ORAL MAXILLARY SQUAMOUS CARCINOMA: AN INDICATION FOR NECK DISSECTION IN THE CLINICALLY NEGATIVE NECK

David M. Montes, DDS,[1] Eric R. Carlson, DMD, MD,[2] Rui Fernandes, DMD, MD,[3] G. E. Ghali, DDS, MD,[4] Joshua Lubek, DDS, MD,[5] Robert Ord, DDS, MD,[5] Bryan Bell, DDS, MD,[6] Eric Dierks, DDS, MD,[6] Brian L. Schmidt, DDS, MD, PhD[7]

[1] Department of Oral and Maxillofacial Surgery, Sanford–MeritCare Health System, Fargo, North Dakota
[2] Department of Oral and Maxillofacial Surgery, University of Tennessee, Knoxville, Tennessee
[3] Department of Oral and Maxillofacial Surgery, University of Florida, Jacksonville, Florida
[4] Department of Oral and Maxillofacial Surgery, Louisiana State University Health Sciences Center, Shreveport, Louisiana
[5] Department of Oral and Maxillofacial Surgery, University of Maryland, Baltimore, Maryland
[6] Legacy Emanuel Hospital, Head and Neck Associates, Portland, Oregon
[7] Department of Oral and Maxillofacial Surgery and Bluestone Center for Clinical Research, New York University, New York, New York. E-mail: bls322@nyu.edu

Accepted 6 September 2010
Published online 6 December 2010 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/hed.21631

Abstract: *Background.* This multicenter study was undertaken to characterize the metastatic behavior of oral maxillary squamous carcinoma and to determine the role of selective neck dissection.

Methods. A retrospective, multicenter study of patients surgically treated for oral maxillary squamous carcinoma was completed. Data collected included primary tumor location, cervical lymph node status, and neck failure rate.

Results. The study included 146 patients. The adjusted regional metastatic rate was 31.4%. Of those N0 (clinically negative) necks treated with or without neck dissection, 14.4% developed cervical metastasis. Within the cohort, 7.5% of patients died with distant disease. The regional salvage rate was 52.9%. None of the patients with locoregional failures were salvaged.

Conclusions. Maxillary palatal, alveolar, and gingival squamous carcinomas exhibit aggressive regional metastatic behavior. Surgical salvage rates for neck failure are low; therefore, selective neck dissection (levels I–III) is recommended at the time of resection of T2, T3, and T4 maxillary squamous carcinomas. © 2010 Wiley Periodicals, Inc. *Head Neck* **33:** 1581–1585, 2011

Keywords: squamous cell carcinoma; maxillary; oral cancer; neck dissection; cervical metastasis

Squamous carcinomas of the hard palate, maxillary gingival, and maxillary alveolus are rare relative to other oral subsites. For maxillary squamous carcinoma there is paucity in published data, particularly regarding management of the clinically negative neck (N0). No randomized, prospective studies are available to guide clinical management of oral maxillary subsite squamous carcinomas. Recently, 2 groups have published their experience with maxillary squamous carcinomas.[1,2] These independent studies suggest that maxillary squamous carcinoma behaves similarly to other well-studied oral cavity subsites with respect to regional metastasis. However, both of these studies are limited by small patient numbers. The current surgical data regarding the rate of cervical metastasis are based on the experience of 2 publications composed of only 40 patients.[1,2] There is no information regarding the highest risk location harboring occult metastasis from maxillary squamous carcinoma nor as to whether cervical lymph nodes become involved without the concomitant parapharyngeal and superficial buccal lymphatic basin metastatic spread.[3–5]

Management of the clinically negative neck in patients with maxillary oral cavity squamous carcinoma has received little attention compared with other oral cavity subsites such as the oral tongue, floor of mouth, and mandibular gingival. Patients at highest risk for regional lymph node metastasis have been difficult to identify based on clinical parameters alone; therefore, a selective neck dissection is commonly recommended for patients with oral squamous carcinoma involving the more well studied oral sites.[6–8] The published regional metastatic rates and survival benefit demonstrate the value of selective neck dissection over a wait-and-watch approach for oral cavity squamous carcinoma.[9–11] A commonly cited study is the decision tree analysis reported by Weiss et al,[12] which proposes that a 20% risk of occult metastasis should be the threshold for elective surgical management of the cervical lymphatics at risk. In a randomized, prospective study, Klingerman et al[13] demonstrated a significant

Correspondence to: B. L. Schmidt

Eric R. Carlson receives royalty from Wiley Blackwell Publishing.

improvement in survival following selective neck dissection for the management of a clinically negative neck in patients with oral tongue squamous carcinoma. Maxillary squamous carcinomas are rare compared with other oral subsites. To appropriately address the question of cervical metastatic rate for these carcinomas, a multicenter study is required. Our multicenter, retrospective study presented here has been undertaken to define the risk of both occult and overall regional metastasis, in an effort to determine the role for selective neck dissection in the management of maxillary squamous carcinoma.

MATERIALS AND METHODS

The project was approved by the Institutional Review Board. The participating institutions in this retrospective review included the University of California, San Francisco; Louisiana State University Health Sciences Center, Shreveport; The University of Tennessee, Knoxville; The University of Maryland, Baltimore; Legacy Emanuel Hospital, Portland, Oregon; and The University of Florida, Jacksonville. Patients treated for maxillary oral cavity squamous cell carcinomas were identified and their records were reviewed. All patients underwent a complete clinical head and neck examination as well as either MRI or CT of the primary tumor site and neck prior to invasive diagnostic interventions (i.e. fine-needle aspiration or open neck biopsy) or surgical treatment. In all, 146 patients met the inclusion criteria defined by (1) squamous carcinoma of the oral maxillary structures (palate, gingival, and alveolus), (2) confirmation that the maxillary squamous carcinoma did not originate in the nasal cavity or paranasal sinus, and (3) primary tumor management was limited to surgical extirpation. Patients who had tumors invading the oropharynx or retromolar trigone and extending to the mandible were not included. Carcinomas that involved maxillary structures but appeared to originate from the buccal vestibule were also excluded.

RESULTS

The study population consisted of 65 men and 81 women, ages ranging from 35 to 93 years. Postsurgical follow-up ranged from 1 to 180 months. The number of patients with regional disease, mode of management for the N0 neck, and the number of regional failures are listed in Table 1. Four patients were lost to follow-up, 2 of whom were known to have developed distant metastasis and died with disease. During initial consultation, cervical disease was identified in 22 patients (15.1%). In 48 of 146 cases, the initial management included a selective neck dissection for stage I and stage II maxillary disease. No patients within the series are known to have suffered an adverse outcome contributable to a selective neck dissection. For patients with early clinical stage (ie, T1 or T2 and N0) who underwent selective neck dissection, pathologic evaluation of the specimen identified an additional 10 patients (6.8%) with occult regional disease. Within the N0 cohort, 15.3% of these individuals (21/131) ultimately experienced failure in the neck after resection of the primary with or without neck dissection. Surgical salvage occurred in 52.9% of these patients. Five patients (3.4%) demonstrated concomitant locoregional failures, none of whom were salvaged. Of the patients who demonstrated regional failures alone, 11 individuals (7.5%) died with distant metastasis. Within this same group of patients who developed distant metastasis, only 8 of 11 initially presented with T3 or T4 carcinomas and only 4 of 11 presented with regional disease on initial workup. None of the patients in this study had metastasis to the pharyngeal lymphatic basins. One patient developed a presumed local failure that extended to the buccal structures and was not thought to represent buccal lymphatic basin failure. Primary oral maxillary tumors >4 cm in size were associated with regional metastatic rates as high as 55%. When considering all patients equally, 29.5% of individuals (43/146) with maxillary squamous carcinoma developed cervical metastasis.

Table 1. The multicenter cohort: squamous cell carcinoma of the maxillary palate, alveolus, and gingival.

No. of patients	Regional disease on presentation	Management for the N0 neck	Regional failures
65 men	14	15 OBS 27 ND 9 RT	10
81 women	8	46 OBS 21 ND 6 RT	11

Abbreviations: OBS, observation only; ND, neck dissection; RT, radiation therapy.

However, within our multicenter review, 1 surgeon routinely prescribes prophylactic radiation to the cervical lymph nodes at risk when locally advanced tumors are extirpated. This resulted in 15 patients (10.3%) with clinically negative necks receiving prophylactic radiation, as opposed to watchful waiting or surgical management with neck dissection. The same N0 necks treated with radiation must be excluded from the overall N0 count, which remains disease free in the postoperative period. In our study, once N0 patients whose neck was by managed by primary elective radiation were excluded from the disease-free observation cohort, oral maxillary squamous carcinoma was associated with an overall regional metastatic rate of 31.4% (see Figure 1).

DISCUSSION

The potential for efferent lymphatic spread of oral squamous cell carcinoma differs for each oral subsite.[14,15] When considering all oral subsites, the least is known regarding the cervical metastatic rate for

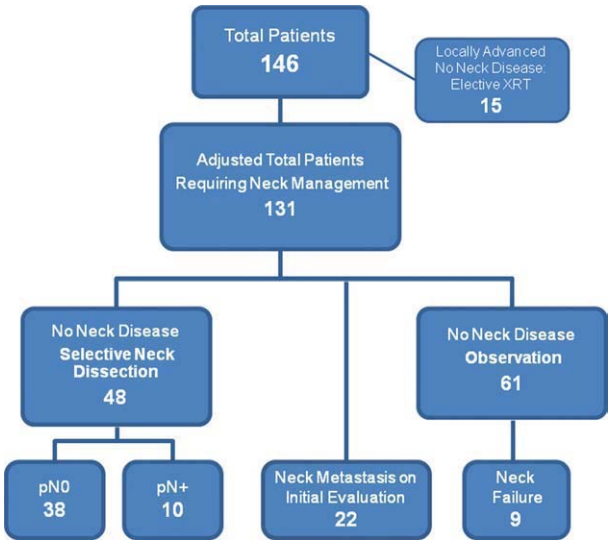

FIGURE 1. Patient distribution flow chart. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

oral cavity maxillary squamous carcinoma. A review of the available published data (Table 2) on maxillary squamous carcinoma shows overall regional metastatic rates that range from 34.6% to 42.9%. These results are based on retrospective studies with a limited number of patients. Our multicenter study provides the largest clinical series to date that characterizes cervical metastasis associated with maxillary squamous carcinoma of the palate, gingival, and alveolar mucosa. In our series, 31.4% of patients with maxillary squamous carcinoma developed cervical metastasis. This rate of cervical metastasis is comparable to that previously reported for maxillary squamous carcinomas,[1,2,16] as well as other oral subsites such as oral tongue and floor of mouth.[17–19] Investigators have yet to identify clinical or molecular parameters that allow clinicians to predict those individuals with the highest risk for metastasis from oral squamous carcinoma. Although tongue and floor of mouth are widely known to exhibit high rates of cervical metastasis, insufficient evidence is available to correlate clinical criteria alone with risk of metastasis.[7] Tumor size alone does not correlate with metastatic risk. Many authors have reported high rates of cervical metastasis for stage I and stage II oral cavity squamous cell carcinoma. Cunningham et al[20] reported that patients with early-stage oral squamous carcinoma who were managed by regional observation alone had a lower survival and salvage rate, compared with patients with early primaries who were managed by selective neck dissection. In this same cohort, completion of a selective neck dissection for stage I oral tongue and floor of mouth squamous carcinomas resulted in a 23% increase in disease-free survival.[20] With regard to maxillary oral palatal, gingival, and alveolar squamous carcinoma, tumor size at presentation may suggest a higher rate of regional metastatic risk (see Figure 2). However, we must consider that 10.3% of the 146 patients presented in this study received prophylactic regional radiation, each being either T3N0 or T4N0. These patients were eliminated from the disease-free observation cohort. Overall, maxillary tumors assessed to be $\leq$4 cm in size demonstrated regional metastatic rates as high as 28%, whereas 55% of T3 and 52% of T4 tumors exhibited regional metastasis (see Figure 2).

Primary tumor location within the maxillary structures likely represents a clinical variable that determines the risk of local recurrence and regional metastasis. In the current study, we were not able to determine whether certain maxillary sites are associated with higher rates of metastasis. Additionally, there are likely differences in the biologic behavior, including metastatic potential, between the different maxillary sites. Resection of the different maxillary sites does present different challenges to the surgeon. Oncologically sound surgical margins are more difficult to achieve in the posterior maxilla relative to the anterior maxilla. Malignant infiltration into the maxillary tuberosity and pterygoid fossa has proven difficult to completely resect. Woolgar and Triantafyllou[21] report a high incidence of positive margins following resection of maxillary alveolar specimens. Given these challenges, adjuvant radiation therapy is liberally

Table 2. Published regional metastatic rates for maxillary squamous cell carcinoma.

Author	No. of patients	Initial N+ disease	N0 neck management	Neck failure rate	Overall metastasis rate
Montes et al, 2008[1]	14	20%	OBS 50% ND 43% RT 7%	21.4%	42.9%
Simental et al, 2006[2]	26	11.5%	OBS 87% ND 11.5% RT 0%	29.2%	34.6%
Ogura et al, 2003[16]	21	28.5%	OBS 100% ND 0% RT 0%	38.0%	38.0%

Abbreviations: OBS, observation only; ND, neck dissection; RT, radiation therapy.

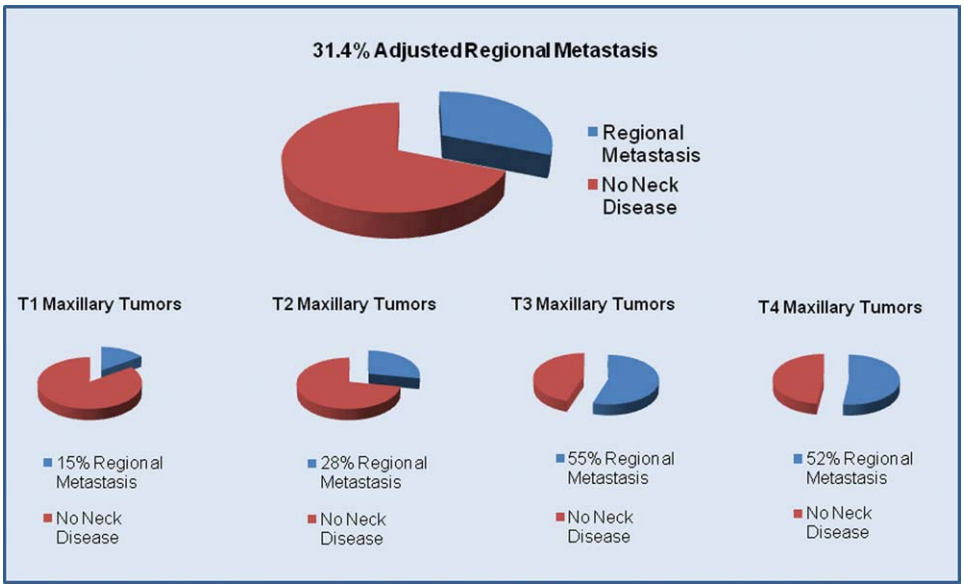

FIGURE 2. Overall and differential metastatic rates for maxillary palatal, alveolar, and gingival squamous carcinoma. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

used for areas of close or positive maxillary resection margins. Radiation therapy to the posterior maxilla carries a number of significant complications, including severe fibrosis and trismus. Therefore, except in locally advanced tumors, radiation therapy should be avoided if oncologically sound margins are realized (ie, >5 mm) following resection and pathologic evaluation. Cheng et al[22] demonstrated maxillary resection margins to be the most stable following resection and pathologic processing compared with other oral cavity sites. Given the stability of maxillary alveolar structures following resection and pathologic processing, precise presurgical planning and exacting intraoperative execution for T1 and T2 tumors will increase the outcome of surgical cure without the need for adjuvant therapy.

For patients with clinically negative necks who are managed by watchful waiting, occult metastasis contributes to regional failures during the early postoperative period. In our adjusted patient cohort of 131 patients, 14.8% of patients (initially classified as N0) managed by regional observation alone developed cervical disease. Yorozu and colleagues[23] published a series of 19 oral cavity maxillary squamous carcinomas treated by radiation alone. The N0 patients in that study had a regional failure rate of 42.1%. Salvage success for regional failures associated with other oral cavity subsite squamous carcinomas remains dismal.[24–26] Recently, Lin and Bhattacharyya[27] published a review that demonstrates maxillary palate and alveolar gingival squamous carcinoma patients have poor survival once regional metastasis occurs. In our study reported here, regional failures were salvaged with either radiation, surgery, or a combination. Our regional salvage rate was 52.9%, a rate comparable to that reported by Simental et al.[2]

In conclusion, this multicenter study of 146 patients with maxillary squamous carcinoma is the largest reported surgical series to date. In this study we have confirmed the much smaller studies that show that oral cavity maxillary squamous carcinomas have a cervical metastatic rate that is higher than expected and approaches that of tongue and floor of mouth. The occult metastatic rate of 6.8% is less than expected. However, some surgeons participating in this study have used a watchful waiting strategy for maxillary squamous cell carcinoma. Also, 10.3% of patients without clinical or radiographic evidence of regional metastasis were prescribed radiation to the cervical lymphatic structures.

Until a prospective study evaluating the efficacy of routine dissection of the N0 neck is completed for maxillary squamous carcinoma, we have only the unacceptably high regional metastatic and disappointing salvage rates to support the recommendation of selective extirpation of the lymphatic contents within levels I to III of the N0 neck. The prognostic benefit provided by pathologic evaluation of regional lymph nodes affords the surgeon and patient an early opportunity for developing management strategy intent for cure, not salvage, following unexpected regional failure. Sparing patients from radiation as a primary management modality reserves this valuable adjuvant for future application should it become necessary. A weakness of this study, and in most multicenter studies, is the variable of the individualized approach by each surgeon contributing to this report. Regardless of a surgeon's individual approach, we can say that early regional failures are a result of unidentified and untreated regional disease at the time of primary resection.

Based on the metastatic rates associated with the different T-classification maxillary squamous carcinomas in this study and the Weiss et al[12] threshold for treatment of the neck, surgeons contributing to this multicenter study recommend a selective neck dissection of levels I to III as a primary management strategy for patients with T2, T3, and T4 oral cavity maxillary squamous carcinoma.

REFERENCES

1. Montes DM, Schmidt BL. Oral maxillary squamous cell carcinoma: management of the clinically negative neck. J Oral Maxillofac Surg 2008;66:762–766.
2. Simental AA Jr, Johnson JT, Myers EN. Cervical metastasis from squamous cell carcinoma of the maxillary alveolus and hard palate. Laryngoscope 2006;116:1682–1684.
3. Kimura Y, Hanazawa T, Sano T, Okano T. Lateral retropharyngeal node metastasis from carcinoma of the upper gingiva and maxillary sinus. AJNR Am J Neuroradiol 1998;19:1221–1224.
4. Umeda M, Minamikawa T, Yokoo S, Komori T. Metastasis of maxillary carcinoma to the parapharyngeal space: rationale and technique for concomitant en bloc parapharyngeal dissection. J Oral Maxillofac Surg 2002;60:408–414.
5. Umeda M, Minamikawa T, Komatsubara H, et al. En bloc resection of the primary tumour and cervical lymph nodes through the parapharyngeal space in patients with squamous cell carcinoma of the maxilla: a preliminary study. Br J Oral Maxillofac Surg 2005;43:17–22.
6. Clark JR, Naranjo N, Franklin JH, de Almeida J, Gullane PJ. Established prognostic variables in N0 oral carcinoma. Otolaryngol Head Neck Surg 2006;135:748–753.
7. Schmidt BL. Molecular biology and clinical behavior of oral cancer. Oral Maxillofac Surg Clin North Am 2006;18:483–491.
8. Woolgar JA, Scott J. Prediction of cervical lymph node metastasis in squamous cell carcinoma of the tongue/floor of mouth. Head Neck 1995;17:463–472.
9. Keski-Santti H, Atula T, Tornwall J, Koivunen P, Makitie A. Elective neck treatment versus observation in patients with T1/T2 N0 squamous cell carcinoma of oral tongue. Oral Oncol 2006;42:96–101.
10. Byers RM, El-Naggar AK, Lee YY, et al. Can we detect or predict the presence of occult nodal metastases in patients with squamous carcinoma of the oral tongue? Head Neck 1998;20:138–144.
11. Haddadin KJ, Soutar DS, Oliver RJ, Webster MH, Robertson AG, MacDonald DG. Improved survival for patients with clinically T1/T2, N0 tongue tumors undergoing a prophylactic neck dissection. Head Neck 1999;21:517–525.
12. Weiss MH, Harrison LB, Isaacs RS. Use of decision analysis in planning a management strategy for the stage N0 neck. Arch Otolaryngol Head Neck Surg 1994;120:699–702.
13. Klingerman J, Lima RA, Soares JR, et al. Supraomohyoid neck dissection in the treatment of T1/T2 squamous cell carcinoma of oral cavity. Am J Surg 1994;168:391–394.
14. Werner JA, Dunne AA, Myers JN. Functional anatomy of the lymphatic drainage system of the upper aerodigestive tract and its role in metastasis of squamous cell carcinoma. Head Neck 2003;25:322–332.
15. Shah JP, Candela FC, Poddar AK. The patterns of cervical lymph node metastases from squamous carcinoma of the oral cavity. Cancer 1990;66:109–113.
16. Ogura I, Kurabayashi T, Sasaki T, Amagasa T, Okada N, Kaneda T. Maxillary bone invasion by gingival carcinoma as an indicator of cervical metastasis. Dentomaxillofac Radiol 2003;32:291–294.
17. Woolgar JA. Detailed topography of cervical lymph-node metastases from oral squamous cell carcinoma. Int J Oral Maxillofac Surg 1997;26:3–9.
18. Hicks WL Jr, Loree TR, Garcia RI, et al. Squamous cell carcinoma of the floor of mouth: a 20-year review. Head Neck 1997;19:400–405.
19. Sessions DG, Spector GJ, Lenox J, et al. Analysis of treatment results for floor-of-mouth cancer. Laryngoscope 2000;1 10:1764–1772.
20. Cunningham MJ, Johnson JT, Myers EN, Schramm VL Jr, Thearle PB. Cervical lymph node metastasis after local excision of early squamous cell carcinoma of the oral cavity Am J Surg 1986;152:361–366.
21. Woolgar JA, Triantafyllou A. A histopathological appraisal of surgical margins in oral and oropharyngeal cancer resection specimens. Oral Oncol 2005;41:1034–1043.
22. Cheng A, Cox D, Schmidt BL. Oral squamous cell carcinoma margin discrepancy after resection and pathologic processing. J Oral Maxillofac Surg 2008;66:523–529.
23. Yorozu A, Sykes AJ, Slevin NJ. Carcinoma of the hard palate treated with radiotherapy: a retrospective review of 31 cases. Oral Oncol 2001;37:493–497.
24. Andersen PE, Cambronero E, Shaha AR, Shah JP. The extent of neck disease after regional failure during observation of the N0 neck. Am J Surg 1996;172:689–691.
25. Wong LY, Wei WI, Lam LK, Yuen AP. Salvage of recurrent head and neck squamous cell carcinoma after primary curative surgery. Head Neck 2003;25:953–959.
26. Ord RA, Kolokythas A, Reynolds MA. Surgical salvage for local and regional recurrence in oral cancer. J Oral Maxillofac Surg 2006;64:1409–1414.
27. Lin HW, Bhattacharyya N. Survival impact of nodal disease in hard palate and maxillary alveolus cancer. Laryngoscope 2009;119:312–315.