Original Article

The Correlation between the Depth of Invasion and Occult Lymph Node Metastasis in Anterior Tongue Cancer

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Objective: To determine the correlation between invasion depth and occult lymph node metastasis in anterior tongue cancer, and to establish the optimal tumor-depth cutoff that predicts nodal metastasis.

Materials and Methods: Retrospective analyses were done for two groups of patients with T1 and T2 clinical N0 oral squamous cell carcinomas of the tongue who were treated between June 1999 and November 2011. Thirty-nine patients were treated with glossectomy coupled with elective neck dissection as a prophylactic measure (the "END group"). Another 10 patients only had glossectomies as their primary treatment, with at least a 2-year follow-up (the "neck-observation group"). Pathological reports were reviewed for the invasion depths at the tongue lesions. Occult cervical node metastasis was defined by node metastasis in neck specimens in the END group, and by recurrence in the neck-observation group.

Results: In the END group, the overall lymph node metastatic rate was 30.8% (n=12/39). The mean invasion depth in positive nodal metastasis was greater than in negative nodal metastasis at 8.68±4.3 mm versus 7.66±3.6 mm, but without significance (p=0.44). As to the neck-observation group, the invasion depth of the 10 patients was 2 to 9 mm (mean 4.4±2.32), and cervical lymph node metastasis occurred in 40%. There was a high incidence of occult metastasis for all tumor depths in the END and neck-observation groups, with minimum depths 2 mm, but no significant correlations were found between nodal metastases and tumor depth.

Conclusion: There were no correlations between invasion depth and occult lymph node metastasis in T1 and T2 anterior tongue cancers. A high occult-metastasis incidence occurred for all invasion depth with minimal depth 2.0-mm.

Keywords: Cancer; Depth of invasion; Lymph node metastasis; Tongue

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Oral squamous cell carcinoma (OSCC) is the sixth most prevalent cancer worldwide. In Asian countries, this prevalence is up to 40%[1]. The oral tongue is the most common site cancer of the oral cavity[2]. In Taiwan, tongue cancer was found in 35.3% of OSCC[3]. Incidence of tongue cancer in Thailand is 2.2 and 1.0 per 100,000 in males and females, respectively[4]. It is aggressive and is associated with a high rate of cervical neck metastasis. The important prognostic factor for recurrence and survival rates is the presence of cervical lymph node metastasis[5,6], which has been shown to reduce the survival rate by approximately 50%[7]. Patients with pathologically negative neck nodes have lower rates of regional recurrence than those with occult node metastasis at 9% versus 50% ($p<0.01$)[8]. T1 and T2 tongue cancers are treated by surgery. Prophylactic neck dissection is recommended when there is a high incidence of occult metastasis at greater than 20%[9], but the procedure is still controversial for T1 and T2 tumors. A prior meta-analysis revealed that elective neck dissections (END) can effectively reduce the risk of death. That study also found that there is significant evidence that the procedure can reduce neck nodal recurrence[6]. Moreover, the reported incidences of occult lymph node metastasis in T1 and T2 tongue cancers have ranged from 22% to 36%[9-17]. Factors have been investigated to determine whether they can be utilized to predict cervical lymph node metastases. They include tumor size, tumor

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depth, and thickness, the grade of differentiation, and perineural and lymphovascular invasion. Microscopic depth of tumor invasion and tumor thickness were the only factors that were found to be significantly correlated with cervical node metastases[12,18,19]. Nevertheless, controversies remain about the use of histopathological depth to determine the existence of occult metastasis, as well as the necessity to perform ENDs[8,20,21].

Materials and Methods

Retrospective analyses were conducted of the medical records of patients who received surgical treatment for stages 1 and 2 (T1 and T2) OSCCs of the tongue at the Department of Otorhinolaryngology, Siriraj Hospital, between June 1999 and November 2011. The staging had been based on the Seventh edition of the American Joint Committee on Cancer (AJCC) cancer staging manual. The study excluded patients who also had other types of cancer, or who had been treated by surgery, irradiation, or chemotherapy that was related to head and neck cancer. In all, 49 patients were enrolled in the present study. Of these, a partial glossectomy with END was performed on 39 patients (the "END group"). The remaining 10 patients had a partial glossectomy alone as their primary treatment, followed by neck observation for at least two years (the "neck-observation group"). According to National Comprehensive Cancer Network (NCCN) Guideline Version 1.2021, END should be strongly considered in tumor with a depth more than 3 mm. For a depth less than 2 mm, elective is only indicated in highly selective situation. For a depth of 2 to 4 mm, clinical judgement is required to determine the suitability of END. In the present study, END depended on surgeon, but tended to have neck surgery in T1 with significant depth and T2, and tended to not operate the neck when T1 was with superficial invasion. Occult cervical node metastasis was defined by node metastasis in neck specimens in the END group, and by recurrence in the neck-observation group. All tissue blocks and slides that had been stained with hematoxylin and eosin were reviewed by a head and neck pathologist. In addition, an ocular micrometer was used to measure the depth of invasion (DOI) from the basement membrane of the normal tongue lining to the deepest part of the cancer.

Statistical analysis

Analyses were conducted of the associations between cervical metastasis and pathological characteristics, clinicopathological factors, and qualitative factors. The factors were gender, alcohol and smoking consumption, cancer stage, and tumor location and characteristics. Pearson's chi-squared test and Fisher's exact test were used for those analyses. As to the DOI and age, given that they were quantitative variable, a two-sample t-test was used for analysis purposes. Survival curves were plotted using the Kaplan-Meier method. Comparison of two survival curves was performed with the log rank test. Statistical calculations were made using SPSS Statistics for Windows, version 16.0 (SPSS Inc., Chicago, IL, USA).

Results

The present study enrolled 49 patients treated for T1 and T2 OSCCs of the tongue between 1999 and 2011. Thirty-nine were in the END group, and the remaining ten were in the neck-observation group. Demographic data of neck-observation group and END group is shown in Table 1. The END-group patients comprised 20 males (51%) and 19 females (49%). Their ages ranged between 23 and 81 (55.7±13.3) years. Most of cases (84.6%) did supraomohyoid neck dissection. Only 12.8% and 2.6% did modified neck dissection area I-V and extended supraomohyoid neck dissection, respectively. Lymph node involvement was found in 12 patients (30.8%). Fifteen patients (38.5%) were T1, while twenty-four (61.5%) were T2. The incidences of occult lymph node metastasis in the T1 and T2 patients were 4/15 (26.7%) and 8/24 (33.3%), respectively (p=0.734). The vast majority of the tumors were on the tongue border (36; 92.3%), two were located on the ventral aspect (5.1%), and one was on the dorsum (2.6%). The growth pattern was mostly ulcerative (21; 53.8%); eleven were exophytic (28.2%), while seven were endophytic (17.9%). The tumors were classified by histological grade into well-differentiated (17, 43.6%), moderately differentiated (19, 48.7%), and poorly differentiated (3, 7.7%). The overall mean DOI was 7.98±3.8 mm (range 2.5 to 16.2). For T1, the mean was 5.85±2.1 mm (range 2.5 to 11.2), whereas for T2, it was 9.30±4.0 mm (range 3.8 to 16.2; p=0.004; 95% CI –5.74 to –1.16). The mean maximal diameters of the T1 and T2 tumors were 1.63±0.35 cm (range 1 to 2) and 3.29±0.6 (range 2 to 4), respectively. The respective mean DOIs in the metastatic and non-metastatic lymph node subgroups were 8.68±4.3 mm and 7.66±3.6 mm. No significant predictive factors of occult lymph node metastasis were found (p=0.440, 95% CI –3.7 to 1.6). The minimum DOI of 2.5 mm was found in two patients, each had T1 cancer, and

Table 1. Demographic data of neck-observation group and END patients

Characteristics	Neck-observation patients (n=10)	END patients (n=39)	PN (–) (n=27)	PN (+) (n=12)	p-value*
Age (year); mean±SD	47.5±15.7	56.5±13.1	55.2±13.0	59.3±13.5	0.384
Sex; n (%)					0.557
Female	4 (40.0)	19 (48.7)	14 (73.7)	5 (26.3)	
Male	6 (60.0)	20 (51.3)	13 (65.0)	7 (35.0)	
Alcohol consumption; n (%)					0.269
No	8 (80.0)	26 (66.7)	16 (61.5)	10 (38.5)	
Yes	2 (20.0)	13 (33.3)	11 (84.6)	2 (15.4)	
Smoking; n (%)					0.872
No	8 (80.0)	22 (56.4)	15 (68.2)	7 (31.8)	
Yes	2 (20.0)	17 (43.6)	12 (70.6)	5 (29.4)	
T classification; n (%)					0.734
T1	8 (80.0)	15 (38.5)	11 (73.3)	4 (26.7)	
T2	2 (20.0)	24 (61.5)	16 (66.7)	8 (33.3)	
Tumor site; n (%)					0.680
Dorsal	1 (10.0)	1 (2.6)	1 (100)	0 (0.0)	
Right or left lateral	8 (80.0)	36 (92.3)	25 (69.4)	11 (30.6)	
Ventral	1 (10.0)	2 (5.1)	1 (50.0)	1 (50.0)	
Growth pattern; n (%)					1.0
Endophytic	1 (10.0)	7 (17.9)	5 (71.4)	2 (28.6)	
Ulcerative	7 (70.0)	21 (53.8)	14 (66.7)	7 (33.3)	
Exophytic	2 (20.0)	11 (28.2)	8 (72.7)	3 (27.3)	
Histological grade; n (%)					0.503
Well-differentiated	8 (80.0)	17 (43.6)	10 (58.8)	7 (41.2)	
Moderately-differentiated	2 (20.0)	19 (48.7)	15 (78.9)	4 (21.1)	
Poorly-differentiated	0 (0.0)	3 (7.7)	2 (66.7)	1 (33.3)	

END=elective neck dissection; PN (–)=pathological status of negative nodes; PN (+)=pathological status of positive nodes; SD=standard deviation

* Probability value of observed results in END group

one had occult nodal metastasis.

The END-group patients were followed up for between 2 and 199 months (mean 81). The primary sites margin were free in 31cases, close in four cases, and could not be assessed in two cases. There were 22 patients followed over five years without recurrent tumor. Seven patients were lost follow-up, nine patients had recurrence, and one patient died from other disease before five years. Locoregional recurrence was found in 9/39 (23%) cases. Of those, 5/39 (12.8%) were in the tongue, 2/39 (5.1%) were in the cervical neck region, and 2/39 (5.1%) were in both the tongue and cervical neck region. Five-year recurrent rate was 23%.

The recurrence periods ranged from 3 to 55 months (mean 16.9). The mean DOI for the no-recurrence subgroup was 8.0±3.7 mm, whereas that of the recurrence subgroup was 7.8±4.3 mm. However, a comparison between the two subgroups showed no statistical difference (p=0.85; 95% CI –2.69 to 3.23).

Metastasis to the cervical lymph nodes in the END-group females (26.3%) was less prevalent than in the males (35%), but it was not statistically significant (p=0.557). The incidence of cervical occult node metastasis in the smoking subgroup was lower than that for the non-smoking subgroup at 29.4% versus 38.5%. As to alcohol consumption, metastasis to the cervical lymph nodes was less frequently found among drinkers than non-drinkers at 15.4% versus 38.5%), but both factors were statistically non-significant (p=0.872 and 0.269, respectively). T2 cancer was found to have more occult node metastasis than T1 at 33.3% versus 26.7%, but this was also without statistical significance (p=0.734). As regards the lesion sites, because most tumors were located at the lateral tongue with only few elsewhere, metastasis to the cervical lymph nodes was inconclusive. The analysis of the growth pattern of the tumors revealed that the ulcerative subgroup had a 33.3% incidence of metastasis to the lymph nodes, followed by the endophytic at 28.6%, and exophytic subgroups at 27.3%. The review of the pathological characteristics

showed the well-differentiated subgroup had the highest lymph node metastasis at 41.2%. Even though the values for the poorly differentiated (33.3%) and the moderately differentiated subgroups (21.1%) were noticeably lower, the differences were statistically nonsignificant (p=0.503).

Of the 15/39 END-group T1-tongue-cancer patients, five were males (33.3%) and ten were females (66.7%). Their ages ranged between 34 and 78 years (mean 57.20±12.76). The respective mean DOIs for the metastatic and non-metastatic subgroups were 6.05±3.68 mm and 5.78±1.42 mm, but there was no statistical significance (p=0.835, 95% CI –3.00 to 2.46). The cutoff DOIs to discriminate between low and high risks for nodal metastasis in T1 cancer are listed in Table 2. Recurrence was found in 3/15 patients (20%) with one occurred in the tongue, another developed in the neck, and the third was located in both the tongue and neck.

In the case of the 24/39 END-group patients who had T2 tongue cancer, the mean DOI in the metastatic and non-metastatic subgroups were 10.01±4.2 mm and 8.95±4.1 mm, respectively. However, the difference was not statistically significant (p=0.556, 95% CI –4.75 to 2.62). The cutoff depths to discriminate between low and high risks for nodal metastasis in T2 are detailed in Table 3. Recurrence was found in six patients (25%), with four instances in the tongue, one in the neck, and one in both the tongue and neck.

Moving on to the neck-observation group, T1 and T2 N0 anterior tongue cancers were initially diagnosed in 12 patients with ten T1 patients (83.33%) and two T2 patients (16.67%). The 12 patients only received surgery on their primary lesions, followed by neck observation. Two of the T1 patients were subsequently excluded from the study. The first of those two had been tracked for seven years, during which time, no spread to the cervical lymph nodes was observed; however, the DOI was unknown. The second patient died from septicemia 10 months after the surgery, but no nodal metastasis was found at the time of death. The ten-remaining neck-observation patients had DOIs ranging from 2 to 9 mm (mean 4.4±2.32). There were eight T1 cases (80%) and two T2 cases (20%). The two cases received post-operative radiation. One after re-surgery of primary site due to not free margin and there was no recurrence in 14-year follow-up, the other due to not free margin and there was recurrence at primary site without a recurrence on the neck at 14 years. The pathological margin of the primary resection in other nine cases were free metastasis to the cervical lymph nodes occurred in 4/10 cases (40%) with three were T1 (depths of 2, 3, and 3 mm), and one was T2 (depth of 5 mm). Two cases recurred at the primary site, but both had no neck recurrence. Five-year recurrent rate was 60%.

Table 2. Cutoff invasion depths for T1 tongue cancer and risks of nodal metastasis for the END group

Cutoff	No. of patients (n=15); n (%)	PN (+); n (%)	p-value	Odds ratio (95% CI)
3 mm			0.476	0.3 (0.01 to 6.38)
≤3 mm	2 (13.3)	1 (50.0)		
>3 mm	13 (86.7)	3 (23.1)		
4 mm			0.476	0.3 (0.01 to 6.38)
≤4 mm	2 (13.3)	1 (50.0)		
>4 mm	13 (86.7)	3 (23.1)		
5 mm			0.560	0.4 (0.04 to 4.00)
≤5 mm	5 (33.3)	2 (40.0)		
>5 mm	10 (66.7)	2 (20.0)		
6 mm			1.000	0.6 (0.04 to 7.67)
≤6 mm	10 (66.7)	3 (30.0)		
>6 mm	5 (33.3)	1 (20.0)		

PN (+)=number of patients with occult metastasis; CI=confidence interval

Table 3. Cutoff invasion depths for T2 tongue cancer and risks of nodal metastasis for the END group

Cutoff	No. of patients (n=24); n (%)	PN (+); n (%)	p-value	Odds ratio (95% CI)
4 mm			0.536	
≤4 mm	2 (8.3)	0 (0.0)		
>4 mm	22 (91.7)	8 (36.4)		
5 mm			0.621	3.2 (0.30 to 33.26)
≤5 mm	6 (25.0)	1 (16.7)		
>5 mm	18 (75.0)	7 (38.9)		
6 mm			0.667	1.8 (0.27 to 11.96)
≤6 mm	8 (33.3)	2 (25.0)		
>6 mm	16 (66.7)	6 (37.5)		

PN (+)=number of patients with occult metastasis; CI=confidence interval

Five-year disease-free survival and 5-year overall survival were 67.9% in END group and 46.7% in neck-observation group. From the Kaplan-Meier survival analysis, it seems like prophylactic neck dissection trends have better survival rate, but statistics is not significant, p=0.521 (Figure 1).

The authors assumed that the metastases to the cervical lymph nodes of the four neck-observation patients at 2, 3, 5, 11 months post operation were due to occult node metastasis, and the authors included those four patients in the present study analyses. By doing so, the following overall proportions for occult node metastasis were reached, T1 patients, 30.4%

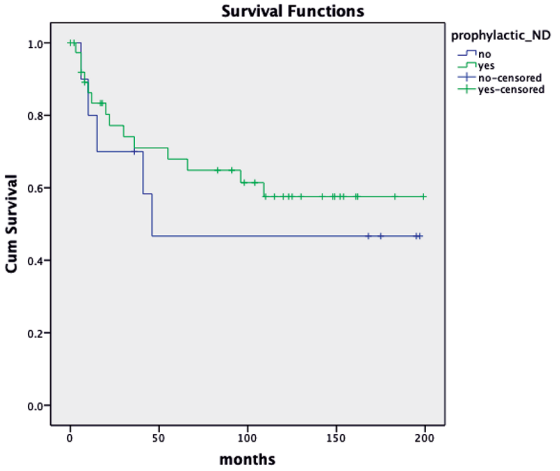

Figure 1. Kaplan-Meier curve in END group and neck-observation group.

(7/23), and T2 patients, 34.6% (9/26, p=0.755, OR 1.2, 95% CI 0.36 to 4.02). The cutoff DOIs and risks of nodal metastasis for the END and neck-observation groups (include T1 and T2) are presented in Table 4. The incidences of nodal metastasis for the END group, the neck-observation group, and the two groups combined are illustrated in Figure 2.

For analysis purposes, the authors divided the DOIs into two subgroups, 2 to 4 mm and larger than 4 mm. When the data of the END and neck-observation groups were combined, the incidences

Table 4. Cutoff depths and risks of nodal metastasis for the END and neck-observation groups include T1 and T2

Cutoff	No. of patients (n=49); n (%)	PN (+); n (%)	p-value	Odds ratio (95% CI)
2 mm			1.000	0.5 (0.03 to 8.01)
≤2 mm	2 (4.1)	1 (50.0)		
>2 mm	47 (95.9)	15 (31.9)		
3 mm			0.195	0.3 (0.06 to 1.55)
≤3 mm	7 (14.3)	4 (57.1)		
>3 mm	42 (85.7)	12 (28.6)		
4 mm			0.709	0.7 (0.16 to 2.80)
≤4 mm	10 (20.4)	4 (40.0)		
>4 mm	39 (79.6)	12 (30.8)		
5 mm			0.478	0.6 (0.19 to 2.19)
≤5 mm	18 (36.7)	7 (38.9)		
>5 mm	31 (63.3)	9 (29.0)		
6 mm			0.755	0.8 (0.25 to 2.75)
≤6 mm	26 (53.1)	9 (34.6)		
>6 mm	23 (46.9)	7 (30.4)		

PN (+)=number of patients with occult metastasis; CI=confidence interval

of nodal metastases were 40% (4/10) for DOIs of 2 to 4 mm, and 30.8% (12/39) for DOIs greater than 4 mm. There were no statistical differences (p=0.709, OR 0.7, 95% CI 0.16 to 2.80).

The staging system for oral carcinomas was updated in the Eighth edition of the AJCC cancer staging manual. The resulting impact on the 39

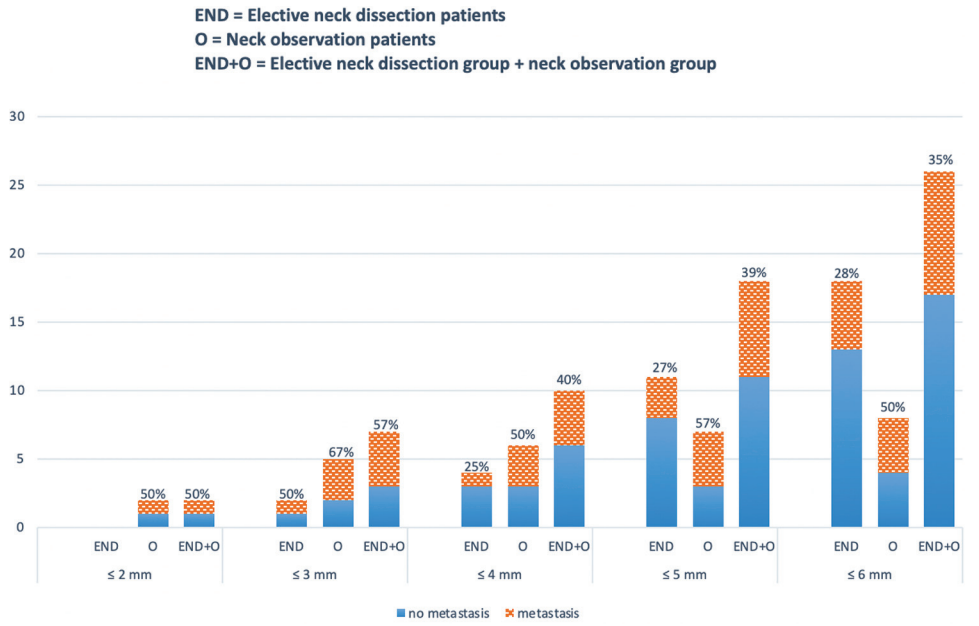

Figure 2. Incidences of nodal metastasis for each depth for the END group, the neck-observation group, and the two groups combined.

END-group patients was substantial. Ten of the 15 T1 cases were reclassified as T2, and nine of the 24 T2 cases were recategorized as T3. Based on the new staging criteria, the proportions of occult node metastases in the END group were amended to T1 patients, 40% (2/5), and T2 patients 28% (7/25). As to the combination of the END and neck-observation groups, the proportions were revised to T1 patients 41.7% (5/12), and T2 patients 33.3% (7/27).

Discussion

The present study investigation found 12 out of 39 cases (30.8%) in the END group had occult node metastases, which is consistent with the other research. The incidences of occult lymph node metastasis in the T1 patients (4/15, 26.7%) and the T2 patients (8/24, 33.3%) were statistically non-significant. This might indicate that the T1 and T2 staging criteria used in the Seventh edition of the AJCC cancer staging manual, which only used the diameters of lesions, were not accurately predicting occult metastases. The DOIs ranged from 2.5 mm to 16.2 mm, with a mean of 7.98±3.79 mm. The mean DOIs for the metastatic subgroup (8.69±4.32 mm) and the non-metastatic subgroup (7.66±3.58 mm) were statistically non-significant (p=0.44, 95% CI –3.71 to 1.65). This indicated that DOI alone was not associated with the incidence of occult metastatic lymph nodes in the neck. In the studies undertaken before 2010, the cutoff DOIs varied from 3 to 9 mm[7,8,11,12,15]. Most studies used a 3 to 5 mm cutoff to signal the risk of node metastasis. The work of Takahiro et al and other studies found a cutoff depth of 4 mm marked the boundary between a high and a low risk of cervical node metastasis[7,15,22-24]. Mann et al found that END improved survival in stage 1 and 2 squamous cell carcinomas of the tongue when the DOI was more than 4 mm[25]. Although the Eighth edition of the AJCC cancer staging manual introduced the use of DOIs of 5 mm or less and more than 5 mm to define T1 and T2 cancers, the depth at which END should be undertaken was not specified. According to NCCN Guideline Version 1.2021, END should be strongly considered in tumor with a depth more than 3 mm. For a depth less than 2 mm, elective is only indicated in highly selective situation. For a depth of 2 to 4 mm, clinical judgement is required to determine the suitability of END. In the present study, END depends on surgeon, but tends to have neck surgery in T1 with significantly invasion, and T2 tended to not operate the neck when T1 with superficial invasion.

In the current investigation, 10 patients only underwent surgery on their primary lesions, followed by neck observation. The neck-observation-group patients with recurrence had a low DOI of 2 to 5 mm. When the depth of this group was analyzed relative to the END group (Figure 2), it was not possible to find the cutoff DOI that separated high and low risks of cervical occult node metastasis. However, a high incidence of occult metastasis was found for all of the analyzed depths. Shintani et al found a 25% incidence of occult metastasis in carcinoma of the tongue when the DOI ranged between 3.0 and 4.9 mm, and an incidence of 51.4% for DOIs over 5.0 mm. In addition, their work revealed that tumors with a reductive bottom of invasion demonstrated a range of tumor depths as well as low involvement of the lymph nodes (23.5%). In contrast, the researchers found that tumors with an expansive bottom of invasion were associated with a deeper depth, and the incidence of lymph node metastasis was high (69.6%)[26]. Lin et al[8] found that tumors with 2.1 to 4.0 mm depths had similar rates of occult node metastasis as tumors with 4.1 to 7.0 mm depths at 25% versus 20%. As well, following neck observation, the regional recurrence rates for tumors with depths of 0 to 2.0 mm, 2.1 to 4.0 mm, and 4.1 to 7.0 mm were 8%, 50%, and 56%, respectively. However, prophylactic neck dissections reduced the regional recurrence rate for the 2.1 to 4.0 mm depth group from 50% to 25%. Therefore, Lin et al recommended that prophylactic neck dissections should be performed in patients with tumors that are more than 2.0 mm in depth. Imai et al[27] retrospectively evaluated 67 patients with squamous cell carcinomas of the tongue that underwent surgery at the primary lesion site, coupled with watchful waiting for neck management. That research team found a 29.9% neck recurrence, with nearly all instances developing within one year of the surgery. Moreover, patients with a tumor depth of 2 mm or more, or muscle invasion were significantly more likely to develop delayed neck metastasis and a worse prognosis[27]. Hori et al[28] investigated 154 patients with early squamous cell carcinomas of the tongue that underwent wide excisions of the primary tumor and watchful waiting alone for neck management. Those researchers found the combination of a tumor depth of 3 mm or more and high-grade tumor budding yielded a high diagnostic accuracy for predicting recurrent neck nodes with positive predictive value 80%, negative predictive value 97%, sensitivity 89%, and specificity 95%. The NCCN Clinical Practice Guidelines in Oncology (version 1.2021) suggest that for tumors with a depth greater than 3 mm, END

should be strongly considered if radiotherapy was not planned. In the case of tumors with a 2 to 4 mm depth, the Guidelines state that clinical judgment must be used to determine the appropriateness of END[29]. In the present study, there was no statistically significant correlation between the DOIs and the incidence of occult node metastasis, and no cutoff depth was found, but there was a high incidence of occult metastasis at greater than 20% for all analyzed depths of 2 mm or more. The authors would like to suggest that END should be considered for T1 and T2 N0 tongue cancers is 2 mm or more in depth.

Limitation

For the present study, it was a retrospective study and small sample size in neck-observation group.

Conclusion

There was no statistically significant correlation between the DOIs and the incidence of occult node metastasis, and no cutoff depth was found. However, there was high incidence of occult-node metastasis rates in both of the END and neck-observation groups with 30.8% and 40%, respectively. Moreover, there was a high incidence of occult metastasis for all analyzed depths of 2 mm or more.

What is already known on this topic?

Controversies remain about the use of histopathological depth to determine the existence of occult metastasis, as well as the necessity to perform ENDs. Although the Eighth Edition of the AJCC cancer staging manual introduced the use of DOIs of 5 mm or less and more than 5 mm to define T1 and T2 cancers, the depth at which prophylactic neck dissection should be undertaken was not specified. According to the NCCN Guideline Version 1.2021, END should be strongly considered in tumor with a depth more than 3 mm. For a depth less than 2 mm, elective is only indicated in highly selective situation. For a depth of 2 to 4 mm, clinical judgement is required to determine the suitability of END.

What this study adds?

There was a high incidence of occult metastasis for all analyzed depths ≥2 mm.

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Conflicts of interest

The authors declare no conflict of interest.

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