tumor invasion. Radiotherapy fields in these circumstances usually incorporated the primary site and the so-called first echelon nodes, ie, the nodes at levels I and II.

Recurrence and survival data were calculated using the Kaplan-Meier method. The site of recurrence was considered the most proximal site. The log rank test was used to compare recurrence and survival rates, and multivariate analysis using logistic regression was used to assess the impact of clinicopathological factors on neck control and survival. Factors analyzed included patient age and sex, primary tumor stage, tumor site, surgical margins, vascular invasion, lymphatic invasion, perineural spread, presence of occult cervical metastases, extracapsular spread, multiple nodal involvement, and the use of postoperative radiotherapy.

<table>
<thead>
<tr>
<th>Tumor Site</th>
<th>Oral Cavity</th>
<th>Oropharynx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral tongue</td>
<td>51</td>
<td>8</td>
</tr>
<tr>
<td>Floor of mouth</td>
<td>37</td>
<td>15</td>
</tr>
<tr>
<td>Alveolus</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>Retromolar trigone</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Lip</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Multiple sites</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>128</td>
<td>34</td>
</tr>
</tbody>
</table>

PATIENTS AND METHODS

circumstances, and so a blanket policy that incorporates only 1 approach for all patients is inappropriate. Issues that confound the debate about elective neck treatment include the following: (1) a lack of evidence from a prospective randomized clinical trial that elective neck treatment improves survival; (2) the additional costs and morbidity of this treatment; and (3) the fact that many patients who have elective neck dissection (END) do not have microscopic disease and, therefore, seem not to benefit. In support of elective neck treatment, however, is the fact that when patients initially managed by observation subsequently return with nodal involvement, their metastatic disease is often advanced, making regional control more difficult. In addition, the increasing use of microvascular free flaps for reconstruction in the oral cavity and oropharynx has meant that the neck is very frequently entered for the reconstructive procedure, and therefore it is appropriate to remove the at-risk nodes during surgical treatment of these patients.

It is our view that the treatment of the neck should not be seen in isolation but rather in the context of the overall management plan. We have described our early experience using such a comprehensive treatment strategy.3
threshold for treatment of the clinically negative neck is when there is a 20% or greater risk of occult disease. This recommendation was based on an analysis of the utility of the management options taking into account the incidence of node involvement, complications of treatment, and disease control rates. This 20% threshold would include most oral cavity cancers staged T2 or higher and nearly all oropharyngeal cancers, including those staged T1. For the past decade, the policy in our department has been to base the management of the clinically negative neck almost exclusively on clinical criteria. Elective neck dissection is recommended when the primary cancer is treated surgically and/or the risk of metastatic disease is 20% or greater. The decision to perform END is based on the tumor site and stage and/or when the neck is entered to facilitate resection of the primary tumor or reconstruction. When radiotherapy is the preferred treatment for the primary site, which is uncommon in our practice, and the risk of metastatic disease is substantial, elective treatment of the neck with radiotherapy is recommended. When the risk of metastatic disease is low, less than 20%, and it is not necessary to enter the neck for resection or reconstruction, observation is recommended. Staging of the neck by means of CT scanning or ultrasound-guided fine-needle aspiration biopsy is never used.

The aim of the present study is to evaluate this treatment approach among patients with primary SCC of the oral cavity and oropharynx and to analyze the rate of control of metastatic disease in the neck in these various clinical settings. It is not the intention of this article to advocate one approach over another, but rather to assess the efficacy of the selective use of neck dissection, radiotherapy, and observation based on clinical criteria.

### RESULTS

A total of 162 patients with primary SCCs of the oral cavity and oropharynx and no evidence of neck metastases were evaluated. Treatment of the primary cancer included surgery alone in 108 patients, surgery and postoperative radiotherapy in 46, and radiation alone in 8.

**Table 2** details management of the neck. Overall, 108 neck dissections were performed in 96 patients (12 bilateral dissections), with 22 patients receiving postoperative radiotherapy to the neck. The neck was observed in 58 patients, and elective irradiation was used in the 8 patients who had definitive radiotherapy to the primary tumor.

**Table 3** outlines the management of the neck based on T stage. A greater proportion of patients with advanced cancers received treatment to the neck while the necks of patients with smaller tumors were more often observed. That is, T stage was significantly predictive of the type of neck management chosen (p < .05). However, 11 patients with clinical T1 cancers had ENDS, and 7 patients with cancers staged T2 or more did not have neck treatment. Among the T1 patients, 2 had oropharyngeal cancers and had a risk of metastatic disease of 20% or more. Five other patients with bulky T1 cancers of the oral cavity had free-flap reconstruction, necessitating entry into the neck. In 3 other patients with midline T1 floor-of-mouth cancers, resection of the primary tumor involved resection of the submandibular duct openings. Rather than reimplanting the ducts or leaving obstructed submandibular salivary glands in situ, a decision was made to carry out bilateral selective dissections of levels I through III. The aim was to remove the submandibular glands within the framework of an oncologically sound operation, even though the likely risk of occult metastatic disease was less than 20%. Finally, 1 patient with a T1 tongue cancer had partial glossectomy with primary closure and an END because follow-up was expected to be unreliable.

In the group of 7 patients staged T2 or more who did not have any neck treatment, 4 patients had superficial T2 tongue tumors, 1 had localized alveolar cancer staged T4 because of local bone invasion, 1 had a bulky but entirely exophytic T3 alveolar cancer, and 1 had a midline lower lip cancer staged T2. In each case the cancers were locally excised, and the defect was either primarily closed or grafted.

**Table 4** details the types of ENDS carried out. The most commonly performed procedures were selective dissections of nodal levels I through III and I through IV, preserving the sternocleidomastoid muscle, the internal jugular vein, and the spinal accessory nerve. Complications following END occurred in 6% of dissected necks. These included 3 hematomas, 3 wound infections, and 1 chyle leak. Free-flap reconstruction was undertaken in 90 patients.

Metastatic SCC was identified in 32 (30%) of 108 neck dissections. The anatomical distribution of in-
volved nodes, as a percentage of the number of times each level was dissected, is given in Table 5. Level II was most often involved, with a frequency of 18%, while level IV was involved with positive nodes in only 5% of cases in which it was dissected. Level V was never histologically involved. Level IV involvement never occurred in isolation and was only associated with the presence of nodal disease at higher levels. The incidence of pathological node involvement did not correlate significantly with T stage or primary tumor site (Table 6).

The cumulative rate of tumor control at the primary site at 3 years was 83% overall. Control rates in the neck at 3 years were 96% among patients who had elective dissection, 100% for radiotherapy alone, and 98% in the observation group where therapeutic neck dissection was performed after metastatic disease developed (Figure 1). Four patients (4%) developed neck recurrence after END. All had pathologically positive necks and all recurred in the dissected field. Two patients had been treated by neck dissection alone while the other 2 received postoperative radiotherapy. Multivariate analysis was performed, but no specific factor was predictive for neck recurrence among patients who had END. Salvage therapy was unsuccessful in each case, and all patients subsequently died of disease. Therefore, 4% of the electively dissected group died with uncontrolled disease in the neck.

A single pathologically positive node was found in 15 of the 32 histologically positive specimens following END. These nodes occurred at level I in 5 patients, level II in 7 patients, and level III in 3 patients. Five patients in this group had postoperative radiotherapy to the primary site and neck. Three of these are alive without evidence of disease, while 2 patients have died of tumor recurrence at the primary site. Ten of the 15 patients found to have a single positive node did not have postoperative radiotherapy to the neck, and no patient in this group has developed recurrent disease in the neck. Two died of recurrence at the primary site, 1 died of a noncancer illness, and 7 remain alive without evidence of disease. There were no instances of recurrence among the patients treated with radiotherapy, but failure at the primary site occurred more frequently in this group.

Five of the 58 patients (9%) in the observation group went on to develop cervical metastases. Four of these patients had clinical stage N2 disease when they presented and 1, who failed to attend follow-up, presented with N3 disease—a massive metastatic node at level III involving skin. Comprehensive neck dissection and radiotherapy were necessary to adequately treat the neck in each case. Disease has been controlled in 4 of these 5 patients, but 1 developed recurrent disease in the neck and died. Therefore, 1 (2%) of 58 patients has died of uncontrolled neck disease.

Overall disease-specific survival was 83% at 3 years, and this was influenced by T stage (Figure 2) and, among patients undergoing END, by the presence of pathologically involved nodes. The actuarial survival results based on the 3 different options of neck treatment are not directly comparable because the clinical T

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**Table 5. Pathological Nodal Distribution for 108 Neck Dissections**

<table>
<thead>
<tr>
<th>Level</th>
<th>No. Dissected</th>
<th>No. (%) Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>108</td>
<td>11 (10)</td>
</tr>
<tr>
<td>II</td>
<td>108</td>
<td>19 (18)</td>
</tr>
<tr>
<td>III</td>
<td>108</td>
<td>9 (8)</td>
</tr>
<tr>
<td>IV</td>
<td>52</td>
<td>3 (6)</td>
</tr>
<tr>
<td>V</td>
<td>13</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

**Table 6. Correlation of Pathological Node Status With T Stage and Site**

<table>
<thead>
<tr>
<th>T Stage</th>
<th>No. Dissected</th>
<th>No. (%) Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11</td>
<td>3 (27)</td>
</tr>
<tr>
<td>2</td>
<td>51</td>
<td>18 (35)</td>
</tr>
<tr>
<td>3</td>
<td>13</td>
<td>5 (38)</td>
</tr>
<tr>
<td>4</td>
<td>21</td>
<td>5 (24)</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>75</td>
<td>25 (33)</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>21</td>
<td>5 (24)</td>
</tr>
</tbody>
</table>

**Figure 1.** Cumulative rates of neck control for the 3 groups treated by elective dissection (n = 96), radiotherapy (n = 8), or observation (n = 58). By 2 years, the respective numbers of patients available for analysis had decreased to 66, 6, and 33; by 4 years, 30, 6, and 24; and by 6 years, 10, 3, and 11.

**Figure 2.** Cumulative survival according to clinical T stage of primary cancers. The respective numbers of patients at risk at the start of the study for T stages 1 through 4 were 62, 61, 16, and 23. At 2 years these respective numbers were 44, 45, 8, and 12; by 4 years they were 30, 23, 4, and 3; and by 6 years, 14, 9, 0, and 1.
The appropriate management of the clinically negative neck among patients with SCC of the oral cavity and oropharynx continues to be a therapeutic challenge. The intention of this article is not to advocate one approach over another but rather to assess the efficacy of selectively treating or observing the neck based on clinical criteria alone. It has not been our practice to attempt to stage the neck by radiological imaging. Magnetic resonance imaging and CT scans are by no means 100% accurate and, in our practice, we believe their usefulness as a staging tool would be very limited. A negative neck CT scan would not preclude END in a patient with a T2 oral cancer and, equally, positive CT scan results are unlikely in patients with T1 oral cancers, thus raising questions of cost-effectiveness. We have recommended that management of the neck be included in the overall treatment strategy for the primary cancer, rather than being viewed in isolation.

The principal aim of treating the clinically negative neck, either by surgery or radiotherapy, is to maximize the rate of control of disease in the neck. Whether this contributes to improved survival remains unproved. However, it is our view that this is of little consequence because there are several other benefits. Among surgically treated patients selective neck dissection facilitates the use of mandibulotomy and mandibular swing, giving access to the posterior oral cavity and oropharynx, and also the use of microvascular free tissue transfer, by allowing isolation of recipient blood vessels in the neck. In both instances, the END obviates the need to subsequently return to the neck should metastatic disease develop. In addition, useful pathological information about the extent of neck disease can be obtained, facilitating selection of patients for adjuvant neck irradiation or systemic therapy.

Our improved understanding of the patterns of metastatic spread in the neck has greatly facilitated the use of selective neck dissections in the prophylactic setting. Supraomohyoid dissection (levels I-III) is widely accepted as the appropriate selective neck dissection for patients with oral cavity cancer and a clinically negative neck. There has been recent debate about whether level IV should be dissected in patients with oral cavity cancer involving the tongue, since a report by Byers et al suggested that involvement of levels III and IV among patients with tongue cancer occurs more frequently than expected and may be a cause of recurrence following supraomohyoid neck dissection. The present experience does not demonstrate a high likelihood of failure at level IV following supraomohyoid neck dissection for oral cavity cancer. In fact, it was previously the practice of one of us (C.J.O.) to carry out selective neck dissection of levels I through IV for both oral and oropharyngeal carcinomas. The technique and indications for this procedure have been described, but because histologically positive nodes have not been demonstrated at level IV, supraomohyoid neck dissection has become our preferred procedure. Since that operation has been used, the development of recurrent disease at level IV has not occurred, despite histologically negative nodes being found at levels I through III. It is recognized, however, that the reported incidence of failure at level IV, in the absence of nodal involvement of levels I through III, is approximately 5%. Certainly, adding the dissection of level IV to a supraomohyoid neck dissection is not technically difficult and adds only a little time to the operative procedure. Individual surgeons will decide their own philosophies in this regard, and our only point is that we have not found it oncologically necessary in our oral cavity cancer group. Among patients with oropharyngeal cancers, however, the likelihood of involvement of level IV nodes approaches 10% in the clinically negative neck. Supraomohyoid dissection is therefore probably not adequate for these patients.

The important issue of whether selective neck dissection is oncologically effective cannot be answered from the present study. A critical question is whether additional treatment to the neck should be given to patients following selective neck dissection in which a single histologically positive node has been found. Patients with multiple positive nodes do not pose this problem because standard practice dictates that they receive adjuvant radiotherapy to the dissected neck, probably bilaterally. The presence of a single positive node without extracapsular spread, however, is not normally an indication for adjuvant radiotherapy, but if the neck has not been completely dissected, further metastatic disease may be present in 1 of the undissected node levels. Again, the main concern is that disease will recur at level IV. In the
present study, 15 patients had a single positive node in their selective neck dissection specimen. Five of these qualified for postoperative radiotherapy because of the presence of extracapsular spread, but 10 had no additional treatment, including 3 patients whose single positive node was at level III. However, the fact that none of these 10 patients experienced recurrence in the neck may be due more to luck than good management. The alternatives in this clinical setting are to do nothing further to the neck, to give radiation to the neck, or to go back and complete the neck dissection. Our current policy is to do nothing further to the neck if the single positive node is at level I or II, but to irradiate the entire neck if the single positive node is at level III or IV. It may be best to avoid supraomohyoid neck dissection and routinely dissect level IV at the initial operation to avoid the dilemma created when a single positive node is found at level III.

When elective radiotherapy is given to the neck, it is important that radiation oncologists observe the same principles as surgeons and incorporate treatment to all the at-risk nodal groups. It would not be logical to simply include the “first echelon of nodes” related to the primary cancer. Good communication between the surgeon and radiation oncologist is therefore important in this setting.

Finally, if a policy of observation is used selectively and applied mainly to patients with early stage disease, few patients will fail in the neck. It is important, however, that patients in this group are observed closely and are not lost to follow-up. Close follow-up will allow early detection of metastatic disease and reduce the likelihood of the being very advanced neck disease when it first detected. However, a likelihood of poor follow-up is, we believe, a valid reason for electively treating the neck.

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REFERENCES