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ORIGINAL RESEARCH

# Cervical level IIb metastases in squamous cell carcinoma of the oral cavity: a systematic review and meta-analysis

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**Purpose:** The aim of this study was to clarify whether level IIb dissection should be performed or avoided in the treatment of oral squamous cell carcinoma by meta-analysis.

**Materials and methods:** Articles that were published before June 2017 were searched electronically in four databases (Web of Science, PubMed, Ovid and China National Knowledge Infrastructure) without any date or language restrictions by two independent reviewers. Abstracts and full-text papers which investigated the cervical metastases to level IIb from primary head and neck cancers and were deemed potentially relevant were screened. Data were analyzed using RevMan 5.3.

**Results:** Four hundred and fifty-five abstracts and 129 full-text papers were screened, and 22 studies were included in the analysis. Among the 2001 patients included, 112 patients had level IIb metastases, the pooled frequency of which was 6% (95% confidence interval [CI]: 4.0–7.0). Among the 400 patients with tongue squamous cell carcinoma from 12 studies, 37 patients had level IIb metastases, the pooled incidence of which was 7% (95% CI: 5.0–10.0). Metastases to level IIb always went together with level IIa, and only three patients were found to have isolated level IIb metastases without involving the other levels.

**Conclusion:** Due to the low frequency of level IIb nodal metastases in oral squamous cell carcinoma patients and rare occurrence of isolated level IIb, level IIb dissection could be avoided when the primary lesions were in early stages (T1 and T2), with the exception of tongue cancer. It is recommended to dissect level IIb tongue cancers without considering the stages of primary lesions and the lymph nodes status. It is also suggested that level IIb dissection should be performed in patients preoperatively or intraoperatively found with multilevel neck metastasis, especially level IIa metastasis.

**Keywords:** level IIb, meta-analysis, neck dissection, oral squamous cell carcinoma, submuscular recess

## Introduction

Oral squamous cell carcinoma (OSCC) is a life-threatening malignant tumor which accounts for 32%–40% of all the head and neck cancers. It characteristically metastasizes via lymphatic vessels to cervical lymph nodes.[1,2] According to statistics, the incidence of clinical cervical metastases from OSCC was as high as 40%.[3] Even among patients with no clinical or radiologic evidence of lymph node metastases preoperatively, occult regional lymph node metastases were revealed by pathohistologic and immunohistochemical analysis with an incidence of 15%–34%.[4] Cervical lymph node status is the most significant prognostic factor in the treatment of patients with OSCC. Once the tumor involves the neck nodes, survival drops by almost 50%.

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Neck dissection, therefore, plays an important role in management of oral cancers, not only as a part of routine treatment, but also as a diagnostic and prognostic approach to determine adjuvant therapy based on their stages and histopathologic characteristics. The techniques of neck dissection have evolved significantly over time, from radical neck dissection to selective neck dissection (SND), with improved functional results. Surgeons have reached a consensus that it is desirable to perform the least radical surgical approach while retaining maximum locoregional control and not sacrificing the survival rate.[5–8] Supraomohyoid neck dissection, an SND, is now the most commonly used surgical technique for detecting occult metastatic cervical lymph nodes and treating the clinically N0 neck. Supraomohyoid neck dissection removes the contents in levels I–III, to which oral cavity cancer most frequently spreads via lymphatic drainage,[9,10] but preserves functionally important anatomic structures, such as the sternocleidomastoid muscle, the internal jugular vein, and the spinal accessory nerve (SAN).

As the cervical level II is one of the most likely regions to which OSCC tends to metastasize, meticulous dissection is needed in this area.[8] However, the posterior region of level II, which is called level IIb, is technically more challenging for surgeons and puts patients at a higher risk because of its crucial anatomic position, difficult accessibility, and important anatomic contents. The SAN splits level II into sublevels IIa and IIb.[11,12] The sublevel IIb, also called submuscular recess, is a triangular area bounded anteromedially by the SAN, superiorly by the skull base, inferiorly by the horizontal plane defined by the hyoid bone, and posteriorly by the posterior border of the sternocleidomastoid muscle. Lymph nodes in this region surround the upper internal jugular vein and SAN. Adequate clearance of level IIb lymph nodes requires traction and elevation of the SAN. This may lead to consequent shoulder problems ranging from a difficulty at overhead abduction to a frozen shoulder due to neurapraxia and devascularization induced by dissection.[13] Therefore, avoiding the dissection of level IIb has been increasingly proposed in order to overcome this complication. Some groups stated that the incidence of metastases to level IIb was rather low in OSCC. But the incidence of metastases to level IIb remains controversial, and despite various published literature, the necessity of level IIb dissection needs to be discussed further.[14–19]

Hence, the purpose of this study is to clarify whether level IIb dissection should be performed or avoided in the treatment of OSCC by analyzing the frequency of metastases to level IIb with meta-analysis. The answer to this question may have some guiding significance on the clinical management strategy for OSCC.

# Materials and methods

## Search strategy

Search terms used were neck dissection, submuscular recess, level IIb, upper jugular lymph nodes, posterior triangle apex, mouth neoplasms, mouth mucosa, oral cavity and squamous cell neoplasms. Electronic searches were conducted in Web of Science, PubMed, Ovid and China National Knowledge Infrastructure for articles that were published until June 2017, without restrictions on dates or language. Studies that were cited in the reference lists of the included papers were also evaluated to ensure inclusion of all relevant studies.

## Inclusion and exclusion criteria

Inclusion criteria were: 1) studies that investigated the frequency of cervical metastases to level IIb from primary head and neck cancers; 2) OSCC patients' data should be extractable from the articles included and 3) the studies included should have histologically analyzed level IIb separately from the other levels for the presence of metastases. Exclusion criteria were: 1) studies on patients who had undergone preoperative radiotherapy and chemotherapy and 2) studies on tumors that relapsed.

## Data extraction

Information was extracted from the included studies, such as authors, publication year, recruitment years, total OSCC cases, cases of IIb metastases and frequency of metastases. Data extraction was independently performed by two authors, Yurong Kou and Tengfei Zhao. Disagreements were solved by discussion or consultation with another author, Shaohui Huang.

## Quality evaluation

Quality evaluation of literature was conducted according to the evaluation criteria for cross-sectional studies recommended by the Agency for Healthcare Research and Quality, as shown in Table 1. Each included literature was evaluated as "yes" or "no" or "unclear" by the 11 entries of the evaluation criteria. If the number of "yes" for a literature was $\geq 7$, the quality of the literature was ranked high; if it was at the range of 4–6, the quality of the literature was ranked medium and if it was $\leq 3$, the quality of the literature was ranked low.

**Table 1** The literature quality evaluation of AHRQ

| Item | Yes | No | Unclear |
|---|---|---|---|
| 1) Define the source of information (survey, record review) | | | |
| 2) List the inclusion and exclusion criteria for exposed and unexposed subjects (cases and controls) or refer to previous publications | | | |
| 3) Indicate the time period used for identifying patients | | | |
| 4) Indicate whether or not subjects were consecutive, if not population based | | | |
| 5) Indicate if evaluators of subject components of the study were masked to other aspects of the status of the participants | | | |
| 6) Describe any assessments undertaken for quality assurance purposes (eg, test/retest of primary outcome measurements) | | | |
| 7) Explain any patient exclusions from the analysis | | | |
| 8) Describe how confounding was assessed and/or controlled | | | |
| 9) If applicable, explain how missing data were handled in the analysis | | | |
| 10) Summarize patient response rates and completeness of data collection | | | |
| 11) Clarify what follow-up, if any, was expected and the percentage of patients for which incomplete data or follow-up was obtained | | | |

**Abbreviation:** AHRQ, Agency for Healthcare Research and Quality.

## Statistical analysis

Data synthesis and statistical analysis were performed with RevMan5.3. Risk difference, standard error and 95% CI were pooled to analyze the incidence of level IIb metastases. As there was no single rate analysis in the RevMan meta-analysis options, generic inverse variance was chosen to calculate the pooled effect, risk difference and rate were logically equivalent. Chi-square based Q test and $I^2$ were used for heterogeneity evaluation. When $P>0.10$ and $I^2<50\%$, a fixed-effects model was used; when $P<0.10$ or $I^2>50\%$, a random effects model was used.

# Results

The search and selection process of the articles is presented in Figure 1. Briefly, based on the selection criteria, a total of 453 articles were identified by the database search and 2 additional articles were found through reviewing articles and reference lists of retrieved articles and preprint online publications. After the duplicates were removed, 203 articles were screened by their titles and abstracts and 60 were subsequently retained. After full-text revision, 38 articles were excluded for various reasons. Thus, 22 studies, all published in English, were included for further analysis.[15,18–38]

## Description of the studies

By quality evaluation, 12 references ranked high, 7 references ranked medium and only 3 references ranked low. Data of 2001 patients were pooled for statistical analysis. In the 22 studies, 112 cases of cervical IIb metastasis were confirmed by pathologic examination or other technologies. But the inclusion criteria and the exclusion criteria of these studies were somewhat inconsistent. Five studies recruited only OSCC patients with clinical N0; seven studies gave the absolute numbers of clinical N0 and N+ cases respectively, while 10 studies provided no information about the clinical lymph node status. Table 2 summarizes the details of the studies included.

Thirteen articles illustrated the characteristics of cervical IIb metastasis patients, which gave details of sites, T stages, isolated IIb metastases and associated metastatic lymph nodes. However, not all the information was complete for each study. The most common primary site for level IIb metastases was the tongue, and tongue cancer particularly has a tendency toward early metastasis (T1 and T2). The other primary sites for level IIb metastases were retromolar trigone, buccal mucosa, floor of the mouth and alveolar ridge and the cases were relatively few. It was also presented that metastases at level IIb always went together with level IIa, and only three patients were found to have isolated level IIb metastases without involving the other levels. Table 3 provides a summary of patient characteristics with level IIb metastases.

Table 4 lists special information about the tongue squamous cell carcinoma (SCC) cervical level IIb metastases. Among 400 tongue SCC patients from 12 studies, metastases to level IIb lymph nodes were found in 37 cases and the frequency of level IIb metastases ranged from 5.00% to 21.74%.

## Results of the pooled analysis

The forest plots for cervical level IIb metastasis rate of OSCC showed that the pooled estimated cervical level IIb metastasis rate was 6% (95% CI: 4.0–7.0) using a random effects model (Figure 2). The corresponding Funnel plots indicated that most of the research was close to axis and there were no publication bias in these studies (Figure 3).

The forest plots for cervical level IIb metastasis rate of tongue SCC showed that the cervical IIb metastasis rate for

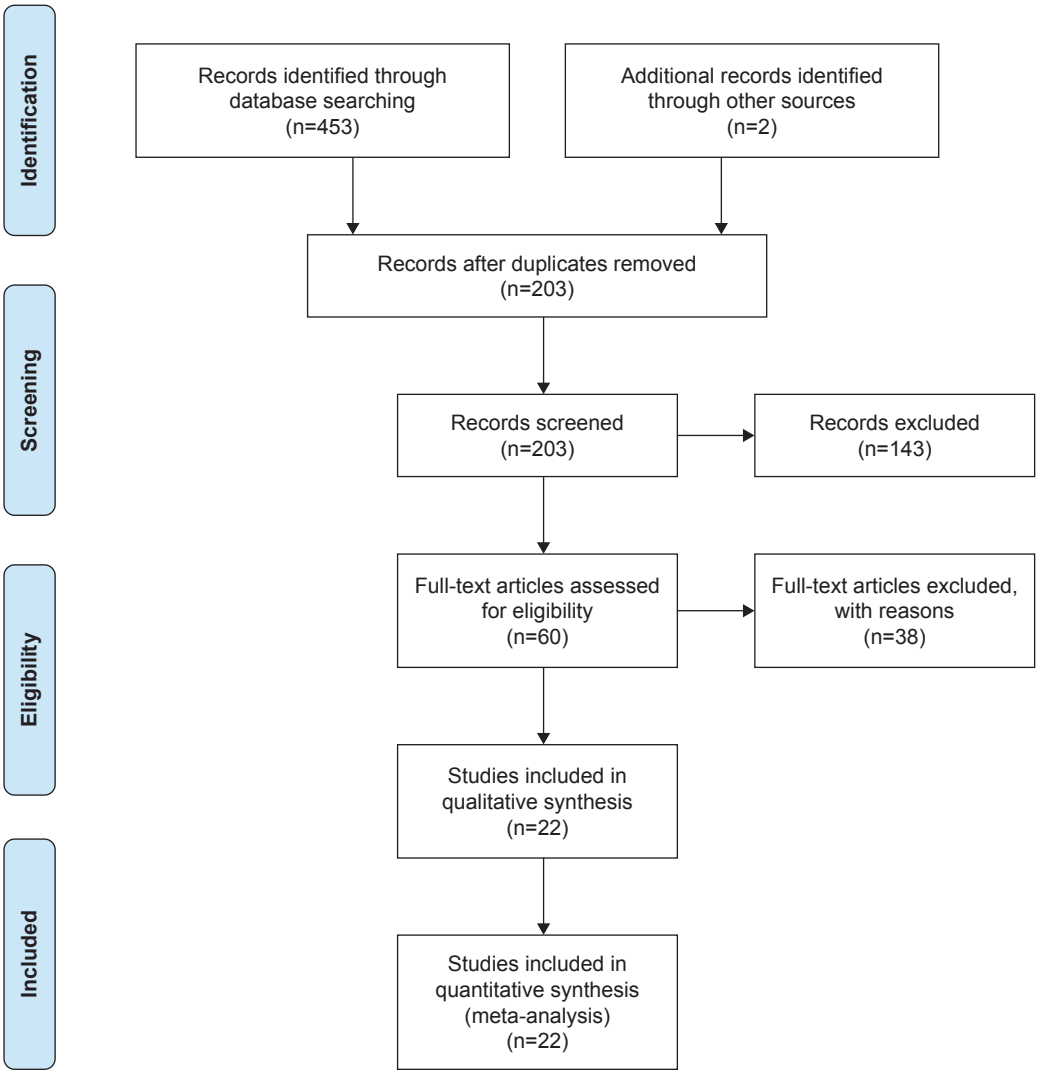


**Figure 1** Flow diagram for the identified published studies included in the meta-analysis.

tongue SCC was 7% (95% CI: 5.0–10.0; Figure 4) using a fixed-effects model. The relevant Funnel plots indicated that there was no publication bias in these 12 studies (Figure 5).

## Sensitivity analysis

Sensitivity analysis was conducted to test the stability of this meta-analysis. The data in the largest and minimum weight were deleted respectively to examine the influence of the deleted data on the pooled rates. With a random effects model, the pooled estimated cervical level IIb metastases rate was 6% (95% CI: 4.0–7.0). When the data in the largest weight[25] were removed, the result was 5% (95% CI: 4.0–6.0), and when the data in the minimum weight[38] were deleted, the result was 5% (95% CI: 4.0–7.0). With a fixed-effects model, the pooled estimated cervical IIb metastases rate for tongue SCC was 7% (95% CI: 5.0–10.0). Then the same method of sensitivity analysis was used for the level IIb pooled metastases rate of tongue SCC and the results were 9% (95% CI: 6.0–13.0) and 10.8% (95% CI: 10.5–11.0), respectively. Deletion of the data in the largest or minimum weight had a negligible influence on the pooled metastasis rate, which indicated the good stability of this meta-analysis.

# Discussion

The aim of SND is to reduce morbidity by preserving the SAN, the sternomastoid muscle and the internal jugular vein. The SAN is important in supplying motor function to the trapezius in the majority of people, and sacrifice of this

**Table 2** Information from 22 studies included in the analysis

| Authors | Year | Recruitment years | Total OSCC cases | cN0 | cN+ | The OSCC cases of IIb metastases | Metastatic rate, % |
|---|---|---|---|---|---|---|---|
| Lim et al[15] | 2004 | 1997–2001 | 74 | 74 | 0 | 4 | 5.00 |
| De Vicente et al[20] | 2015 | 2010–2011 | 56 | 27 | 29 | 1 | 1.80 |
| Maher and Hoffman[21] | 2014 | 2006–2013 | 71 | 71 | 0 | 4 | 5.60 |
| Koerdt et al[18] | 2016 | 2011–2014 | 112 | – | – | 16 | 12.60 |
| Bartella et al[22] | 2016 | 2012–2015 | 183 | 116 | 67 | 6 | 3.30 |
| Manola et al[19] | 2011 | 2002–2006 | 38 | 16 | 22 | 8 | 21.00 |
| Smith et al[23] | 2007 | 2002–2004 | 34 | – | – | 3 | 8.00 |
| Hoyt et al[24] | 2008 | 2002–2006 | 78 | 46 | 32 | 5 | 6.40 |
| Agarwal et al[25] | 2016 | 2011–2015 | 231 | 231 | 0 | 2 | 0.86 |
| Bhattacharya et al[26] | 2015 | – | 30 | – | – | 2 | 6.67 |
| Corlette et al[27] | 2005 | 1998–2003 | 56 | – | – | 4 | 7.14 |
| Chone et al[28] | 2000 | 1988–1997 | 25 | – | – | 1 | 3.60 |
| Elsheikh et al[29] | 2005 | 2001–2004 | 48 | 48 | 0 | 5 | 10.40 |
| Talmi et al[30] | 1998 | 1995–1996 | 33 | – | – | 2 | 6.06 |
| Santoro et al[31] | 2008 | 2004–2007 | 47 | 40 | 7 | 1 | 2.13 |
| Silverman et al[32] | 2003 | 1998–2001 | 35 | – | – | 1 | 2.86 |
| Pantvaidya et al[33] | 2014 | 2008–2011 | 583 | – | – | 22 | 3.80 |
| Villaret et al[34] | 2007 | 2003–2005 | 111 | 54 | 57 | 11 | 9.91 |
| Dabholkar and Kapre[35] | 2016 | 2011–2012 | 65 | – | – | 7 | 10.44 |
| Ghantous et al[36] | 2016 | 2000–2011 | 70 | 35 | 35 | 5 | 7.14 |
| Paleri et al[37] | 2007 | – | 10 | – | – | 1 | 2.60 |
| Chiesa et al[38] | 2000 | 1997–1998 | 11 | 11 | 0 | 1 | 9.09 |
| Total cases | | | 2001 | 769 | 249 | 112 | |

**Note:** "–", Data not provided.
**Abbreviation:** OSCC, oral squamous cell carcinoma.

nerve causes significant shoulder dysfunction and pain. Some authors have reported that even if the SAN is preserved, some degree of shoulder morbidity could occur.[13,39] Leipzig et al concluded that there may be a degree of shoulder dysfunction associated with any type of neck dissection, even when the SAN is minimally dissected or stretched.[40] Kraus et al reported that 50% of patients who underwent SAN-sparing procedures experienced shoulder drop, while 30% of those

**Table 3** A summary of patient characteristics among those with level IIb metastases

| Authors | Year | Cases | IIb metastases cases | IIb metastases patients' specific information | | | | | | Isolated IIb metastases | Distribution of positive level lymph nodes (for cases IIb+) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | Site | Cases | T (no) | | | | | |
| | | | | | | T1 | T2 | T3 | T4 | | |
| Lim et al[15] | 2004 | 74 | 4 | Tongue | 4 | – | 4 | – | – | 0 | I, IIa, III |
| De Vicente et al[20] | 2015 | 56 | 1 | Tongue | 1 | 1 | – | – | – | 0 | IIa, III |
| Maher and Hoffman[21] | 2014 | 71 | 4 | Tongue | 3 | – | 2 | 1 | – | 2 | IIa, III |
| | | | | Retromolar trigone | 1 | – | – | – | 1 | – | – |
| Smith et al[23] | 2007 | 34 | 3 | – | – | – | 1 | – | 2 | – | – |
| Hoyt et al[24] | 2008 | 78 | 5 | – | – | – | 2 | 1 | 2 | – | – |
| Agarwal et al[25] | 2016 | 231 | 2 | Buccal mucosa | – | – | – | – | – | – | – |
| Bhattacharya et al[26] | 2015 | 30 | 2 | Anterior alveolus mandible | 1 | 1 | – | – | – | 0 | IIa |
| | | | | Buccal mucosa | 1 | – | 1 | – | – | – | – |
| Elsheikh et al[29] | 2005 | 48 | 5 | – | – | – | – | – | – | 0 | IIa |
| Talmi et al[30] | 1998 | 33 | 2 | Tongue | 1 | – | – | – | – | – | – |
| | | | | Alveolar ridge | 1 | – | – | – | 1 | – | – |
| Santoro et al[31] | 2008 | 47 | 1 | – | – | – | 1 | – | – | 0 | IIa |
| Silverman et al[32] | 2003 | 35 | 1 | – | – | – | – | – | 1 | 0 | IIa, III |
| Paleri et al[37] | 2007 | 10 | 1 | FOM | – | – | – | – | 1 | 1 | – |
| Chiesa et al[38] | 2000 | 11 | 1 | Tongue | 1 | 1 | – | – | – | – | – |

**Note:** "–", Data not provided.
**Abbreviation:** FOM, floor of mouth.

**Table 4** Special information about the tongue squamous cell carcinoma

| Authors | Year | Total tongue SCC cases | Tongue SCC cases of IIb metastases | Tongue SCC IIb metastases rate, % |
|---|---|---|---|---|
| Lim et al[15] | 2004 | 51 | 4 | 7.84 |
| De Vicente et al[20] | 2015 | 20 | 1 | 5.00 |
| Maher and Hoffman[21] | 2014 | 27 | 3 | 11.11 |
| Koerdt et al[18] | 2016 | 40 | 3 | 7.50 |
| Manola et al[19] | 2011 | 38 | 8 | 21.05 |
| Elsheikh et al[29] | 2005 | 23 | 5 | 21.74 |
| Talmi et al[30] | 1998 | 16 | 1 | 6.25 |
| Silverman et al[32] | 2003 | 16 | 1 | 6.25 |
| Pantvaidya et al[33] | 2014 | 121 | 6 | 5.00 |
| Dabholkar and Kapre[35] | 2016 | 29 | 3 | 10.34 |
| Ghantous et al[36] | 2016 | 8 | 1 | 12.50 |
| Chiesa et al[38] | 2000 | 11 | 1 | 9.09 |
| Total cases | | 400 | 37 | |

**Abbreviation:** SCC, squamous cell carcinoma.

patients who underwent a minimal SAN dissection had pain and shoulder dysfunction.[41] This may be due to traction and elevation of the nerve during dissection of the submuscular recess, namely, level IIb. Therefore, it is very significant to clarify whether to perform or avoid cervical level IIb dissection for the postoperative quality of life in patients with OSCC.

Tongue is the most common primary site for OSCC. Some studies reported that the primary site for level IIb metastasis has no statistical significance.[26,35] But many scholars strongly recommended that dissection of level IIb in patients with tongue SCC should be incorporated into the procedures. Elsheikh et al found the incidence of metastasis at level IIb in patients with primary tumors located in the tongue to be 22%. Thus, they defended that level IIb should be included in the neck dissection in the case of tongue cancer.[29] Maher and Hoffman found cervical level IIb lymph node metastases in 4 of 71 (5.6%) patients with primary OSCC and they also presented a relatively high incidence of level IIb metastasis from the tongue (11%).[21] Bhattacharya et al stated that tongue cancers and cancers of the retromolar trigone had the highest incidence of metastases at level IIb.[26] However, Bartella et al demonstrated that metastases at level IIb resulted preferentially from malignant lesions on the soft palate, alveolar crest of the mandible and the buccal mucosa.[22] In this analysis, it was found that the frequency of level IIb metastases of tongue SCC was higher than that of OSCC; tongue SCC patients, even in their early stages (T1 and T2), were prone to level IIb metastases. The possible reason for the propensity of tongue SCC to metastasize was that the tongue possesses extensive lymphatic network. Although there were still some other primary sites for OSCC

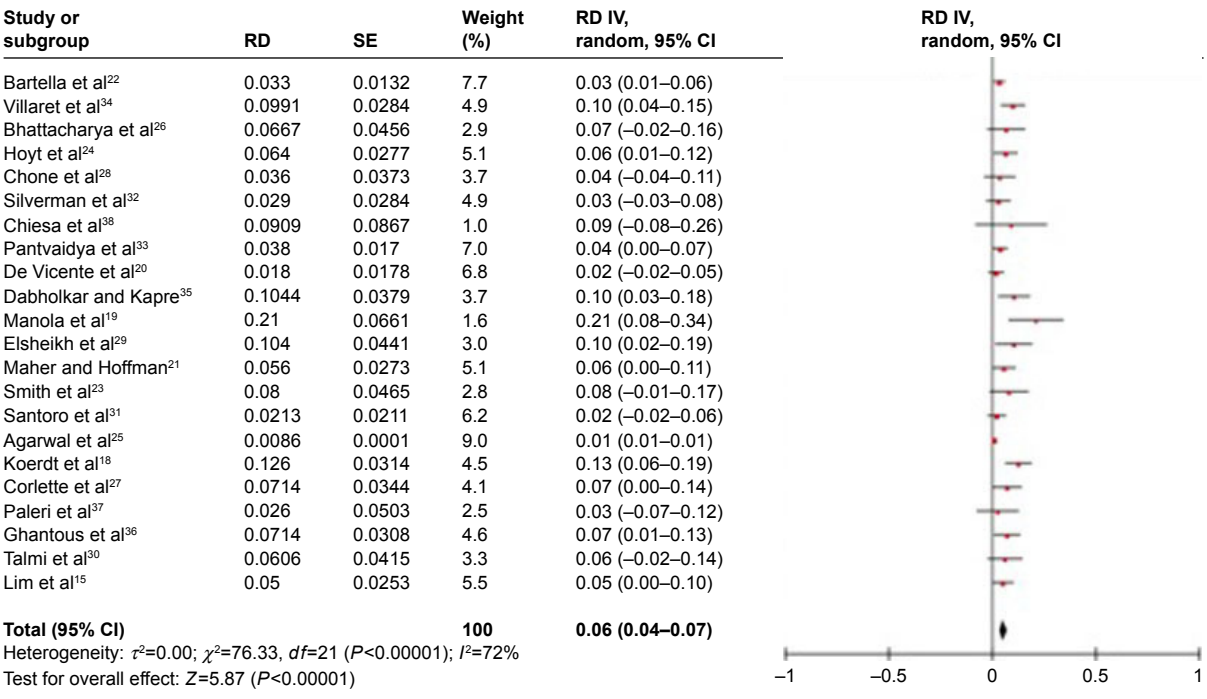


**Figure 2** Forest plot for cervical level IIb metastasis rate for OSCC.
**Note:** Chi-square based Q test was used for heterogeneity evaluation of these studies ($\chi^2$=0.00, $I^2$=72%, $P$<0.1), so the random effects model should be used and the cervical IIb metastatic rate for OSCC was 6%.
**Abbreviations:** *df*, degrees of freedom; IV, inverse variance; OSCC, oral squamous cell carcinoma; RD, risk difference; SE, standard error.

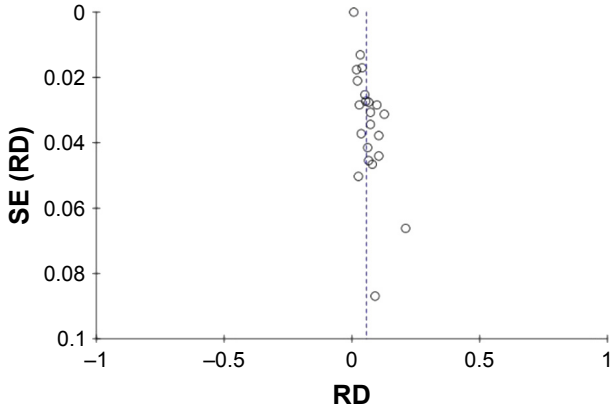


**Figure 3** Funnel plot for cervical level IIb metastasis rate for OSCC.
**Note:** Plot indicates that there was no publication bias in these studies.
**Abbreviations:** OSCC, oral squamous cell carcinoma; RD, risk difference.

patients with level IIb metastases, the number of cases was relatively low for each primary site and the patients were usually in terminal stages (T3 and T4). With no doubt, level IIb dissection should be routinely performed when patients have been found in their terminal stages, no matter where the primary sites are. However, when it comes to the cases in early stages, especially with N0 neck, researchers have different opinions about the extent of the neck dissection.[42] Manola et al believed that sentinel node biopsy with the aid of lymphoscintigraphy appears to be a good technique for early tongue cancer.[19] Yet, on the basis of our study, we suggest that level IIb dissection should better be performed in the case of tongue SCC, even in the early stages. Of course, our proposal still needs further verification due to the lesser number of cases of primary sites, except the tongue. More prospective, multicenter, large-scale trials would help to aid decision making for OSCC management in the future.

In this analysis, it was revealed that the prevalence of metastases at level IIb was low (6%) and isolated level IIb metastases were rarely found. Thus, we suggest that it might not be always necessary to dissect level IIb lymph nodes in OSCC patients to avoid postoperative shoulder disability. Preservation of level IIb was conditional on the stages of primary lesions and the lymph node status. Level IIb dissection could be avoided when the primary lesions were in early stages, yet with the exception of tongue cancer, as we discussed earlier. Pantvaidya et al found that metastases at level IIb were associated with metastases at level IIa in 68.1% of dissections, while only 11.3% of all level IIa metastases had positive nodes at level IIb.[33] Bhattacharya et al also reported that always there were positive nodes in level IIa in patients with positive level IIb nodes.[26] So, it was proposed that the assessment of level IIa should be focused on using preoperative fine-needle aspiration cytology or intraoperative frozen section, thereby to guide further dissection of levels IIb and V.[33] Level IIb dissection is recommended to be conducted in OSCC patients with multilevel neck metastasis, especially level IIa metastasis found preoperatively or intraoperatively.

The reason for the discrepancy in reported incidences of metastases may be partly due to the inconsistency of techniques utilized to detect the neck metastases. Traditional techniques for pathologic analysis of neck specimens by light microscopy with ordinary hematoxylin and eosin staining may fail to detect isolated micrometastases, while new and highly sensitive technologies such as immunohistochemical and molecular analysis may identify subpathologic micrometastases. Hence, the incidence of metastases detected

| Study or subgroup | RD | SE | Weight (%) | RD IV, fixed, 95% CI |
|---|---|---|---|---|
| Silverman et al[32] | 0.0625 | 0.0605 | 4.6 | 0.06 (–0.06–0.18) |
| Chiesa et al[38] | 0.0909 | 0.0867 | 2.2 | 0.09 (–0.08–0.26) |
| Pantvaidya et al[33] | 0.0496 | 0.0198 | 42.8 | 0.05 (0.01–0.09) |
| De Vicente et al[20] | 0.05 | 0.0487 | 7.1 | 0.05 (–0.05–0.15) |
| Dabholkar and Kapre[35] | 0.1035 | 0.0565 | 5.3 | 0.10 (–0.01–0.21) |
| Manola et al[19] | 0.2105 | 0.0661 | 3.8 | 0.21 (0.08–0.34) |
| Elsheikh et al[29] | 0.2174 | 0.086 | 2.3 | 0.22 (0.05–0.39) |
| Maher and Hoffman[21] | 0.1111 | 0.0605 | 4.6 | 0.11 (–0.01–0.23) |
| Koerdt et al[18] | 0.075 | 0.0416 | 9.7 | 0.07 (–0.01–0.16) |
| Ghantous et al[36] | 0.125 | 0.117 | 1.2 | 0.13 (–0.10–0.35) |
| Talmi et al[30] | 0.0625 | 0.0601 | 4.6 | 0.06 (–0.06–0.18) |
| Lim et al[15] | 0.0784 | 0.0376 | 11.9 | 0.08 (0.00–0.15) |
| **Total (95% CI)** | | | **100** | **0.07 (0.05–0.10)** |

Heterogeneity: $\chi^2$=9.77, *df*=11 (*P*=0.55); $I^2$=0%
Test for overall effect: *Z*=5.73 (*P*<0.00001)

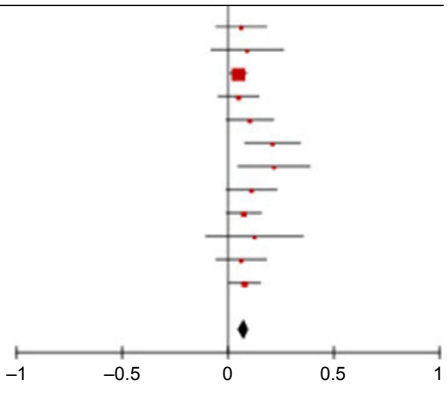


**Figure 4** Forest plot for cervical level IIb metastasis rate for tongue SCC.
**Note:** Chi-square based Q test was used for heterogeneity evaluation of these studies ($\chi^2$=9.77, $I^2$=0%, $P$<0.1), so the fixed-effects model was used and the cervical IIb metastasis rate for tongue SCC was 7%.
**Abbreviations:** *df*, degrees of freedom; IV, inverse variance; SCC, squamous cell carcinoma; RD, risk difference; SE, standard error.

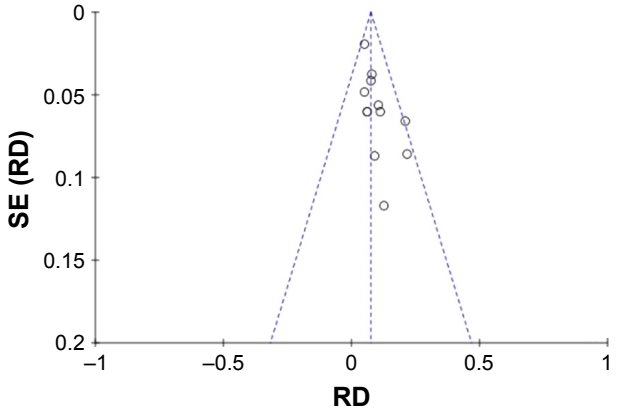


**Figure 5** Funnel plot for cervical level IIb metastasis rate for tongue SCC.
**Note:** Plot indicates that there was no publication bias in these studies.
**Abbreviations:** RD, risk difference; SCC, squamous cell carcinoma; SE, standard error.

has been found to be higher than previously indicated.[43–46] Among the eight included studies which mentioned stain method, new technologies were used in two studies to detect metastases. Manola et al used molecular markers such as cytokeratin and epithelial membrane antigen and identified 8 cases with IIb metastases in 38 tongue SCC patients.[19] Elsheikh et al found that the prevalence of metastases at level IIb was 6% (3/48) by pathologic analysis, but 10% (5/48) by CK20 nested reverse transcription-polymerase chain reaction, with the primary tumors located in the tongue.[29] Thus, they stated that determination of *CK20* gene expression by nested reverse transcription-polymerase chain reaction proved a good tool for detection.

It must be admitted that this study has limitations. First, there is inherent heterogeneity among the studies included. The inclusion and exclusion criteria, specimen processing methods and techniques for metastasis detection were variable. In addition, the limited data available and the relatively small sample size discounted the authority of this analysis. A large prospective multi-institutional cohort study with standardized intraoperative methods of dissecting level IIb and sensitive pathology detection for level IIb lymphonodus would help to make a definitive decision on the management strategy of OSCC in the future.

## Conclusion

Based on the evidence that the frequency of level IIb metastasis in OSCC was low, level IIb dissection could be avoided when the primary lesions were in early stages (T1 and T2), yet with the exception of tongue cancer. It is recommended to dissect level IIb for tongue cancers without considering the stages of primary lesions and the lymph node status. It is also suggested that level IIb dissection should be performed in patients preoperatively or intraoperatively found with multilevel neck metastases, especially IIa metastases. When considering the merits of preservation of level IIb, the benefit of preservation of SAN function has to be weighed against potentially reduced oncologic control.

## Disclosure

The authors report no conflicts of interest in this work.

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