Cervical metastases of oral maxillary squamous cell carcinoma: A systematic review and meta-analysis

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Accepted 12 September 2015
Published online 18 February 2016 in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/hed.24274

ABSTRACT: Cervical treatment of oral maxillary squamous cell carcinoma (SCC) remains controversial. We determined the metastases incidence and evaluated its predictive factors. Systematic review and meta-analysis was conducted of 23 Chinese and English-language articles retrieved from PubMed, Ovid, Embase, Cochrane Library, China National Knowledge Infrastructure, and Chinese Scientific and Technological Journal databases. Total cervical metastases and occult metastases rate was 32% and 21%, respectively. Positive lymph node detection was likeliest from levels I to III. The maxillary gingival metastases rate was higher than that of the hard palate. Advanced-stage tumors had higher metastatic risk than early-stage tumors. Well-differentiated tumors had a significantly higher metastases rate than medium and poor-differentiation tumors. N0 cases had survival benefit compared with N+ cases. Metastases rate of oral maxillary SCC correlates significantly with T classification and pathological stage. T and N classifications impact outcome significantly. Therefore, levels I to III selective neck dissection is recommended for patients with T3/4 cN0 disease. © 2016 Wiley Periodicals, Inc. *Head Neck* **38**: E2335–E2342, 2016

KEY WORDS: squamous cell carcinoma, maxillary gingiva, hard palate, cervical metastases, elective neck dissection

INTRODUCTION

Squamous cell carcinoma (SCC) is the most common malignant tumor in the oral cavity. Cervical metastases is a well-known behavior of oral SCC and may have a distinct influence on prognosis and clinical outcome.[1,2] That SCC of the tongue, floor of the mouth, and mandibular gingiva has a strong tendency for cervical metastases has been well-documented. Elective neck dissection is well accepted in such patients.[3–8] However, the management of the clinically negative (cN0) neck of patients with hard palate, maxillary alveolar, or gingival SCC remains on a "watch and wait" basis, given the low metastases rate. It was only recently that studies focused on cervical metastases in maxillary SCC. Some results indicate that the metastatic risk is much higher than expected, and elective neck dissection should be recommended for these patients. However, most of the studies are retrospective, with relatively small sample sizes.[9–31] Studies with high level of evidence, such as prospective studies and clinical trials, are still lacking, and treatment of the cN0 neck is still controversial. With the development of evidence-based medicine, meta-analysis, a convincing and effective tool, has become increasingly popular in clinical studies.[32–37] Thus, the primary purpose of this systematic review was to identify the risk of cervical metastases in patients with maxillary SCC and to evaluate the predictive factors for metastases.

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Contract grant sponsor: The Science and Technology Committee of Beijing, China (no. Z131107002213116) and the National Supporting Program for Science and Technology (no. 2014BAI04B06).

Additional Supporting Information may be found in the online version of this article.

MATERIALS AND METHODS

Study identification

An initial online search was performed using the PubMed, Ovid, and Embase databases for English-language literature, and the China National Knowledge Infrastructure and Chinese Scientific and Technological Journal databases for Chinese literature (from January 2000 to December 2013). A broad search strategy was used, utilizing the following keywords: "squamous cell carcinoma," "cervical metastases," "maxillary gingiva," "hard palate," and "elective neck dissection." Two reviewers screened the titles and abstracts of the retrieved articles. We obtained full articles for relevant studies and studies in which the title and abstract information were insufficient for us to make a clear decision. The reference lists of the selected articles were also screened, and the relevant citations were included in the next phase.

Study selection

Two reviewers obtained and evaluated the full text of articles retrieved from the first round of searching and

from the reference list search. Studies were included according to the following criteria: (1) tumors were pathologically confirmed as SCC originating from maxillary gingival or hard palate; (2) tumors were staged according to the Union for International Cancer Control (UICC) classification criteria; and (3) the primary treatment was surgery only. The exclusion criteria were: (1) SCC originating from the maxillary sinus; (2) lacking of TNM classification information; and (3) primary tumor invading soft palate, oropharynx, and retromolar area. Single case reports and articles in languages other than English and Chinese were also excluded.

In the retrieving procedure, the first reviewer reviewed the abstract and selected the studies according to the inclusion and exclusion criteria. The second reviewer then reviewed and checked all the abstracts again and made his selection also based on the same criteria. The whole text of the selected studies was reviewed again by both the reviewers in details. After that, the 2 reviewers discussed any differences encountered, and disagreement was managed by consultation with a third party.

Study design

The studies included for review were randomized controlled trials, controlled clinical trials, retrospective studies, and cross-sectional studies. There was no restriction on publication date or status.

Outcome measures

We identified the risk of cervical metastases of maxillary SCC according to the cervical metastases rate, which included the rates of total metastases and occult metastases. The primary site, T classification, and pathological grade were evaluated as predictive factors for cervical metastases. We assessed the prognostic factors, including N classification and neck treatment strategy. There were several methods used to identify cN+ cases before surgery according to the published studies: (1) palpable enlarged lymph nodes with physical examination; (2) lymph nodes larger than 10 mm with suspicions of liquefaction examined by the CT/MRI scans; (3) metastases detected by positron emission tomography (PET)-CT scan; and (4) pathologically confirmed by fine-needle aspiration (FNA).

Data extraction and analysis

The first reviewer collected the data and imported it into electronic database form (Microsoft Excel, Redmond, WA). The second reviewer checked the extracted data for omissions or inaccuracies. The 2 reviewers discussed any differences encountered, and disagreement was managed by consultation with a third party.

We used R software[38] for the meta-analysis of the metastases rate. The difference between rates was evaluated using odds ratios (ORs). The 95% confidence interval (95% CI) was also calculated. A Q test was used for evaluating heterogeneity. The fixed-effect model was used when there was no heterogeneity ($p > .1$; $I^2 < 50\%$); the random-effect model was used when there was heterogeneity ($p < .1$; $I^2 > 50\%$). Publication bias was evaluated using the Begg plots.

RESULTS

We retrieved 539 articles from the database search (PubMed, 234; Ovid, 165; Embase, 98; and China National Knowledge Infrastructure and Chinese Scientific and Technological Journal Database for Chinese Technical Periodicals, 42). After identification and selection, 23 articles met the inclusion criteria for further assessment.

Of the 23 articles, 21 were retrospective studies, 1 was a cohort study, and 1 was a cross-sectional study. The studies included 2139 cases in total (Table 1).

Rates of cervical metastases and occult metastases

The rates of cervical metastases and occult metastases were analyzed in 22 of the 23 articles; the exception being the study by Lin and Bhattacharyya (Table 2).[25] In the 22 studies, metastases was confirmed by pathological examination. The overall metastases rate was defined as the ratio between the number of pN+ cases and total cases. The occult metastases rate was defined as the ratio between the number of cN0pN+ cases and total cN0 cases. Especially for the patients without neck dissection initially, those presenting with regional metastases or recurrence during the follow-up period would also be counted as pN+ cases. However, patients who presented with regional recurrence in the setting of local recurrence were not defined as occult metastases and were excluded from the analysis of occult metastases rate. The forest plots in Figures 1 and 2 show that the overall cervical metastases rate and occult metastases rate were 32% and 21%, respectively. The Begg plots presented with a symmetric distribution and indicated that there was no publication bias in this series (Supplementary Figures S1 and S2, online only).

Primary sites

Seven articles focused on the correlation between primary site and metastases rate (Table 3). The metastases rate of tumors originating from the maxillary gingiva was 35% and from the hard palate was 28%. The OR was 0.66 ($p > .01$), which suggested there was not significant relation between primary site and metastases (Supplementary Figures S3–S5, online only).

T classification

We compared the incidence of maxillary SCC cervical metastases in early-stage (T1/2) and advanced-stage (T3/4) disease, according to the TNM classification criteria (UICC 2010), identifying and including 17 articles for this purpose (Table 4). The meta-analysis determined a significantly higher metastases rate in advanced-stage disease compared to early-stage disease (19%), with an OR of 0.37 ($p < .0001$; Supplementary Figures S6–S8, online only). There was no publication bias in this series (Supplementary Figure S9, online only).

Pathological grade

We evaluated the effect of different pathological features on the cervical metastatic risk of patients with maxillary SCC according to the World Health Organization (WHO, 2005) pathological classification criteria for oral SCC. As only 4 articles met this criterion, we divided this

TABLE 1. Information of included studies and the identification for outcome measures.

Authors	Year	study design	Cases	Outcome measurements						
				Metastatic rate	Primary site	T classification	Pathological grade	Metastatic region	Survival rate	Effect of elective neck dissection
Dalal[9]	2013	Retrospective	30	√	√	√		√		√
Feng[10]	2013	Retrospective	129	√		√				√
Eskander[11]	2013	Cohort	97	√		√				
Yang[12]	2013	Retrospective	64	√	√	√	√	√	√	
Sagheb[13]	2013	Retrospective	135	√		√	√			
Chen[14]	2012	Retrospective	63	√	√	√	√	√		
Brown[15]	2012	Retrospective	43	√						
Poeschl[16]	2011	Retrospective	74	√		√				√
Beltramini[17]	2011	Retrospective	65	√	√	√				
Montes[18]	2011	Retrospective	131	√						
Liu[19]	2010	Retrospective	127	√	√	√			√	
Lubek[20]	2010	Retrospective	37	√		√				
Nicolai[21]	2010	Retrospective	55	√		√				
Wang[22]	2010	Retrospective	79	√		√				
Valentino[23]	2010	Retrospective	19	√						
Morris[24]	2010	Retrospective	139	√		√		√		
Lin[25]	2009	Cross-section	725			√			√	
Kruse[26]	2009	Retrospective	30	√		√	√			
Mourouzis[27]	2009	Retrospective	17	√	√	√			√	
Montes[28]	2008	Retrospective	14	√	√	√				
Simental[29]	2006	Retrospective	26	√						
Ogura[30]	2003	Retrospective	21	√						
Yorozu[31]	2001	Retrospective	19	√						
Total cases			2139	1414	423	1890	292	296	933	233

series into 2 groups: grade I (well-differentiated) and grade II and III (medium and poorly differentiated), to reduce the small-sample effect (Table 5). The meta-analysis determined that the metastases rate of well-differentiated tumors was 16%, which was significantly lower than that of medium or poorly differentiated tumors, where the rate was 37% (OR = 0.32; $p = .0424$; $p < .05$; Supplementary Figures S10–S12, online only).

Nodal levels of maxillary squamous cell carcinoma

Among the 23 articles, 4 were retrieved for evaluation of the metastatic region of maxillary SCC (Table 6). We

TABLE 2. Clinical studies on cervical metastasis of maxillary squamous cell carcinoma.

Author	Year	Study design	Cases	cN+		cN0		Overall metastatic rate	Occult metastatic rate
				Total	pN+	Total	pN+		
Dalal[9]	2013	Retrospective	30	7	7	23	8	50.0%	34.8%
Feng[10]	2013	Retrospective	129	0	0	129	31	24.0%	24.0%
Eskander[11]	2013	Cohort	97	28	23	69	17	41.2%	24.6%
Yang[12]	2013	Retrospective	64	13	6	51	5	17.2%	9.8%
Sagheb[13]	2013	Retrospective	135	40	40	95	12	38.5%	12.6%
Chen[14]	2012	Retrospective	63	13	9	50	8	27.0%	16.0%
Beltramini[17]	2011	Retrospective	65	8	8	57	6	21.5%	10.5%
Montes[18]	2011	Retrospective	131	22	22	109	19	31.3%	17.4%
Liu[19]	2010	Retrospective	127	49	49	78	11	47.2%	14.1%
Lubek[20]	2010	Retrospective	37	2	2	35	4	16.2%	11.4%
Nicolai[21]	2010	Retrospective	55	5	5	50	7	21.8%	14.0%
Wang[22]	2010	Retrospective	79	7	7	72	10	21.5%	13.9%
Valentini[23]	2010	Retrospective	19	1	1	18	1	10.5%	5.6%
Morris[24]	2010	Retrospective	139	12	9	127	34	30.9%	26.7%
Lin[25]	2009	Cross-section	725	–	–	–	99	13.7%	–
Kruse[26]	2009	Retrospective	30	4	4	26	7	36.7%	26.9%
Mourouzis[27]	2009	Retrospective	17	4	4	13	2	35.3%	15.4%
Montes[28]	2008	Retrospective	14	3	3	11	3	42.9%	27.3%
Simental[29]	2006	Retrospective	26	2	2	24	7	34.6%	29.2%
Ogura[30]	2003	Retrospective	21	6	6	15	8	66.7%	53.3%
Yorozu[31]	2001	Retrospective	19	5	5	14	3	42.1%	17.6%

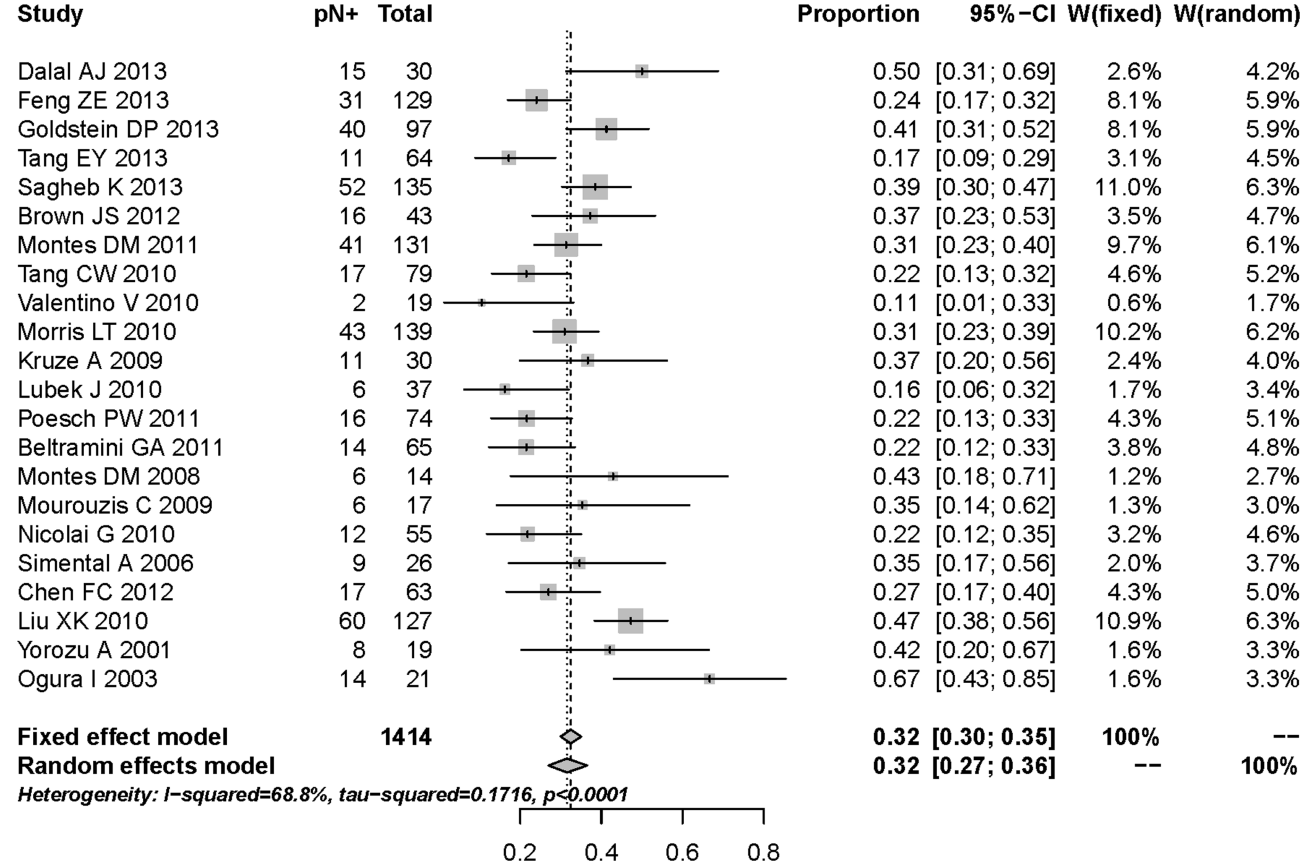

FIGURE 1. Forest plot for overall cervical metastasis rate of oral maxillary SCC. The Q test presented with heterogeneity of these studies ($\chi^2 = 0.1716$,I2 = 68.8%, $p < 0.1$), so the random effects model should be used and the overall metastatic rate was 32%.

divided the cervical lymph nodes into 5 levels according to the American Joint Committee on Cancer (AJCC) classification. There were 86 pN+ cases in the 4 studies, and 172 positive lymph nodes were detected and metastases was confirmed by pathological examination. Of these, 64 were level I (37.2%), 81 were level II (47.1%), and 19 were level III (11.1%). Level IV and V metastases were relatively rare (4.6%).

DISCUSSION

SCC is the most common malignant tumor in the oral cavity; cervical metastasis is one of its most common features and can affect prognosis significantly. Many studies have proven that SCC in oral subsites, such as the tongue, floor of the mouth, buccal mucosa, and mandibular gingiva, present higher risk of cervical metastases, and elective neck dissection is necessary in such patients.[39–44] However, the risk of cervical metastases of maxillary gingiva and hard palate SCC is considered lower than that of SCC in other primary sites, and management of cN0 patients is to "watch and wait." The National Comprehensive Cancer Network (NCCN)[45] proposed guidelines for treatment strategies for head and neck cancer, suggesting levels I to III selective neck dissection for cN0 patients with SCC of the tongue, floor of the mouth, mandibular gingiva, and buccal mucosa. However, there is still no specific strategy for cN0 cases of maxillary SCC.

Only recently, several studies[9–31] reported that cervical metastasis of maxillary SCC ranges from 21.5% to 66.7%, which is much higher than expected and comparable to that of other primary oral sites. However, almost all were retrospective studies with relatively small sample sizes, and there is still a lack of high level evidence-based studies, such as prospective studies, therefore, treatment of the cN0 neck remains controversial.

With the development of evidence-based medicine, systematic review, especially meta-analysis, has become increasingly popular in clinical studies.[32–37] Currently, some researchers have performed systematic reviews and meta-analyses of studies on cervical metastases of SCC of oral sites, such as the tongue, buccal mucosa, or floor of the mouth, and the management of cN0 neck.[42,46] However, there is no such research on maxillary SCC.

In our review, we included all studies on cervical metastasis of maxillary SCC. Via meta-analysis, we identified the incidence of cervical metastasis rate and occult metastatic risk, and evaluated the risk factors. We also performed a systematic review of the management and prognosis of the cN0 neck.

In the 23 articles included, the cervical metastases rate ranged from 13.7% to 66.7%. The meta-analysis results

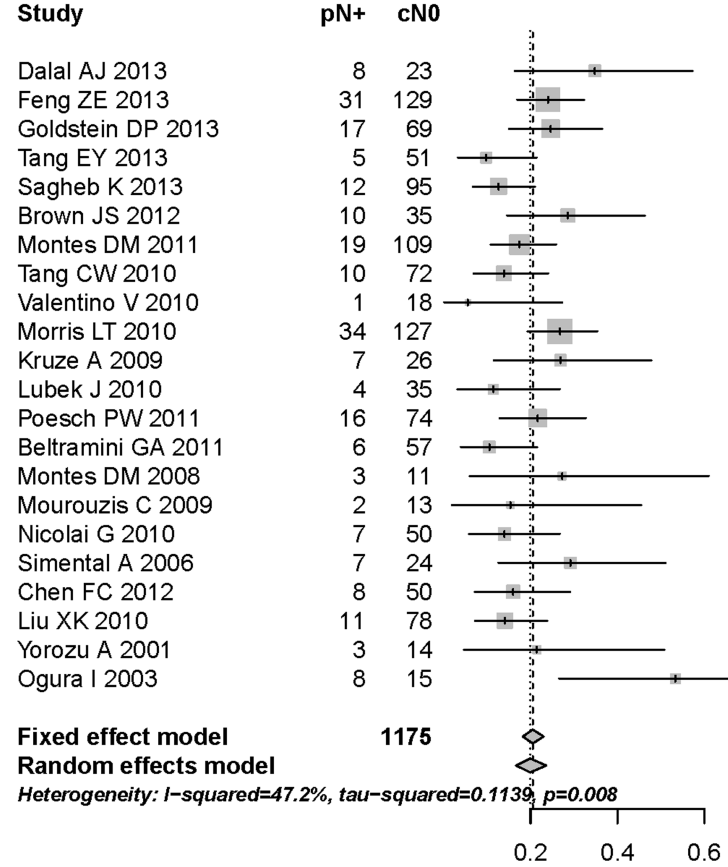

FIGURE 2. Forest plot for occult metastasis rate of oral maxillary SCC. The Q test presented with very small heterogeneity of these studies ($\chi^2 = 0.1139$,I2 = 47.2%, $p < 0.1$), so the fixed effects model should be used and theoccult metastatic rate was 21%.

indicated that the overall metastases rate was 31%, which was similar to the metastatic risk of SCC of the tongue or floor of the mouth.[4–7] Given the high recurrence rate of oral cancer, an increasing number of studies has raised their concerns about occult metastases. The occult metastases were identified as the situation that positive lymph nodes were found in the cN0 neck after elective neck dissection. More than 60% of patients with oral cancer were T1/2 N0 at the time of study, but there was occult metastases in 6% to 46%.[47] An important factor in prognosis is that occult metastases is likely responsible for regional recurrence and can reduce survival rates by 50%.[1,28] In our review, meta-analysis determined that the occult metastases rate was 20%. Previous studies have reported that the occult metastases rate of SCC of the tongue, floor of the mouth, and mandibular gingiva was 20% to 30%. It is obvious that the risk of cervical metastases of maxillary SCC is equal to that of other subsites of the oral cavity. Consequently, evaluation of occult metastases risk and management of the cN0 neck are of great importance and significance in clinical work.

The AJCC and NCCN suggest that cervical metastasis of oral SCC follows the cascade theory: lymph nodes close to the primary site are likely to be involved before

TABLE 3. Cervical metastasis rate of maxillary squamous cell carcinoma by primary site.

				Maxillary gingival			Hard palate		
Author	Year	Study design	Cases	N0	N+	Metastasis rate	N0	N+	Metastasis rate
Dalal[9]	2013	Retrospective	30	14	7	33.3%	6	3	33.3%
Yang[12]	2013	Retrospective	64	24	7	22.6%	29	4	12.1%
Chen[14]	2012	Retrospective	63	31	12	27.9%	15	5	25.0%
Beltramini[17]	2011	Retrospective	65	26	10	27.8%	24	5	17.2%
Lin[25]	2009	Cross-section	725	221	190	46.2%	121	193	61.5%
Mourouzis[27]	2009	Retrospective	17	6	4	40.0%	5	2	28.6%
Montes[28]	2008	Retrospective	14	7	6	46.2%	1	0	0.0%

TABLE 4. Cervical metastasis rate of maxillary squamous cell carcinoma by T classification.

Author	Year	Study design	Cases	T1/2			T3/4		
				N0	N+	Metastasis rate	N0	N+	Metastasis rate
Dalal[9]	2013	Retrospective	30	3	0	0.0%	12	15	55.6%
Feng[10]	2013	Retrospective	129	55	11	16.7%	43	20	31.7%
Eskander[11]	2013	Cohort	97	40	18	31.0%	19	20	51.3%
Yang[12]	2013	Retrospective	64	36	2	5.3%	17	9	34.6%
Sagheb[13]	2013	Retrospective	135	61	21	25.6%	22	31	58.5%
Chen[14]	2012	Retrospective	63	16	0	0.0%	30	17	36.2%
Beltramini[17]	2011	Retrospective	65	19	2	9.5%	32	12	27.3%
Poeschl[16]	2011	Retrospective	74	22	0	0.0%	36	16	30.8%
Lubek[20]	2010	Retrospective	37	20	2	9.1%	11	4	26.7%
Wang[22]	2010	Retrospective	79	32	0	0.0%	30	17	36.2%
Morris[24]	2010	Retrospective	134	51	12	3.2%	41	30	42.3%
Nicolai[21]	2010	Retrospective	55	19	9	32.1%	24	3	11.1%
Liu[19]	2010	Retrospective	127	42	31	42.5%	36	18	33.3%
Lin[25]	2009	Cross-section	725	307	35	10.2%	319	64	16.7%
Kruse[26]	2009	Retrospective	30	13	10	43.5%	6	1	14.3%
Mourouzis[27]	2009	Retrospective	17	5	0	0.0%	6	6	50.0%
Montes[28]	2008	Retrospective	14	6	4	40.0%	2	2	50.0%

TABLE 5. Cervical metastasis rate of maxillary squamous cell carcinoma according to pathological grade.

Author	Year	Study design	Cases	Grade I			Grade II–III		
				N0	N+	Metastasis rate	N0	N+	Metastasis rate
Yang[12]	2013	Retrospective	64	29	5	14.7%	24	6	20.0%
Sagheb[13]	2013	Retrospective	135	24	2	7.7%	59	50	45.9%
Chen[14]	2012	Retrospective	63	23	7	23.3%	23	10	30.3%
Kruse[26]	2009	Retrospective	30	7	0	0.0%	12	11	47.8%

the distal lymph nodes. The tumor cells invade the lymphatic vessels in the surrounding tissue, proliferate in the lymph nodes, and reach the distal lymph nodes via the lymphatic network.[45] SCC of the tongue, floor of the mouth, and mandibular gingiva is likely to metastasize to levels I to III. There are 2 pathways for maxillary SCC metastases to the neck. Lymph from the maxillary gingiva drains to the submandibular lymph nodes through the buccal lymphatic system, which includes the gingivalbuccal complex, whereas lymph from the hard palate drains directly to the deep cervical lymph nodes through the parapharyngeal or retropharyngeal lymphatic system.[17] In our review, we retrieved data on lymph node involvement from 4 articles. We divided 172 positive lymph nodes in 86 pN+ cases into levels I to V, among which >95% of metastatic lymph nodes were levels I to III. Morris et al[24] performed a retrospective study of 139 patients with maxillary SCC. Eleven cN0 patients underwent elective neck dissection and 32 patients underwent radical neck dissection after regional recurrence. In their series, cervical metastases, mostly levels I to III, was confirmed by pathological examination.

The involvement of regional lymph nodes in head and neck cancer depends on various factors, including primary site, size, depth, and other histological features of the primary tumor.[17]

The study by Ma[48] proposed that the occult metastatic risk of oral cancer should be related to the primary site. The rich lymphatic network and flexibility of the tissue leads to a high risk of metastases. SCC of the posterior

TABLE 6. Metastatic regions of maxillary squamous cell carcinoma.

Author	Year	Total cases	pN+ cases	No. of positive lymph nodes	Levels				
					I	II	III	IV	V
Dalal[9]	2013	30	15	15	6	5	4	0	0
Yang[12]	2013	64	11	30	15	12	2	1	0
Chen[14]	2012	63	17	67	15	41	7	2	2
Morris[24]	2010	139	43	60	28	23	6	1	2
Total		296	86	172	64	81	19	4	4
%					37.2	47.1	11.1	4.6	4.6

oral sites has a relatively higher metastatic risk. Metastases are more likely to occur in mandibular gingival SCC than in maxillary SCC. Our meta-analysis determined that maxillary gingival SCC had a higher metastatic risk than hard palate SCC. The maxillary gingiva is close to the vestibular sulcus, which is more likely to be involved in the gingival-buccal complex, which has a rich lymphatic network. In contrast, the hard palate mucosa is thin, inflexible, and lacks lymphatics, which renders the risk of metastases much lower. Beltramini et al[17] reported that the metastatic risk increases as the tumor approaches the soft palate.

According to the TNM classification system (UICC 2010), T classification represents tumor size, depth of invasion, and relation with the surrounding tissue. There is little chance of cervical metastases for very early-stage tumors. However, the risk increases with tumor size. Therefore, some surgeons believe that, with the exception of T1 patients, elective neck dissection should be performed for all patients with oral cancer.[49,50] Others believe that even T1 cases face occult metastatic risk; therefore, any patient with a primary tumor >1 cm should receive elective neck dissection. It was worth noting that 17 of the included 23 articles considered T classification a risk factor of metastases in maxillary SCC. The results suggest that patients with advanced-stage (T3/4) disease face a significantly higher risk of metastases. Montes et al[18] and Lin and Bhattacharyya[25] reported that the cervical metastases rate of maxillary SCC was strongly correlated with T classification. Ogura et al[30] used radiography to evaluate tumor size and depth of invasion, and found that invasion of maxillary bone (T4) indicated higher metastatic risk.

We used the WHO criteria (2005) to evaluate the histological features of maxillary SCC, which are an important indicator for assessing malignancy. It was believed that capillary invasion is the most significant histological feature of metastases.[24] Acharya et al[51] suggested that the metastatic risk of well-differentiated maxillary SCC was lower than that of poorly differentiated cases. There is a lack of similar studies, and we retrieved only 4 articles for meta-analysis of this aspect. The results also indicated higher metastatic risk in medium or poorly differentiated cases. However, given the small sample size and lack of similar studies, there would be publication bias and selective bias, and prospective studies with large sample sizes are still required.

As with other types of oral cancer, regional recurrence occurs in patients with maxillary SCC, especially in untreated cN0 cases. Cervical metastases or recurrence could have an impact on the prognosis of maxillary SCC. Yorozu et al[31] suggested that N classification was the only remarkable factor in the survival rate of patients with maxillary SCC. We performed a systematic review of 4 retrospective studies and 1 cross-sectional (descriptive) study and found that N0 patients had higher 5-year survival rates than N+ patients (Supplementary Table 7, online only). We expect that there will be more studies with larger sample sizes and prospective studies on this aspect.

It was reported that elective neck dissection should be performed on cN0 patients with oral cancer when the occult metastases rate is >20%.[52,53] It has also been accepted that elective neck dissection should be performed routinely for SCC of the tongue, floor of the mouth, mandibular gingiva, and other oral subsites.[54–56] However, controversy over treatment of the cN0 neck in patients with maxillary SCC remains. Traditional management involves observation, but studies have found that elective neck dissection for cN0 patients at primary tumor resection is beneficial. Based on our meta-analysis, we suggest that the incidence of cervical metastases in maxillary SCC is higher than expected and that the occult metastatic risk is similar to that of other oral subsites. The metastatic risk is much higher for advanced-stage and poorly differentiated tumors. Therefore, we suggest that elective neck dissection be considered for maxillary SCC.

There are few studies on the correlation between elective neck dissection and prognosis of maxillary SCC; there have been no randomized controlled trials either. In this article, we reviewed the only 3 retrospective studies on the topic in the last decade, and our findings indicate that elective neck dissection benefits patients by reducing the recurrence rate and improving the survival rate.

Although our study has collected all the related studies, the quantity, quality, and type of these studies still may limit the level of evidence of this meta-analysis. Most of the studies included in this review were retrospective types and even some with small sample sizes. Heterogeneity of these studies existed in this meta-analysis. There were not adequate data and studies for the meta-analysis of prognosis and treatment strategy, and we cannot control for variables associated with metastases without getting patient level data. Thus, more prospective studies or random clinical trials with larger sample sizes are expected in the future.

CONCLUSIONS

Based on our literature review and meta-analysis, we conclude that the risk of cervical metastases for SCC originating from the maxillary gingiva and the hard palate is higher than expected and is comparable to that of other oral sites. The metastases rate correlates strongly with T classification and pathological staging. Advanced T classification and higher-grade tumors presents significantly higher metastatic risk. Both T and N classification affect the outcome of maxillary SCC. Based on the limited number of studies addressing the impact of elective neck dissection on survival, there seems to be some benefit, however, further studies are still required. We recommend levels I to III selective neck dissection for T3/4 cN0 patients.

Acknowledgments

The authors thank Zhi-xia Li and Zhi Qu from the Department of Epidemiology and Biostatistics, Peking University Health Science Center for Statistical Analysis Support and the professional editor of Elixigen Company for revising and modifying the English language of this manuscript.

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