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Lymph node yield, depth of invasion, and survival in node-negative oral cavity cancer

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A R T I C L E I N F O

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A B S T R A C T

Objective: To determine the effects of nodal yield on survival in early stage oral cavity squamous cell carcinoma (OCSCC) in the context of primary tumor depth of invasion (DOI).

Materials and methods: Patients with early-stage clinically node-negative OCSCC who underwent upfront surgery at the primary site were identified using the National Cancer Database between 2004 and 2015.

Results: There were 3384 patients with < 4 mm DOI and 1387 patients with ≥4 mm DOI identified. Management of the neck included observation (40%), END with < 18 nodes harvested ± postoperative radiation (ND < 18, 16%), and END with ≥18 nodes harvest ± postoperative radiation (ND ≥ 18, 44%). When adjusted for relevant covariates, ND ≥ 18 demonstrated statistically significant improvements in overall survival for both DOI < 4 mm and ≥4 mm (DOI < 4 mm: HR 0.67, 95%CI 0.54–0.85; DOI ≥ 4 mm: HR 0.47, 95%CI 0.34–0.64). However, ND < 18 showed no significant difference from observation of the neck regardless of DOI (DOI < 4 mm: HR 0.82, 95%CI 0.63–1.07; DOI ≥ 4 mm: HR 0.72, 95%CI 0.51–1.03). Of patients undergoing END, the most significant factors associated with obtaining a nodal yield of 18 or more were age less than 40 years (HR 2.58, 95%CI 1.84–3.63) and treatment at an academic facility (HR 2.47, 95%CI 2.06–2.96).

Conclusions: END with 18 or more nodes is associated with improved survival outcomes in patients with early stage OCSCC regardless of DOI. END with less than 18 nodes, however, does not appear significantly different than observation of the neck alone. Achieving a lymph node yield of 18 or more is multifactorial and includes both patient and provider factors.

Introduction

Despite decreasing tobacco use nationwide, oral cavity cancer remains an important public health issue. In 2019, an estimated 35,130 individuals will be diagnosed with this malignancy in the United States and another 7410 will die from it [1]. Patients with early T-stage clinically node-negative disease represent an important group with a good prognosis whose oncologic outcomes should be optimized to maximize survival while limiting the morbidity of treatment. In a recent randomized trial, D'Cruz, et al. [2] demonstrated a survival benefit for elective neck dissection (END) in patients with early T-stage node-negative oral cavity cancer. Although not powered for subset analysis, in this trial the survival advantage appeared to apply only to patients with a primary tumor depth of invasion (DOI) of 4 mm or greater. Although the sample size was limited, < 6% of patients in this study with DOI of < 4 mm had occult nodal disease. By convention, based on historical decision-tree analyses [3], in clinically node-negative head and neck cancer, neck dissection is generally recommended when the risk of occult nodal disease is at least 20%. Current NCCN guidelines support this conclusion, and recommend END for oral cavity with less than 4 mm DOI only in highly select situations based on clinical judgement [4].

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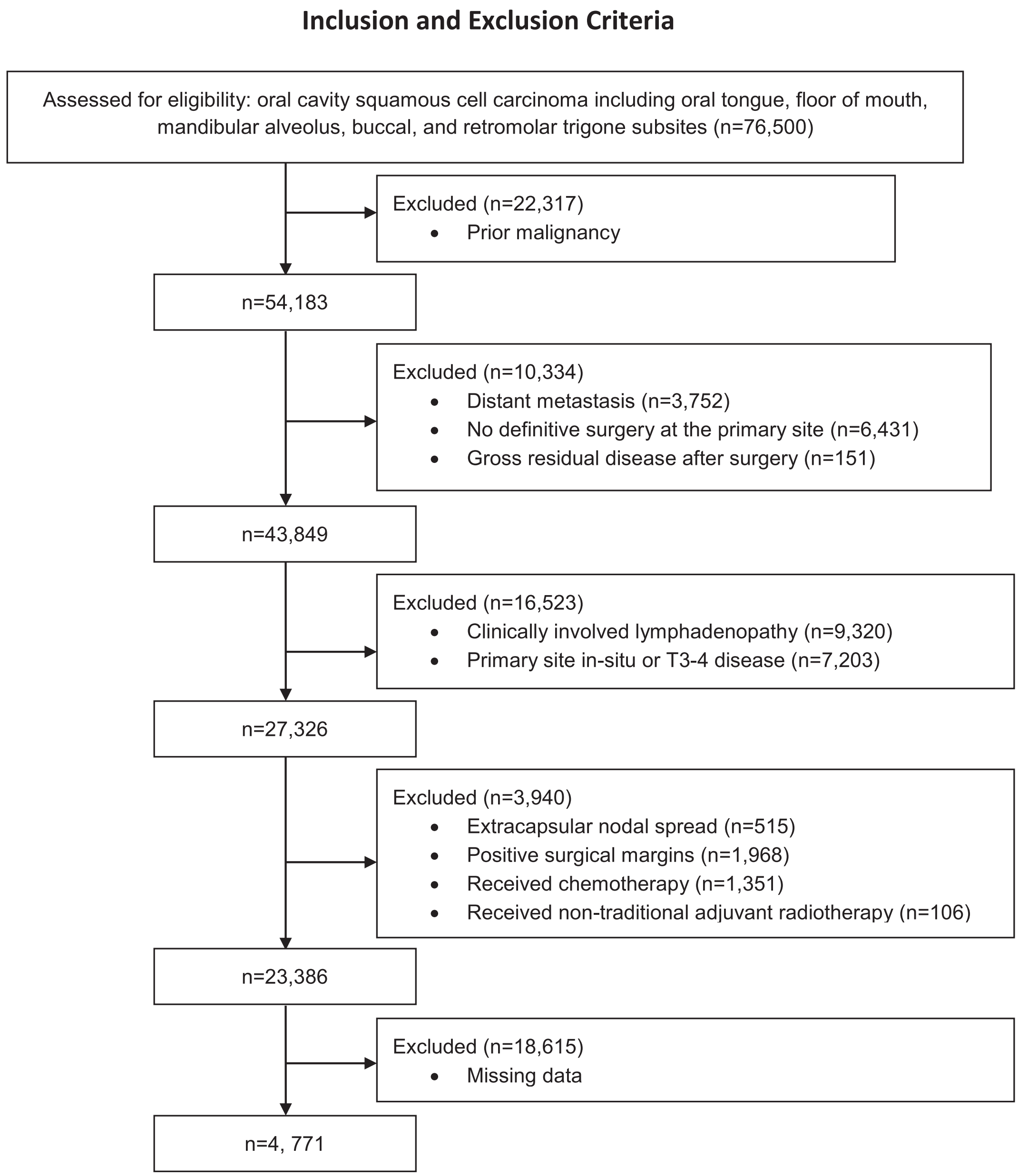

Fig. 1. Flow diagram delineating inclusion and exclusion criteria.

Given the low risk of a modern functional neck dissection and the morbidity and mortality associated with regional recurrence of head and neck cancer, other authors have questioned the validity of the 20% threshold [5–8]. Further, these cut offs for DOI and occult nodal risk in considering END do not account for nodal yield. In recent years, higher nodal counts from neck dissection in head and neck cancer have been associated with improved survival outcomes [9]. The evidence for this has been most robust in oral cavity cancer in which both multi-institutional prospective trials and large database analyses have found an association with high nodal yields from neck dissection, particularly 18 or greater, and oncologic outcomes [10–13].

There is little evidence to-date, however, to interpret the effect of END on survival for clinically node-negative oral cavity cancer in the context of both primary tumor DOI and lymph node yield from neck dissection. The objectives of this report, therefore, are to determine the association of END with oncologic outcomes in a large cohort of early stage oral cavity cancer patients stratified by DOI, and to further determine if survival outcomes in these groups are influenced by nodal yield.

Methods

The 2015 participant user file from the National Cancer Database (NCDB) was analyzed for this study, including patients diagnosed between 2004 and 2015. The NCDB is a joint project between the American College of Surgeons Commission on Cancer and the American Cancer Society. Established in 1989, it is a nationwide, facility-based, comprehensive clinical surveillance oncology database which includes approximately 70% of all newly diagnosed cancers in the United States.

Patients were identified using the International Classification of Diseases for Oncology, Third Edition. Topographical codes were identified for the oral cavity, including codes for tongue (C02.0, C02.1, C02.2, C02.3, C02.8, C02.9), floor of mouth (C04.0, C04.1, C04.8, C04.9), mandibular alveolus (C03.1), buccal (C06.0), and retromolar trigone (C06.2) areas. Patients with a diagnosis of standard keratinizing squamous cell carcinoma were included (8070, 8071) while those with less common variants of squamous cell carcinoma which may affect management or prognosis (such as spindle cell [8074] or basosquamous [8094] variants) were excluded. Patients with prior malignancies, distant metastases, or no definitive surgery at the primary site were excluded. Those with gross residual disease after surgery were also excluded, as these patients were considered to have undergone surgical debulking or biopsy without the intent of complete surgical resection. To identify patients with early T-stage tumors at risk for occult nodal disease, patients with clinically involved lymphadenopathy and those with either in-situ only or T3-4 staging (AJCC 7th edition) were excluded. Patients with tumors less than 4 cm in diameter but with a depth of invasion greater than 1 cm (T3 by recent AJCC 8th edition criteria) were included and analyzed as a subgroup because until recently, these patients were staged and managed as early-stage primary tumors. Patients with zero to four lymph nodes harvested were excluded as they were felt likely to have undergone some form of excisional biopsy rather than a true attempt at a formal neck dissection [9]. To improve the transparency and stability of statistical modeling, other confounding variables which may affect prognosis apart from nodal yield and DOI were excluded, including patients with extracapsular nodal spread, positive margins, and those receiving any chemotherapy (pre- or post-operatively) or non-traditional adjuvant radiotherapy techniques (radioisotopes, brachytherapy, pre-operative or intraoperative radiation). Finally, patients with missing data regarding survival, tumor staging, DOI, margin status, neck dissection, nodal yield, or adjuvant therapies were excluded.

Statistical analysis was performed using SPSS (SPSS v24, IBM, Chicago, IL). Descriptive statistics were used to define the study population. Univariable and multivariable Cox survival analyses were used to investigate the relationship between demographic, tumor, and treatment factors and overall survival. Based on NCCN guidelines and evidence from a prior randomized trial [2,4], models were stratified by DOI of < 4 mm and ≥ 4 mm. Variables reaching statistical significance in univariable analysis and those considered clinically relevant were included in a multivariable model. The effects of lymph node yield from neck dissection were dichotomized around 18 nodes as this been significantly associated with recurrence and survival in previous reports [9–15]. To evaluate the limits of effectiveness for neck dissection in early stage oral cancer, an additional separate sub-analysis was performed using a threshold of 2 mm depth of invasion. Finally, factors associated with higher lymph node yields were investigated with uni- and multivariable logistic regression analyses.

Results

There were 76,500 patients diagnosed with oral cavity squamous cell carcinoma in the National Cancer Database between 2004 and 2015. Of these, 4771 patients were included in the final analysis (Fig. 1). Median follow up was 35 months. Demographic, tumor, and treatment characteristics are shown in Table 1. Overall, 2851 (60%) patients underwent neck dissection, while 1920 (40%) were observed. Of the 2851 patients undergoing neck dissection, 2077 (73%) had a nodal yield of 18 or greater, while 774 (17%) had a nodal yield of less than 18. Of 3384 patients with primary tumor DOI < 4 mm, 1820 (54%) underwent neck dissection, while of 1387 patients with primary tumor DOI ≥ 4 mm, 1031 (74%) underwent neck dissection. Nodal yield, pathological nodal stage, and adjuvant radiotherapy are shown in Table 2, stratified by DOI. None of the patients who underwent observation of the neck received adjuvant radiotherapy.

Multivariable Cox survival regression analyses were performed, stratified by DOI. For patients with DOI < 4 mm, young age (HR 0.60, 95%CI 0.37–0.97), private insurance (HR 0.42, 95%CI 0.34–0.51), low comorbidity index (HR 0.70, 95%CI 0.58–0.85), pathological T1 and N0 staging (T1 vs T2: HR 0.56, 95%CI 0.46–0.68; pN + vs pN0/x: HR 2.40, 95%CI 1.81–3.19), low-/moderate-grade (HR 0.55, 95%CI 0.43–0.71), and neck dissection with 18 or greater nodes harvested (HR 0.67, 95%CI 0.54–0.85) were associated with improved survival (Table 3). Patients with less than 18 nodes harvested demonstrated no significant survival difference from neck observation alone (HR 0.82, 95%CI 0.63–1.07, Fig. 2A). For patients with DOI ≥ 4 mm, young age (HR 0.53, 95%CI 0.26–1.09), private insurance (HR 0.64, 95%CI 0.49–0.83), low comorbidity index (HR 0.69, 95%CI 0.53–0.90), pathologic T1 and N0 staging (T1 vs T2: HR 0.60, 95%CI 0.46–0.77; pN + vs pN0/x: HR 1.42, 95%CI 1.00–2.01), low-/moderate-grade (HR

Table 1
Demographics, tumor, and treatment characteristics.

	N = 4771
Age (years)	
• < 40	358 (8%)
• ≥ 40	4413 (92%)
Gender	
• Male	2716 (57%)
• Female	2055 (43%)
Insurance	
• Private	2478 (52%)
• Other*	2293 (48%)
Education	
• Zip code < 7% no high school diploma	1322 (28%)
• Zip code ≥ 7% no high school diploma	3449 (72%)
Income ($ per year)	
• ≥ 63,000	3065 (64%)
• < 63,000	1715 (36%)
Distance from treatment facility (miles)†	
• ≥ 17 or more	2313 (49%)
• < 17 miles	2442 (51%)
Facility type	
• Academic cancer center	4173 (48%)
• Other**	4579 (52%)
Charleson-Deyo comorbidity index	
• 0	3605 (76%)
• ≥ 1	1166 (24%)
Year of diagnosis	
• 2004–2011	1502 (32%)
• 2012–2015	3269 (68%)
Clinical T-stage	
• T1	3219 (68%)
• T2	1552 (33%)
Pathological T-stage (AJCC 7th edition)	
• T1	3527 (74%)
• T2	1244 (26%)
Depth of invasion (mm)	
• < 4mm	3384 (71%)
• ≥ 4mm < 10 mm	978 (21%)
• ≥ 10 mm	409 (9%)
Subsite	
• Oral tongue	3477 (73%)
• Other††	1294 (27%)
Tumor grade	
• Low/moderate	4105 (86%)
• High/undifferentiated	460 (10%)
Adjuvant Therapy	
• None	4166 (87%)
• Radiation	605 (13%)
Management of the neck	
• Observation	1920 (40%)
• Neck dissection < 18 nodes harvested ± adjuvant radiation	774 (16%)
• Neck dissection ≥ 18 nodes harvested ± adjuvant radiation	2077 (44%)

* Other insurance includes Medicare, Medicaid, other governmental insurance, and uninsured.

† 16 patients had unknown distance from treatment facility.

** Other facility types include community cancer program, comprehensive community cancer program, integrated network cancer program, and other specified types of cancer programs.

†† Other subsites including floor of mouth, mandibular alveolus, buccal, and retromolar trigone.

Table 2
Tumor and treatment characteristics of the neck in patients managed with neck dissection.

Depth of invasion	Treatment characteristics	Neck dissection < 18 nodes	Neck dissection ≥18
All patients	Pathologic nodal disease		
	• pN0	676 (87%)	1727 (83%)
	• pN+	98 (13%)	350 (17%)
	Adjuvant treatment		
	• None	643 (83%)	1603 (77%)
	• Radiotherapy	131 (17%)	474 (23%)
< 4mm	Pathologic nodal disease		
	• pN0	445 (90%)	1117 (84%)
	• pN+	48 (10%)	210 (16%)
	Adjuvant treatment		
	• None	427 (87%)	1056 (80%)
	• Radiotherapy	66 (13%)	271 (20%)
≥4mm	Pathologic nodal disease		
	• pN0	231 (82%)	610 (81%)
	• pN+	50 (18%)	140 (19%)
	Adjuvant treatment		
	• None	216 (78%)	547 (73%)
	• Radiotherapy	65 (22%)	203 (27%)

0.68, 95%CI 0.50–0.93), omission of radiotherapy (HR 1.43, 95%CI 1.03–1.98), and neck dissection with 18 or greater nodes harvested were associated with improved survival (HR 0.47, 95%CI 0.34–0.64, Table 4). Again, patients with less than 18 nodes harvested demonstrated no significant survival difference from neck observation alone in this cohort (HR 0.72, 95%CI 0.51–1.03, Figure 2B). A separate subanalysis using a threshold of 2 mm depth of invasion was performed. Similarly, regardless of depth of invasion in these stratified groups, neck dissection with less than 18 nodes demonstrated no significant difference from neck observation alone. Neck dissection with 18 or more nodes harvested was associated with improved survival for patients with DOI ≥ 2 mm over observation (HR 0.74, 95%CI 0.59–0.92, Fig. 3B), but this difference did not reach statistical significance for patients with < 2 mm DOI (HR 0.80, 95%CI 0.61–1.05, Fig. 3A). Factors associated with achieving a nodal yield from neck dissection of 18 or more are demonstrated in Table 5.

Discussion

The results of this study confirm the survival advantage of END in early stage clinically node-negative oral cavity cancer, with several important qualifications. As supported by a recent randomized trial [2] and current NCCN guidelines [4], patients with DOI of ≥4 mm demonstrated an association between improved overall survival and END. However, when adjusting for relevant covariates, a significant survival benefit was seen only in patients who received a neck dissection with 18 or more nodes harvested. Additionally, contrary to current guidelines, END was also associated with improved survival for patients with a primary tumor DOI of < 4 mm. Again, however, this appeared limited to patients with a nodal yield of 18 or greater. Regardless of DOI, overall survival for patients undergoing END with less than 18 lymph nodes was not statistically different than observation of the neck in this patient population. These results may have important implications for both when and how END dissection should be performed in early stage oral cavity cancer.

There are several potential explanations for these findings. As the NCDB does not include disease-specific or disease-free survival, the benefit of higher nodal yield from neck dissection may be a proxy measure for global quality of cancer care, rather than a direct mechanism to decrease risk of recurrent disease. In addition, increasing nodal harvests were strongly associated with treatment at academic centers, suggesting that lymph node yield may be associated with the delivery of high-quality care.

Alternatively, increasing nodal yield may have a direct effect on survival. This report excluded patients with other confounding factors at the primary site and neck which can influence oncologic outcomes, including advanced T-stage, positive margins, extracapsular extension, and the addition of chemotherapy. This limits the study population to a more homogeneous group in which management strategy of the neck is more likely to have an oncologic impact. Higher nodal yields from neck dissection may allow increased detection of occult nodal disease and lead more patients to receive the adjuvant radiotherapy they require. Further, higher nodal yields may also contribute to greater clearance of occult nodal disease and decreased regional recurrence. This could apply to pathologically negative neck dissections as well, as microscopic disease which was missed by the pathologist during routine sectioning may have been surgically cleared [16].

Whether a proxy metric for the quality of care or a direct mechanism to decrease disease recurrence, END with 18 or more nodes demonstrated an association with survival regardless of DOI. Numerous previous reports, however, have not shown a significant survival benefit to END in patients with DOI < 4 mm [2,17–19]. There are several potential reasons for this discrepancy. Firstly, prior studies of oral cavity cancer with DOI < 4 mm did not evaluate survival outcomes in the context of nodal yield. Whether due directly to the extent of lymphadenectomy or an indication of global quality of care, END with 18

Table 3
Univariable and multivariable survival analyses for overall survival of patients with T1-2N0 oral cavity cancer with depth of invasion < 4 mm (n = 3384).

	Univariable HR (95%CI)	Multivariable HR (95%CI)
Age (< 40 vs ≥40 years)	**0.41 (0.25–0.66)**	**0.60 (0.37–0.97)**
Gender (male vs female)	1.15 (0.96–1.36)	
Insurance (private vs other)	**0.37 (0.31–0.45)**	**0.42 (0.34–0.51)**
Education (zip code < 7% no high school diploma vs ≥7% no high school diploma)	0.90 (0.75–1.10)	
Income (≥$63,000 vs < $63,000 per year)	**0.72 (0.60–0.87)**	0.87 (0.72–1.06)
Distance from treatment facility (≥17 vs < 17 miles)	0.87 (0.74–1.04)	
Facility type (Academic cancer center vs other)	0.90 (0.76–1.06)	
Charleson-Deyo comorbidity index (0 vs ≥1)	**0.59 (0.50–0.71)**	**0.70 (0.58–0.85)**
Year of diagnosis (2012 or later vs prior to 2012)	1.04 (0.86–1.25)	
Pathological T-stage (T1 vs T2 or greater)	**0.49 (0.41–0.59)**	**0.56 (0.46–0.68)**
Subsite (oral tongue vs other)	0.96 (0.80–1.16)	
Tumor grade (low/moderately vs high/undifferentiated)	**0.49 (0.39–0.63)**	**0.55 (0.43–0.71)**
Pathological N-stage (pN + vs pN0/x)	**2.92 (2.32–3.66)**	**2.40 (1.81–3.19)**
Adjuvant therapy (radiation vs observation)	**1.84 (1.46–2.32)**	1.19 (0.89–1.58)
Surgical management of the neck		
– Neck dissection ≥ 18 nodes harvested vs observation	1.00 (0.83–1.21)	**0.67 (0.54–0.85)**
– Neck dissection < 18 nodes harvested vs observation	1.21 (0.95–1.54)	0.82 (0.63–1.07)

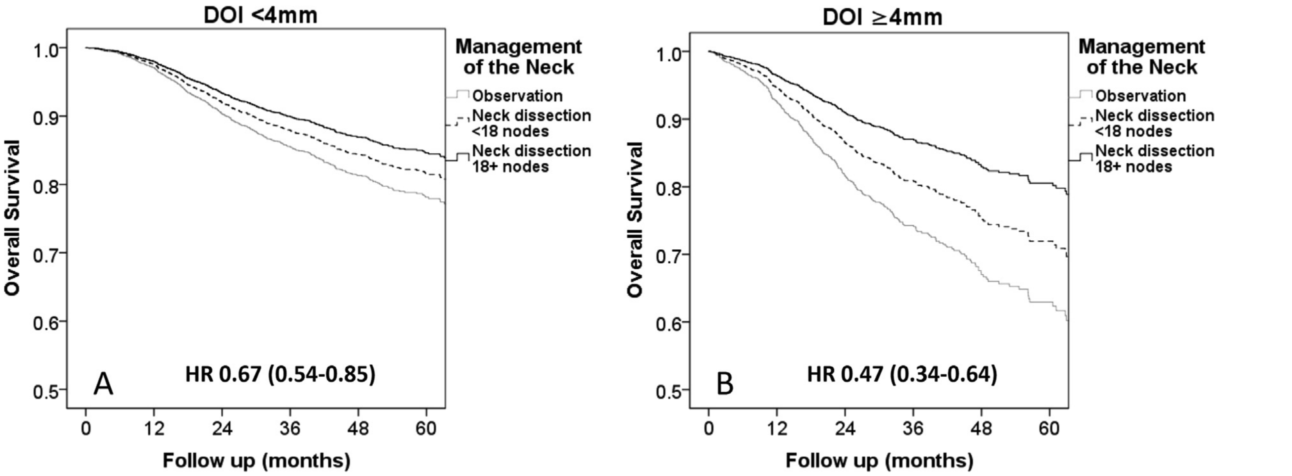

Fig. 2. Association between management of the neck and overall survival for T1-2N0 oral cavity squamous cell carcinoma stratified by depth of invasion (A) < 4 mm and (B) ≥ 4 mm, and adjusted for relevant covariates. Hazard ratios (HR) refer to survival outcomes of patients undergoing neck dissection with ≥18 nodes as compared to observation.

Table 4
Univariable and multivariable survival analyses for overall survival of patients with T1-2N0 oral cavity cancer with depth of invasion ≥ 4 mm (n = 1387).

	Univariable HR (95%CI)	Multivariable HR (95%CI)
Age (< 40 vs ≥40 years)	**0.34 (0.17–0.68)**	**0.53 (0.26–1.09)**
Gender (male vs female)	1.24 (0.97–1.58)	
Insurance (private vs other)	**0.53 (0.42–0.69)**	**0.64 (0.49–0.83)**
Education (zip code < 7% no high school diploma vs ≥7% no high school diploma)	0.93 (0.71–1.22)	
Income (≥$63,000 vs < $63,000 per year)	**0.74 (0.57–0.96)**	0.84 (0.64–1.09)
Distance from treatment facility (≥17 miles vs < 17 miles)	0.94 (0.74–1.20)	
Facility type (Academic cancer center vs other)	0.86 (0.68–1.09)	
Charleson-Deyo comorbidity index (0 vs ≥1)	**0.65 (0.50–0.84)**	**0.69 (0.53–0.90)**
Year of diagnosis (2012 or later vs prior to 2012)	0.95 (0.74–1.24)	
Pathological T-stage (T1 vs T2 or greater)	**0.55 (0.44–0.70)**	**0.60 (0.46–0.77)**
Depth of invasion (< 1cm vs ≥1 cm)	**0.67 (0.52–0.85)**	0.85 (0.65–1.10)
Subsite (oral tongue vs other)	**0.73 (0.57–0.95)**	0.83 (0.64–1.08)
Tumor grade (low/moderately vs high/undifferentiated)	**0.67 (0.49–0.92)**	**0.68 (0.50–0.93)**
Pathological N-stage (pN + vs pN0/x)	**1.59 (1.17–2.15)**	**1.42 (1.00–2.01)**
Adjuvant therapy (radiation vs observation)	**1.54 (1.18–2.02)**	**1.43 (1.03–1.98)**
Surgical management of the neck		
– Neck dissection ≥18 nodes harvested vs observation	**0.67 (0.51–0.88)**	**0.47 (0.34–0.64)**
– Neck dissection < 18 nodes harvested vs observation	0.98 (0.71–1.36)	0.72 (0.51–1.03)

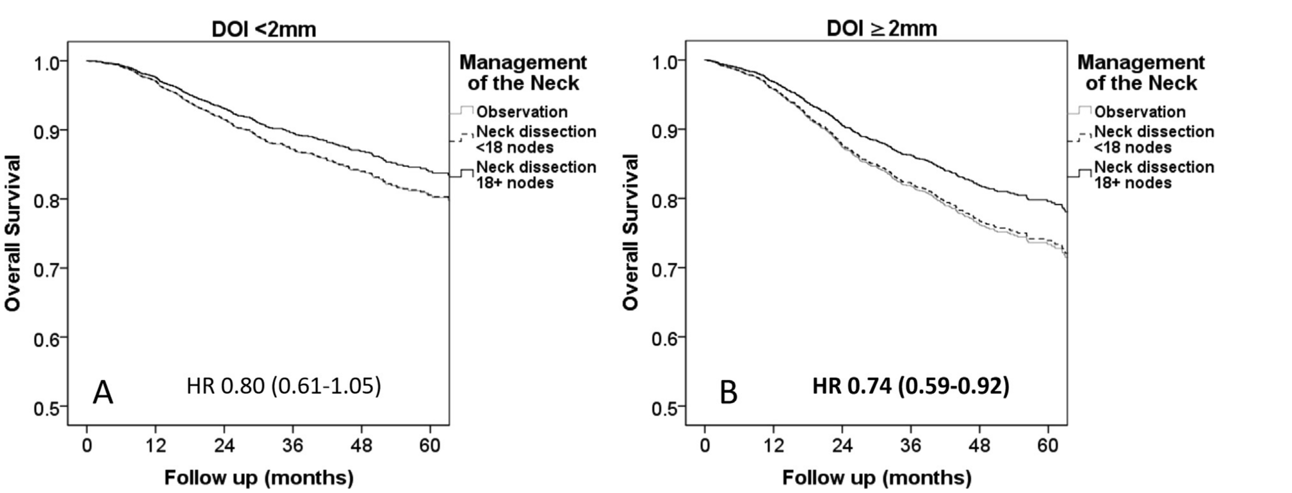

Fig. 3. Association between management of the neck and overall survival for T1-2N0 oral cavity squamous cell carcinoma stratified by depth of invasion (A) < 2 mm and (B) ≥ 2 mm, and adjusted for relevant covariates. Hazard ratios (HR) refer to survival outcomes of patients undergoing neck dissection with ≥18 nodes as compared to observation.

Table 5
Univariable and multivariable analyses for factors associated with ≥18 lymph nodes harvested in patients with T1-2N0 oral cavity cancer undergoing neck dissection.

	Univariable HR (95%CI)	Multivariable HR (95%CI)
Age (< 40 vs 40 or more years)	**1.53 (1.11–2.12)**	**2.58 (1.84–3.63)**
Gender (male vs female)	**1.32 (1.12–1.56)**	**1.34 (1.13–1.60)**
Insurance (private vs other)	1.06 (0.90–1.25)	
Education (zip code < 7% no high school diploma vs ≥7% no high school diploma)	1.03 (0.86–1.25)	
Income ($63,000 or more vs less than $63,000 per year)	**1.22 (1.02–1.45)**	**1.21 (1.01–1.45)**
Distance from treatment facility (17 or more miles vs < 17 miles)	**1.45 (1.23–1.72)**	**1.28 (1.07–1.52)**
Facility type (Academic cancer center vs other)	**2.25 (1.90–2.66)**	**2.47 (2.06–2.96)**
Charleson-Deyo comorbidity index (0 vs 1 or more)	1.13 (0.94–1.36)	
Year of diagnosis (2012 or later vs prior to 2012)	1.13 (0.94–1.35)	
Pathological T-stage (T1 vs T2 or greater)	**0.79 (0.67–0.93)**	**0.77 (0.64–0.92)**
Depth of invasion (< 4mm vs ≥4 mm)	1.01 (0.85–1.20)	
Subsite (oral tongue vs other)	0.94 (0.78–1.13)	
Tumor grade (low/moderately vs high/undifferentiated)	1.13 (0.88–1.45)	

or more nodes appears significantly prognostic and was not included in prior studies of patients with DOI < 4 mm. Secondly, such prior studies may have been underpowered to detect a survival difference for END. Most individual institutions will treat only a few dozen early stage node-negative oral cavity cancers per year and, as a result, individual institutional studies may not identify a survival difference for END in patients with DOI < 4 mm. However, thousands of early stage node-negative oral cavity cancers are managed in the United States annually and tens of thousands worldwide. In that way, a small but significant improvement in survival for END in patients with DOI < 4 mm would be a significant finding. Given the absence of available high-level data for this population, however, there is substantial variation nationwide in management of patients with primary tumor DOI < 4 mm, with just over half undergoing END in this study.

There are several limitations to these conclusions. These data are retrospective and subject to the omissions and inaccuracies of the medical record. Importantly, the NCDB does not distinguish between DOI and tumor thickness. While these are not interchangeable values, they are often very similar and recent evidence suggests that for the purpose of retrospective survival analysis, it is reasonable to impute tumor thickness for depth when it is otherwise unavailable [20]. The NCDB additionally does not specify the number or extent of elective neck dissections. Therefore, those undergoing bilateral neck dissections or inclusion of level 4 may have contributed to the observed results. Additionally, several important risk factors and outcomes were not available in the dataset including lymphovascular invasion, perineural invasion, and locoregional recurrence, as well as tobacco and alcohol use. It also does not include important elements of patient and physician decision-making. Although END for oral cavity cancer with a DOI < 4 mm may have a small statistical survival advantage in a large cohort, this does not account for the risks and complications of a neck dissection, patient preferences and goals of care, surveillance strategies, nor the individual and societal costs. Patients whose livelihoods depend on physical labor may want to avoid risk to the spinal accessory nerve. Others may desire close follow up with short interval ultrasound imaging to avoid a neck dissection incision or the associated risks [21].

Further, other demographic and pathological risk factors must be considered. While historically young patients with oral cavity cancer were thought to have intrinsically aggressive disease and lower survival, in this study of early T-stage clinically-node negative disease adjusted for relevant covariates, young patients were found to have significantly improved survival [22,23]. Patients with smaller primary tumors and low-grade pathobiology also had improved survival. In that way, patients with a constellation of good prognostic factors may be at such low risk of metastases that neck dissection may not be beneficial. Further, while this study included a large number of patients with DOI < 4 mm, there were too few events to separate the cohort into individual millimeter or sub-millimeter DOI groups and these data may not apply to patients with very thin primary tumor depth. In support of this, a separate sub-analysis performed did not demonstrate a statistically significant difference between any neck dissection and observation for very thin (< 2mm) tumors. Ultimately, however, rather than establish strict threshold values above which neck dissection is required, the available data should serve to guide decision-making in the context of patient values, oncologic outcomes, and societal resources. Nonetheless, the findings of this study suggest that in the appropriate context, neck dissection with 18 or more lymph nodes harvested may provide oncologic benefit in oral cavity cancer patients with a primary tumor DOI < 4 mm, and in particular, those with 2–3 mm DOI. These findings will require validation in future large-scale trials. While an individual institutional study or a randomized multi-center design are likely not feasible given sample size requirements, other prospectively maintained national databases should be explored to understand the implications of nodal yield and DOI on survival in oral cavity cancer.

Conclusion

In patients with early T-stage clinically node negative oral cavity cancer, neck dissection with a nodal yield of 18 or more improved overall survival as compared with observation of the neck, in both patients with thick (DOI ≥ 4 mm) and thin (DOI < 4 mm) tumors. Survival outcomes of patients with harvest of less than 18 nodes was not significantly different than observation in either group. Several other demographic and pathobiological factors were also associated with improved survival including young age, low grade disease, and T1 and N0 pathological staging. The most significant factors associated with lymph node harvest of 18 or more were young age and treatment at an academic institution. In the appropriate patient and context, a thorough neck dissection may provide an overall survival benefit in patients with thin (DOI < 4 mm) oral cavity cancers.

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Declaration of Competing Interest

The authors have no conflicts of interest or disclosures.

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