To Operate or Not to Operate N0 Neck in Early Cancer of the Tongue? A Prospective Study

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Abstract Squamous cell carcinoma (SCC) of the tongue is a common cancer across the globe. These cancers have a high predilection for nodal metastasis and a high incidence of occult metastasis. The management of clinically negative neck nodes (N0) remains controversial. We have undertaken a prospective study to evaluate the rate of occult nodal metastasis, the characteristic of metastasis, and assess the usefulness of tumor depth as a predictor of metastasis and as a guide to treat the neck. Prospective study between January 2000 to December 2005. Patients with SCC of the anterior 2/3rd of tongue with N0 neck were included. Wide excision of the primary and subsequent modified radical neck dissection (in patients with tumor depth >4 mm) was performed. Postoperative radiotherapy was given in patients with lymph node metastasis. Patients who had no node metastasis (p N -ve) were observed. The total number of eligible patients was 180. Occult lymph node metastasis (p N +ve) was seen in 122 (62.2%) patients ($p < 0.001$), multiple levels of node involvement in 79 (70.5%) patients and extracapsular spread (ECS) in 38 (33.6%) patients. Patients in the p N +ve group who were disease free was 63.1% as compared to 68.2% in the p N -ve group ($p = 0.36$). Recurrence was seen in 28 (36.8%) patients of p N +ve group and 14 (31.8%) patients of p N -ve group. Early cancer of tongue with tumor depth >4 mm was associated

with predominantly high grade tumors, high incidence of occult nodal metastasis, multiple levels of nodal involvement and ECS. The disease free status of patients with occult metastasis who were treated was similar to that of patients with no nodal metastasis. Elective neck dissection appears essential for early oral tongue cancer with tumor depth >4 mm as there is no investigational modality which can reliably identify patients without occult metastasis.

Keywords Tongue cancer · Elective neck dissection · N0 neck · Oral cancer

Introduction

Cancer of the anterior two-thirds of the tongue is a common malignancy across the globe. Because of the rich vascular and lymphatic supply of the tongue, there is a high propensity for the cancer to spread to the cervical lymph nodes. The incidence of occult cervical lymphatic metastasis for early cancer is also higher when compared to other sites in the oral cavity [1]. Management of patients with clinically negative nodes (N0) with early tongue cancer is controversial. The various treatment modalities advocated include elective neck dissection (END), radiotherapy or wait and watch policy with therapeutic neck dissection in the event of neck recurrence. To date four randomized control trials (RCT) have been conducted to address this issue. Two of these included only cancer of the tongue [2, 3] and the other two [4, 5] have included other early cancers of the oral cavity. However, the results of these trials have not provided a satisfactory answer to the controversy. Fakih et al. found that a tumor depth of greater than 4 mm was associated with higher potential of lymph nodal metastasis. They however did not find a survival difference if these patients were observed or subjected to

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END [2]. Studies have shown that a significant number of patients with early oral cavity cancers who are observed will develop neck recurrence and many of these patients will be of advanced stage with poor prognostic factors such as extra-capsular spread (ECS) [6]. The salvage rates in these patients with recurrences were found to be only 30% [1]. We feel that early cancers of the tongue with tumor depth >4 mm constitute a high risk group requiring elective treatment of the neck. We undertook this single institute prospective study in this subset of patients i.e. early tongue cancer with tumor depth >4 mm and N0 neck. The aim of the study is to evaluate the rate of occult nodal metastasis and the characteristics of the metastasis. We also wanted to study the usefulness of tumor depth as a predictor of nodal metastasis and assess if it could be used as a guide to treat the neck.

Patients and Methods

This is a prospective study conducted between January 2000 and December 2005, at Kidwai Memorial Institute of Oncology, Bangalore. All patients with histologically proven squamous cell carcinoma of the anterior two-thirds of the tongue with N0 neck were included in the study. The nodal status of the neck was evaluated clinically by two experienced surgeons in all the cases. Informed consent was obtained from all the patients. The initial surgical management consisted of two stages. The first stage included wide excision of the tongue lesion and histopathological examination. Those patients who had a tumor depth of >4 mm underwent stage two of the treatment 6 weeks later. This stage consisted of a modified radical neck dissection sparing the internal jugular vein and spinal accessory nerve. The specimen was mounted and marked to identify the levels of lymph nodes. If the primary specimen showed positive margins, revision of the involved margins were done during this stage. Patients who were found to have lymph node metastasis (p N +ve) were given adjuvant radiotherapy. Patients with no lymph node metastasis (p N –ve) were observed. All patients were kept on close follow-up and evaluated periodically with clinical examination. Recurrences were proven by fine needle aspiration of the lesion.

The data was subjected to statistical analysis using SPSS (version 13.0). Univariate tables were generated. Comparison of two groups for statistical significance was done using proportions test. Any *p* value less than or equal to 0.05 was considered to be statistically significant.

Results

A total of 1819 cases of cancer of the anterior two-thirds of tongue were encountered by us. Of these, 217 (11.9%)

patients had N0 neck. The number of patients with tumor depth >4 mm was 211. The total number of patients who completed both stages of surgical management was 180 and this formed our evaluable group. The mean follow-up we had was 65.5 months. There were no post operative deaths. The male-to-female ratio was approximately 6:4 (106:74) with a male preponderance. The laterality of the lesions was right sided 98 and left sided 82. Ulcero-proliferative, ulcero-infiltrative and exophytic lesions accounted for 49.4%, 40.6% and 10% of cancers respectively. Lesions with infiltration of depth between 4 and 10 mm were 47 (48.3%), 11–15 mm depth were 72 (40%) and >15 mm were 21 (11.7%).

Table 1 shows the tumor grades in the primary lesion. Sixty (33.4%) patients had a tumor grade of III and 32 (17.7%) had a grade of IV. Margin positivity of the primary was seen in 27 (15%) patients and all these margins were revised during the second stage of surgery. Occult cervical lymph nodal metastasis was seen in 112 (62.2%) patients. Sixty eight (37.8%) patients had no metastasis in the lymph nodes ($p < 0.001$). The number of lymph nodes was one in 19 patients, 2 to 5 in 69 patients and greater than 5 in 24 patients. ECS was seen in 38 (33.9%) patients. Multiple levels of lymph node involvement were seen in 79 (70.5%) patients. Table 2 shows the different levels of lymph node involvement. Level II was the most common site involved (49 patients) and level IV was involved in 23 patients. Table 3 shows the follow-up data and recurrence pattern of the patients. The p N +ve group had 36 (32.2%) patients and the p N –ve group had 24 (35.3%) patients lost to follow-up. Patients found to be disease free in the p N +ve group were 48 (63.1%) and disease free in the p N –ve group were 30 (68.2%). This was not found to be statistically different ($p = 0.36$). Recurrences occurred in 28 (36.8%) patients in the p N +ve group and 14 (31.8%) in the p N –ve group. In the p N +ve group the recurrence occurred at the primary site in 18 patients, neck in 7 patients and both primary and neck in 3 patients. In the p N –ve group the recurrence occurred in the primary, neck and primary and neck in 10, 2 and 2 patients respectively.

Discussion

Cervical node metastasis in head and neck cancer is a poor prognostic feature and decreases the survival by 50% [7]. It

Table 1 Tumor grade of primary lesion ($n = 180$)

Tumor grade	Number (%)
Grade I	42 (23.4%)
Grade II	46 (25.5%)
Grade III	60 (33.4%)
Grade IV	32 (17.7%)

Table 2 Levels of lymph node involvement

Lymph node levels	Number
I a	03
I b	35
II	49
III	37
IV	23
V	05

is obvious that patients with clinically involved nodes require treatment of the neck. However, controversy exists in the management of patients with early cancers and N0 neck. Weiss et al. suggested that END is necessary if the incidence of occult metastasis is greater than 20% [8]. The proponents of wait and watch policy argue that 80% of patients with N0 neck would be over treated, and subjected to additional morbidity and costs. Though this argument may apply to most oral cavity tumors, the cancer of the tongue must be viewed as a separate entity. The incidence of nodal metastasis is higher for early cancer of the tongue when compared with other sites of the oral cavity. AK D’cruz et al. found the incidence of nodal metastasis to be 37.5% in T1 lesions and 62.5% in T2 lesions of the oral tongue [9]. Andersen et al. studied the results of neck failure following observation of N0 necks. They found that 60% of patients had N2 disease and 49% had ECS. Either or both these adverse prognostic factors were present at the time of surgery in 77% of patients [6]. The surgery required at this stage would be a more radical procedure with increased morbidity.

Four RCTs have been performed to compare END with wait and watch policy. Two of the trials were conducted purely on early oral tongue cancers. Fakih et al.’s study on T1 and T2 lesions compared END (radical neck dissection) with observation. They found that there was no survival difference between the two groups. They however found that a tumor depth of >4 mm was associated with higher rates of involved nodes and suggested that these set of patients may benefit from END [2]. A more recent RCT

from Hong Kong compared END (supra-omohyoid neck dissection) versus observation for T1 and T2 lesions of the oral tongue. They had a robust follow-up protocol of clinical and ultrasonographic examination of the neck to detect recurrences. They were able to salvage all neck recurrences in the observational arm and thus found no survival differences between the two arms [3]. All the above RCTs had small numbers and consisted of methodology flaws making their conclusions difficult to inculcate into clinical practice.

In our study we found that about 50% of patients with tumor depth >4 mm had grade III and IV tumors. The incidence of occult metastasis was 62.2%, which is significantly higher than for other subsites of the oral cavity. Thirty eight (33.9%) patients with occult metastasis had ECS, which is a poor prognostic feature. Another poor prognostic indicator we detected was multiple levels of nodal involvement in 79 (70.5%) patients. As expected most of the lymph nodes were localized to levels I, II and III. But level IV was involved in 23 patients. We therefore feel that if supra-omohyoid neck dissection would have been done, it might have been an inadequate procedure. In the mean follow-up period of 65.5 months we had almost one-third of patients lost to follow-up. Patients in the p N +ve group who were disease free was 63.1% as compared to 68.2% in the p N –ve group. This difference was not found to be statistically significant ($p=0.36$). This suggested that patients with occult metastasis when treated adequately have the same disease free status as those with no nodal metastasis. The recurrence pattern was not very different between the two groups.

It is evident from our data that 36% of patients had no neck metastasis. Unfortunately to date there is no investigational modality which can identify these patients and thereby avoid un-necessary surgery. The only investigation which has shown to have potential in identifying nodal recurrence is ultrasound of the neck with ultrasound guided fine needle aspiration cytology [10]. However, it is a highly operator dependent investigation. It also requires additional manpower and time, thus making its routine use difficult in a high volume cancer centre.

Table 3 Follow-up data ($n=180$)

	P N+ve (112)	P N –ve (68)
Mean follow-up	65.5 months	65.5 months
Lost to follow-up	36 (32.2%)	24 (35.3%)
Evaluable	76 (67.8%)	44 (64.7%)
No evidence of disease	48 (63.1%)	30 (68.2%) ($p=0.36$)
Recurrence	28 (36.8%)	14 (31.8%)
Primary	18	10
Neck	7	2
Primary + Neck	3	2

Conclusion

Cancers of the oral tongue with tumor depth of >4 mm should be considered as an entity separate from those of the other sites of the oral cavity. We found that most of the tumors are high grade with high incidence of occult cervical metastasis. The nodal metastasis involved multiple levels and had ECS in a significant number. Level IV was involved in a high number of patients thereby making only a supra-omohyoid neck dissection an inadequate procedure.

Patients with occult metastasis when adequately treated with surgery and adjuvant radiotherapy had the same disease free status as those with no nodal metastasis. There is no reliable investigational modality to accurately identify patients with occult nodal metastasis. We therefore conclude that patients with early cancer of the oral tongue with >4 mm tumor depth and N0 neck should be treated with END with clearance of ipsilateral cervical nodes of level I–IV. Wait and watch policy can be under taken in fully informed complaint patients and in institutions with facilities to provide a robust follow-up protocol.

Conflict of Interest None.

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