LETTERS TO THE EDITOR

ELECTIVE NECK DISSECTION IN EARLY-STAGE ORAL SQUAMOUS CELL CARCINOMA

To the Editor:

We read with great interest the paper by Capote et al. The elective neck dissection in clinically N0 early-stage squamous cell carcinoma of the oral cavity is indeed a very interesting and challenging topic. Selecting the patients with high risk of positive lymph nodes is the best way to avoid performing a neck dissection in all the cases, and sentinel node mapping may help to accomplish this. Some evidence supports clinical and pathological features (such as tumor thickness) as predictors of tumor aggressiveness. Other prognostic factors as well as the significance of early disease in the lymph nodes are still under investigation.

This article helps emphasize accumulating evidence that delayed lymph node metastasis portend a particularly poor prognosis. However, we are concerned by 1 aspect of the study design that makes it almost impossible to accurately interpret the results: in Materials and Methods, the authors mention that patients with positive lymph nodes were excluded from the study. With this, all previously staged clinical N0 (cN0) upstaged to pathological N positive (pN+) after a neck dissection are excluded, making the 2 groups incomparable. This results in comparing a group of pN0 (with confirmed absence of disease in the neck) to a group cN0 (in which some patients may have microscopic disease in the neck). It is thus expected to see that the group with neck dissection does better than the control group. Similarly, it can be anticipated that the control patients will have more neck recurrences than those who were treated with a neck dissection, and were pN0 (because the patients with pN+ were excluded). Therefore, it is not possible to conclude that the neck dissection per se was associated with better outcome.

Moreover, the patients who did not have a neck dissection had a higher recurrence rate at the primary site, which theoretically has nothing to do with the neck dissection. The authors did not comment on this or test for significance nor did they compare the 2 groups with regard to primary tumor characteristics such as thickness or perineural spread. Assuming equivalent technique for the transoral resection of the primary tumor, an additional explanation for the differences in regional recurrence and survival could be that the control group had more aggressive tumors. This further reinforces the fact that the groups may not be comparable to start with.

In the discussion, the authors infer that the “rate of occult lymph nodes metastases was 26.8%, because it was the incidence of neck recurrences in the group of watchful-waiting policy of the neck.” This inference overlooks natural tumor progression if disease persisted at the primary site, patients were lost to follow-up, or patients died from unrelated conditions. To estimate the percent of occult lymph node metastases, it would have been more accurate to study the cN0 group.
who underwent a neck dissection and review the number of patients whose disease was upstaged to pN+. Even this would have been inaccurate because of the selection bias, but one could have said that this is the incidence of pN+ in patients with cN0 when a neck dissection was performed.

We would be very much interested in seeing the results of this group with inclusion of patients with pN+ in the neck dissection group. Not only would it make the groups more comparable, but it would also help answer the important question of whether there is a significant difference in outcome between initial neck dissection versus salvage neck dissection after neck recurrence in watchful waiting policy.

The importance and clinical significance of micrometastases (cN0 pN+) in oral cavity squamous cell carcinoma is being elucidated. This is more thoroughly studied with the advent of sentinel lymph node biopsy prior to performing selective neck dissection. Finally, it is important to mention tumor thickness as a prognostic factor in early-stage oral cavity squamous cell carcinoma, since there is evidence supporting it.

Despite the limitation of retrospective institutional studies on head and neck cancer, good study design and careful interpretation of the results are of utmost importance. This is the only way to learn from past experience and big case series, and the most effective way to develop a knowledge base for prospective study design.

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Reply:
We also read with great interest the Letter to the Editor, by Dr. Sargi et al, about our article, “Elective Neck Dissection in Early-Stage Oral Squamous Cell Carcinomas—Does It Influence Recurrence and Survival?” However, we have some clarifications regarding their comments on the study design and patient selection.

Our aim was to study the influence of neck dissection therapy on the prognosis of early-stage oral carcinomas. Classically, elective neck dissection has been recommended in all T3 and T4 oral squamous cell carcinomas, but its effect in T1 and T2 carcinomas has been controversial. Recent studies have demonstrated that neck recurrence in patients with small tumors <4 cm and with negative necks is not unheard of and that neck relapse plays a role in poor survival rates. Our aim was to demonstrate the positive effect of performing a prophylactic neck dissection in patients with those tumors in which the disease is confined to oral mucosa (early-stage), which according to the classic literature should have a good prognosis.

We considered all histologically confirmed pT1N0M0 and pT2N0M0 cases as early-stage. In the group of patients in which no neck dissection was performed, we selected tumors smaller than 4 cm after histological examination (pT1 and pT2). In this group, we have to assume a clinically negative neck, confirmed radiologically, in which local resection alone with wide margins was the indicated therapy. In the group of patients with neck dissection, we selected only patients with pT1N0M0 and pT2N0M0 disease that met the 2 criteria for early-stage (stage I and II): tumors smaller than 4 cm (T classification) and pathologically negative neck (pN0), as a pN+ status is considered to be advanced stage (stages III and IV). We did not consider pN+ cases because they were not early-stage and thus beyond the purpose of our study.

We understand that the cN0 group may have microscopic disease in the neck and subsequent recurrence, but in this study we sought to determine whether these differences in recurrence and survival were statistically significant, which
would lead us to reevaluate indications for neck dissection. Therefore, the main characteristic between the 2 groups is that the tumors were of comparable size, T1 and T2 tumors smaller than 4 cm, the main factor of early-stage. We showed that, in these cases, neck dissection also influenced the prognosis. Certainly, it would be of interest to perform another study including all stages (pN+ patients) to compare neck dissection treatment, and it would be an aim of our team for future investigations.

Regarding the comment in the third paragraph in which the authors asked about the significance of higher local recurrences in the no-neck-dissection group: we included these data for descriptive purposes; a comparative analysis was not an aim of the study. Probably, this difference is related to differences in tumor aggressiveness that may exist between the 2 groups, and the study of prognostic factors could be of great interest, as tumor thickness or perineural spread which would also be analyzed in future studies.

The implications of sentinel lymph node biopsy in oral squamous cell carcinoma have been the main subject of several studies. Its value has been demonstrated in other tumors, such as cutaneous melanoma, but the results in oral cancer remain controversial. In this way, we have to consider that skip metastases in intraoral tumors are not infrequent and that positive nodes may appear in unusual lymph node levels than tumor drainage. Thus, we must interpret the results of this technique with care, and elective neck dissection is probably the main classification method that we have at present. This is another reason that supports elective neck treatment in early-stage disease and that allowed our study.

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