Neck recurrence of oral squamous cell carcinoma in unusual sites: Retrospective study of 1658 cases

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ABSTRACT: *Background.* The purpose of this study was to explore the frequency and prognosis of irregular neck recurrences in the prelaryngeal, parotid, and lateral retropharyngeal regions in patients with oral squamous cell carcinoma (OSCC).

Methods. We conducted a retrospective study.

Results. Twenty-four patients (1.4%) had irregular neck recurrences: 17 in the parotid (1.0%), 4 in the prelaryngeal (0.2%), and 3 in the lateral retropharyngeal (0.2%) regions. The 1-year/5-year overall survival rates after the N-relapse date for these areas were 40.0%/25.0%, 42.9%/20.0%, and 33.3%/0%, respectively. Patients with irregular neck recurrences had a poorer salvage success rate than controls (21.7% vs 68.8%, respectively; $p < .001$) as well as a significantly lower 5-year disease-specific survival (23.8% vs 60.8%, respectively; $p < .001$).

Conclusion. Patients with OSCC with irregular neck recurrences were extremely rare and had poor prognoses. The management of irregular metastases in patients with OSCC remains challenging for surgeons. Further study will be worthwhile to evaluate the best diagnostic and management strategies for unusual neck recurrences of OSCC. © 2015 Wiley Periodicals, Inc. *Head Neck* **38**: E680–E686, 2016

KEY WORDS: oral squamous cell carcinoma, neck recurrence, prelaryngeal area, parotid area, lateral retropharyngeal area

INTRODUCTION

The prognosis of patients with oral squamous cell carcinoma (OSCC) with neck lymph node recurrences remains dismal, especially when the recurrence occurs at an unusual site.[1] Our previous studies of cervical metastases have demonstrated that the regions where OSCC occurs most frequently are at neck levels I to III.[2–4] Neck recurrences outside levels I to V have been shown to be extremely rare.[5,6] Moreover, the outcomes of patients with OSCC with neck recurrences have been demonstrated to be largely dependent on whether the regions are salvageable.[7] However, few studies have focused on the frequency, salvage rate, and prognosis of lymph node recurrence in irregular regions. Although uncommon, an awareness of this issue is essential for head and neck surgeons. In our department, the most common irregularly located neck recurrences have been at the prelaryngeal, parotid, and lateral retropharyngeal regions. In this study, we retrospectively reviewed the data from cases with at least 2 years of follow-up in our department to evaluate the incidence rate and oncologic outcomes in patients with OSCC who had undergone radical surgery with or without postoperative adjuvant therapy.

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PATIENTS AND METHODS

Patients

The Institutional Review Board of the Stomatological Hospital of Peking University approved this study. Because of the retrospective nature of this study, an exemption was granted by the Institutional Review Board. The eligibility criteria were as follows: (1) histological diagnosis of OSCC; (2) no previous treatment; and (3) a primary tumor without evidence of distant metastasis. Exclusion criteria included second metachronous malignancies and/or refusal or inability to receive definitive treatment for the disease.

All of the study participants underwent an extensive preoperative evaluation, including preoperative CT, MRI, and/or positron emission tomography scans to determine the extent of the tumor and a baseline chest X-ray. Complete blood counts and blood chemistries were also obtained. Clinical staging was based on the clinical and imaging findings, according to the 2009 Union for International Cancer Control/American Joint Committee on Cancer staging criteria (seventh edition).

Primary treatment

All of the patients were initially treated with surgery. The surgical procedure was selected by the surgeons,

according to tumor site and local practice. Standard surgeries, including radical tumor resection, neck dissection, and tissue defect reconstructions, as necessary, were performed. Local excision of the primary tumor was performed with margins of at least 15 mm. The tumor margins then were cryosectioned. If a margin was positive, additional tissue was excised and cryosectioned to ensure that the margin was tumor free. Postoperative radiotherapy (RT) was advised for patients with positive lymph nodes. RT was scheduled within 4 to 8 weeks after the operation at the prescribed dose of 1.8 to 2 Gy per fraction per day, administered 5 days per week. The total radiation dose was 66 Gy for patients with multiple positive neck lymph nodes and 60 Gy for the remaining patients. Concomitant chemoradiotherapy (CCRT) with cisplatin (30 mg/m^2 weekly) was recommended for patients with multiple, pathologically proven nodal metastases and/or extracapsular spread (ECS), as described in our previous study.[8]

Salvage therapy for patients with locoregional recurrence considered salvageable consisted mainly of surgery with or without adjuvant RT or CCRT. Of those patients who had nodal recurrence in the prelaryngeal area, extensive local excision or therapeutic neck dissection was performed according to local practice. Patients who had parotid lymph nodal recurrence underwent total parotidectomy, whereas patients with parotid-tail recurrence underwent partial parotidectomy. Palliative therapy with RT/CCRT was performed for those patients with low surgical curability.

For routine histopathological analysis of neck dissection specimens, nodes were placed in different specimen containers based on the neck level from which they were resected. The laterality and neck level of the nodes were delineated using orienting stitches that were added immediately after the removal of the specimens. Standard hematoxylin-eosin staining was performed.

Statistical analysis

The cutoff date for all follow-up encounters among surviving patients was September 1, 2014. All of the included patients had follow-up examinations for at least 24 months after surgical treatment or until death. Descriptive statistics are summarized using frequencies, percentages, and means ± SDs. The baseline demographic data between the 2 groups were compared using the chi-square test for categorical variables and the t test for continuous variables. Second primary carcinoma was defined as a metachronous invasive solid cancer developing ≥6 months after an index OSCC, according to criteria of Morris et al.[9] Specifically, if the second cancer was of nonsquamous cell origin, or if it developed in a different location, it was coded as an second primary carcinoma. If the second cancer was OSCC and developed in the same region as the index cancer, it was only coded as a second primary carcinoma if >60 months had passed since the index diagnosis.

The primary outcome assessment parameter was the success rate of salvage treatment, defined as the percentage of successfully salvaged patients who received surgery-based salvage treatment for neck recurrence in unusual sites. The secondary endpoint was the 5-year disease-specific survival (DSS), which was calculated from the time of the first operation to the time of death or last follow-up; patients who died from causes other than OSCC were censored at the time of death. The Kaplan–Meier method was used to provide estimates of the 5-year DSS. Statistical significance was determined by the log-rank test. All tests were 2-sided, and p values $< .05$ were considered statistically significant. All statistical analyses were performed using the Statistical Package for Social Science for Windows, version 19.0 (SPSS, Chicago, IL).

RESULTS

Patient characteristics

A total of 1658 eligible patients with previously untreated OSCC who underwent surgery between June 1991 and September 2012 were enrolled in this study. The median age was 60 years (range, 5–90 years). There were 948 men (57.2%) and 710 women (42.8%). The primary sites were the tongue in 692 patients (41.7%), the lower gingiva in 291 patients (17.6%), the buccal mucosa in 251 patients (15.1%), the floor of the mouth in 181 patients (10.9%), the upper gingiva in 182 patients (11.0%), and the hard palate in 61 patients (3.7%). The clinical stages were as follows: T1 ($n = 405$; 24.4%), T2 ($n = 642$; 38.7%), T3 ($n = 177$; 10.7%), and T4 ($n = 434$; 26.2%). With regard to pathologic grade, 837 patients (50.5%) were grade I, 701 (42.3%) were grade II, 77 (4.6%) were grade III, and 43 (2.6%) could not be evaluated. The pathological nodal statuses were as follows: pNx, no neck dissection ($n = 323$; 19.5%), pN0 ($n = 773$; 46.6%), pN1 ($n = 251$; 15.1%), pN2b ($n = 250$; 15.1%), and pN2c ($n = 61$; 3.7%).

A total of 366 consecutive cases were available for the analysis of histologic signs of severity (eg, perineural invasion, vascular/lymphatic emboli, diffuse infiltration), and 302 consecutive cases were available for the analysis of ECS status. Specifically, perineural invasion was present in 52 cases, absent in 288 cases, and missing in 26 cases. Vascular/lymphatic emboli were present in 9 cases, absent in 331 cases, and missing in 26 cases. Diffuse infiltration was present in 85 cases, absent in 255 cases, and missing in 26 cases. The ECS status was positive in 78 cases, negative in 205 cases, and missing in 19 cases.

Of these 1658 patients, 24 patients (1.4%; group A) had regional recurrence in unusual sites, including the parotid (17 cases; 1.0%), prelaryngeal (4 cases; 0.2%), and lateral retropharyngeal (3 cases; 0.2%) regions. The remaining 1634 patients were analyzed as controls (group B). The first relapses of the primary tumor in group B were as follows: 240 (14.7%) developed local recurrences (43 coupled with a neck recurrence), 164 (10.0%) had neck recurrences alone, 207 (12.7%) had second primary carcinoma (19 coupled with a neck recurrence), and 75 (4.6%) had distant metastases. The differences in baseline data between group A and group B are listed in Table 1.

Baseline data, treatment, and prognosis of patients in group A

The baseline data, treatment, and prognosis for patients with OSCC with neck recurrences in unusual sites are listed in Table 2. All of the primary tumors were completely excised, and the margins were negative. All 24

TABLE 1. Differences in baseline data between group A and group B.

Variables	Group A ($n = 24$)		Group B ($n = 1634$)		p value
	No. of patients	%	No. of patients	%	
Age, y: mean ± SD	58.5 ± 11.8		59.0 ± 12.4		.849
Sex					
Male	18	75.0	930	56.9	.075
Female	6	25.0	704	43.1	
Sites					
Tongue	13	54.2	679	41.6	.867
Lower gingival	4	16.7	287	17.6	
Buccal mucosa	4	16.7	247	15.1	
Floor of the mouth	1	4.1	180	11.0	
Upper gingival	2	8.3	180	11.0	
Hard palate	0	0.0	61	3.7	
T classification					
T1	5	20.8	400	24.5	.431
T2	9	37.5	633	38.7	
T3	5	20.8	172	10.5	
T4	5	20.8	429	26.3	
Pathological nodal status					
N-	9	37.5	764	46.8	.041
N+	15	62.5	547	33.5	
Nx (no neck dissection)*	0	0.0	323	19.7	
pN2					
No	14	58.3	1010	61.9	.032
Yes	10	41.7	301	18.4	
Nx (no neck dissection)*	0	0.0	323	19.7	
Level IV/V metastases					
No	23	95.8	1264	77.4	> .999
Yes	1	4.2	47	2.9	
Nx (no neck dissection)*	0	0.0	323	19.7	
Pathologic grade					
I	14	58.3	823	50.4	.878
II	9	37.5	692	43.4	
III	1	4.2	76	4.7	
Missing	0	0.0	43	2.6	
Growth pattern					
Exophytic	7	29.2	543	33.2	.406
Ulcerative	6	25.0	446	27.3	
Infiltrative	11	45.8	484	29.6	
Missing	0	0.0	161	9.9	
Smoking history					
Smoker	14	58.3	694	42.7	.147
Nonsmoker	10	41.7	900	55.1	
Missing	0	0.0	40	2.4	
Alcohol history					
Drinker	12	50.0	512	31.3	.063
Nondrinker	12	50.0	1082	66.2	
Missing	0	0.0	40	2.4	
ECS					
Absence	4	28.6	201	74.7	.001
Presence	10	71.4	68	25.3	
Perineural invasion					
Absence	11	55.0	277	86.6	< .001
Presence	9	45.0	43	13.4	
Vascular/lymphatic emboli					
Absence	15	75.0	316	98.8	< .001
Presence	5	25.0	4	1.3	
Diffuse infiltration					
Absence	6	30.0	249	77.8	< .001
Presence	14	70.0	71	22.2	
Neck dissection					
No	0	0.0	323	19.8	.008
Yes	24	100	1311	80.2	

TABLE 1. *Continued*

Variables	Group A ($n = 24$)		Group B ($n = 1634$)		p value
	No. of patients	%	No. of patients	%	
Bilateral neck dissection					
No	20	83.3	1106	84.3	> .999
Yes	4	16.7	206	15.7	
Combined therapy					
Surgery	10	41.7	959	58.7	.093
Surgery + RT/CCRT	14	58.3	675	41.3	

Abbreviations: Nx, no neck dissection; ECS, extracapsular spread; RT, radiotherapy; CCRT, concurrent chemoradiotherapy.
*Cases of Nx were excluded from the statistical analysis.

patients in group A received neck dissection: unilateral supraomohyoid neck dissection in 9 cases, unilateral comprehensive neck dissection (CND) in 11 cases, both CND and supraomohyoid neck dissection in 2 cases, bilateral CND in 1 case, and bilateral supraomohyoid neck dissection in 1 case. Tissue reconstruction using a free-flap transfer was performed in 12 cases: radial forearm flap in 5 cases, fibular flap in 4 cases, anterolateral thigh flap in 2 cases, and lateral crural flap in 1 case.

During the follow-up period, 17 of the 24 patients (70.8%) died, all as a result of cancer-related causes. There were 8 patients (33.3%) who developed irregular nodal recurrences coupled with comprehensive neck metastasis or distant metastasis. The node-related mortality rate was 62.5% (15/24), and nodal recurrence was found after a median follow-up of 8.5 months (range, 2–115 months).

Close follow-up and early diagnosis were the crucial factors to improve the salvage rate of patients in group A

Because tumor relapse often occurred within 2 years, patients were routinely advised to make regular return visits every 2 to 3 months during the first 2 years after treatment. CT or MRI scanning was also recommended at regular 6-month intervals after the operation. However, in this study, 12 patients (50.0%) experienced a delayed diagnosis of their irregular neck recurrence (relapsed time >6 months) because the majority of the patients did not comply with our follow-up strategy. Ultimately, of those 24 patients who developed an irregular nodal recurrence, only 12 patients had salvage surgical excision, including 10 locally extensive excisions (total parotidectomy, 2 cases; partial parotidectomy, 5 cases; prelaryngeal area, 2 cases; and lateral retropharyngeal area, 1 case), and 2 therapeutic neck dissections (prelaryngeal area recurrence only). Furthermore, 5 of the above 12 patients also underwent postoperative RT/CCRT, and 1 patient had postoperative chemotherapy. Unfortunately, another 12 patients underwent only palliative RT/CCRT/chemotherapy or opted not to receive therapy because of incurable nodal recurrence or recurrence coupled with distant metastasis. The patients whose irregular neck recurrences were diagnosed early had a significantly higher rate of salvage success compared with patients with delayed diagnoses (41.7% vs 0.0%; $p < .001$).

Patients in group A had worse prognoses than patients in group B

At the end of the study, the survival analysis of the patients in group B revealed 972 patients (59.5%) were living, 493 (30.2%) had died, and 169 (10.3%) were lost to follow-up. Thirty-six patients died as a result of causes unrelated to cancer, including cardiac failure and stroke (15 patients), multiple organ failure (6 patients), respiratory failure (8 patients), acute gastrointestinal hemorrhage (2 patients), suicide (2 patients), sepsis (1 patient), and uncertain causes (2 patients).

Patients in group A had a poorer success rate of salvage therapy than patients in group B (21.7% vs 68.8%; $p < .001$; Figure 1). Further analysis showed a significantly lower 5-year DSS in group A patients compared with group B patients (23.8% vs 60.8%; $p < .001$; Figure 2).

DISCUSSION

The lymphatic drainage routes of head and neck cancers, including the prelaryngeal area in thyroid and laryngeal cancer, the parotid area in facial skin cancer, and the lateral retropharyngeal area in oropharyngeal cancer, are well recognized.[10–12] For oral cancer, the frequency of involvement of the prelaryngeal, parotid, and lateral retropharyngeal areas seems to be extremely low. The current medical literature contains few case reports or studies on unusual site metastases,[13–15] and it was very difficult to draw a conclusion from the treatment strategies or outcomes of these previous reports. Recently, a large cohort study from a betel nut-chewing area showed that all 26 patients with OSCC with regional nodal recurrence at unusual sites died within 15 months after salvage therapy, indicating that the prognosis of irregular neck recurrences is poor. For further validation, the authors of that study proposed that a meta-analysis across different areas, primary treatment modes, and etiologies using either a cohort or well-designed prospective study is warranted.[1] Another large cohort study of recurrence in parotid areas in oral and oropharynx cancer found a 20.0% (5 of 10) salvage success rate and recommended aggressive surgery-based combined therapy.[16] In our study, the success rates after surgical salvage treatment were 50.0% (2 of 4) for patients with recurrence in prelaryngeal areas, 42.9% (3 of 7) for parotid areas, and 0.0% (0 of 1) for lateral retropharyngeal areas. However, all of the patients

TABLE 2. Baseline data, treatments, and prognoses of patients with oral squamous cell carcinoma with neck recurrence in unusual sites ($n = 24$).

Patient #	Age, y	Sex	Site	pTNM classification	Pathological grade	Growth pattern	Tobacco use	Alcohol use	Primary neck treatment	Recurrence sites	Recurrence time, mo	Salvage treatment	Censor (mo)
1	64	M	Tongue	T2N1	II	Infiltrative	Yes	No	S	Inferior parotid	17	S + RT	Death (167)
2	68	F	Lower gingival	T1N0	I	Exophytic	No	No	S	Inferior parotid + neck	2	S + RT	Death (45)
3	58	F	Floor of mouth	T1N0	II	Ulcerative	No	No	S	Parotid	115	S	Survival (148)
4	50	F	Tongue	T2N0	I	Exophytic	No	No	S	Inferior parotid + neck	9	S + CCRT	Death (20)
5	37	M	Tongue	T2N0	I	Infiltrative	Yes	Yes	S	Lateral retropharyngeal	6	RT	Death (11)
6	46	F	Buccal	T3N2b	II	Ulcerative	Yes	No	S + RT	Parotid	4	S	Survival (99)
7	72	M	Upper gingival	T1N1	I	Exophytic	No	No	S	Lateral retropharyngeal + neck	13	S + RT	Death (59)
8	52	M	Lower gingival	T4N2c	I	Infiltrative	Yes	Yes	S + RT	Inferior parotid	9	S	Death (18)
9	65	F	Tongue	T3N0	I	Ulcerative	No	No	S	Prelaryngeal	9	S + RT	Survival (86)
10	62	M	Tongue	T1N0	I	Ulcerative	Yes	Yes	S + RT	Prelaryngeal	7	S	Survival (66)
11	68	M	Upper gingival	T3N1	II	Infiltrative	No	No	S + RT	Parotid	8	Quit	Death (24)
12	58	M	Tongue	T2N2b	I	Infiltrative	Yes	Yes	S + RT	Prelaryngeal + neck	8	S + CT	Death (15)
13	62	M	Lower gingival	T3N0	I	Exophytic	No	No	S	Parotid + distance	18	RT	Death (24)
14	32	M	Tongue	T2N1	I	Ulcerative	Yes	Yes	S + RT	Prelaryngeal	3	S	Death (9)
15	50	M	Tongue	T1N2b	II	Infiltrative	Yes	Yes	S + RT	Prelaryngeal + neck	8	Quit	Death (11)
16	55	M	Tongue	T2N2c	III	Infiltrative	Yes	Yes	S + RT	Lateral retropharyngeal + neck	18	Quit	Death (25)
17	63	M	Tongue	T4aN2c	II	Infiltrative	Yes	Yes	S + RT	Inferior parotid	16	RT	Survival (24)
18	67	M	Buccal	T2N0	I	Exophytic	No	No	S	Inferior parotid	30	RT	Death (35)
19	59	M	Buccal	T4aN2b	II	Infiltrative	Yes	No	S + RT	Parotid	3	Quit	Death (5)
20	68	F	Tongue	T2N1	I	Exophytic	No	No	S + CCRT	Parotid	6	Quit	Death (8)
21	78	M	Lower gingiva	T4aN0	I	Exophytic	No	Yes	S + RT	Parotid	14	CT	Death (15)
22	43	M	Tongue	T4N2b	II	Infiltrative	Yes	Yes	S + RT	Parotid	8	Quit	Survival (27)
23	50	M	Tongue	T3N2b	II	Infiltrative	Yes	Yes	S + RT	Inferior parotid	3	S	Lost to follow-up
24	77	M	Buccal	T2N2b	I	Ulcerative	Yes	Yes	S	Parotid + neck	9	CCRT	Death (15)

Abbreviations: S, surgery; RT, radiotherapy; CCRT, concurrent chemoradiotherapy; CT, chemotherapy.

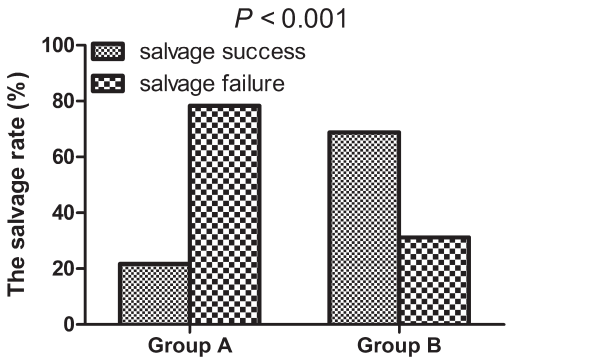

FIGURE 1. Success rates of salvage therapy of patients in group A and group B.

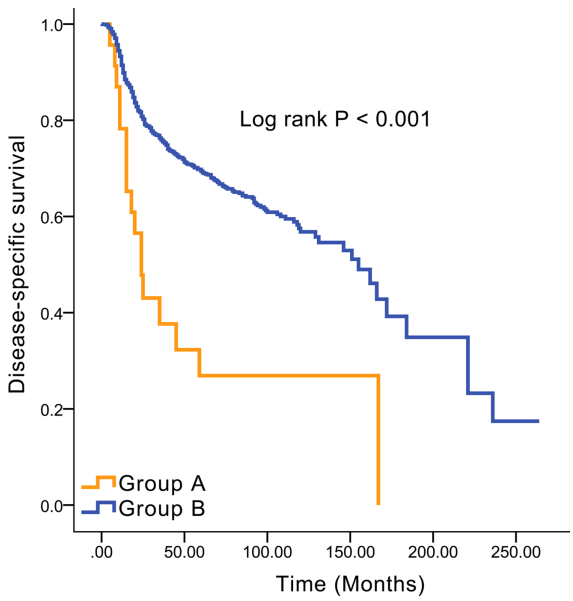

FIGURE 2. Differences in 5-year disease-specific survival (DSS) between group A and group B.

with irregular local metastases who underwent only palliative RT/CCRT or who opted not to receive therapy died of cancer. We believe that neck recurrences in the prelaryngeal and parotid areas may be successfully salvaged by surgical-based combined therapy on the premise of early diagnosis. If the neck recurrence is in the lateral retropharyngeal region, the outcome is likely to be poor. Therefore, clinicians should (1) increase their awareness of the potential of OSCC to metastasize to the prelaryngeal, parotid, and lateral retropharyngeal regions, (2) suggest that patients return for regular postoperative visits, and (3) prescribe adjuvant CT/MRI or positron emission tomography/CT examinations that may help diagnose irregular neck recurrence early to provide a perspective on treatment.

In this study, we found that advanced pN status, ECS, perineural invasion, vascular/lymphatic emboli, diffuse infiltration, and neck dissection were closely associated with neck recurrence in unusual sites. Among our 1658 patients with OSCC, all of the irregular lymph node metastases were found in treated patients with OSCC with disease relapse; no patients had unusual site lymph node disease at their initial presentation. Additionally, all patients with irregular neck recurrences underwent primary neck dissections with or without adjuvant RT/CCRT. Furthermore, we did not find that patients who adopted a neck observation strategy had delayed neck recurrences in the prelaryngeal, parotid, or lateral retropharyngeal region. These results differed from previous reports by Liao et al.[1] Therefore, we propose that irregular metastases from OSCC occur more frequently after normal cervical lymphatic flow has been disrupted. Surgery, RT, and widely advanced neck disease have all been shown to markedly alter normal patterns of cervical lymph flow.[17]

This study is retrospective and may be restricted to patient subsets with similar clinicopathological data. However, it is very challenging to implement prospective, evidence-based studies for neck recurrences in unusual sites because of their low incidence rate compared with other outcome assessment parameters. Currently, large-cohort observational studies with detailed clinical data may be the best available evidence to answer these questions. Aiming to exclude selection bias, consecutive patients who met all of the inclusion criteria were enrolled in this study. Therefore, the results from this study are reliable. Based on this series of 24 patients, we are unable to define clear treatment concepts, but some generalizations are possible. Our results highlight the importance of careful clinical and radiographic evaluation for unusual sites in which the clinician routinely examines a postoperative patient who has received neck dissection and/or RT. For patients with neck recurrences in the prelaryngeal or parotid region who are eligible for salvage surgery, aggressive surgery-based therapy is the recommended management.

CONCLUSION

In conclusion, irregular neck recurrences in patients with OSCC were extremely rare and had poor prognoses. The management of irregular metastases in patients with OSCC remains challenging for surgeons. Further study will be worthwhile to evaluate the best diagnostic and management strategies for unusual neck recurrences of OSCC.

REFERENCES

1. Liao CT, Lin CY, Fan KH, et al. Outcome analyses of unusual site neck recurrence in oral cavity cancer. *Ann Surg Oncol* 2013;20:257–266.
2. Feng Z, Li JN, Niu LX, Guo CB. Supraomohyoid neck dissection in the management of oral squamous cell carcinoma: special consideration for skip metastases at level IV or V. *J Oral Maxillofac Surg* 2014;72:1203–1211.
3. Feng Z, Li JN, Li CZ, Guo CB. Elective neck dissection versus observation in the management of early tongue carcinoma with clinically node-negative neck: a retrospective study of 229 cases. *J Craniomaxillofac Surg* 2014;42:806–810.
4. Guo CB, Feng Z, Zhang JG, et al. Supraomohyoid neck dissection and modified radical neck dissection for clinically node-negative oral squamous cell carcinoma: a prospective study of prognosis, complications and quality of life. *J Craniomaxillofac Surg* 2014;42:1885–1890.
5. Feng Z, Li JN, Li CZ, Guo CB. Elective neck dissection versus observation for cN0 neck of squamous cell carcinoma primarily located in the maxillary

gingiva and alveolar ridge: a retrospective study of 129 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2013;116:556–561.
6. Feng Z, Gao Y, Niu LX, Peng X, Guo CB. Selective versus comprehensive neck dissection in the treatment of patients with a pathologically node-positive neck with or without microscopic extracapsular spread in oral squamous cell carcinoma. *Int J Oral Maxillofac Surg* 2014;43:1182–1188.
7. Liao CT, Chang JT, Wang HM, et al. Salvage therapy in relapsed squamous cell carcinoma of the oral cavity: how and when? *Cancer* 2008;112:94–103.
8. Feng Z, Niu LX, Yuan Y, Peng X, Guo CB. Risk factors and treatment of contralateral neck recurrence for unilateral oral squamous cell carcinoma: a retrospective study of 1482 cases. *Oral Oncol* 2014;50:1081–1088.
9. Morris LG, Sikora AG, Patel SG, Hayes RB, Ganly I. Second primary cancers after an index head and neck cancer: subsite-specific trends in the era of human papillomavirus-associated oropharyngeal cancer. *J Clin Oncol* 2011;29:739–746.
10. Ljumanovic R, Langendijk JA, Hoekstra OS, Leemans CR, Castelijns JA. Distant metastases in head and neck carcinoma: identification of prognostic groups with MR imaging. *Eur J Radiol* 2006;60:58–66.
11. Nuyens M, Schüpbach J, Stauffer E, Zbären P. Metastatic disease to the parotid gland. *Otolaryngol Head Neck Surg* 2006;135:844–848.
12. Iyer NG, Shaha AR, Ferlito A, et al. Delphian node metastasis in head and neck cancers–oracle or myth? *J Surg Oncol* 2010;102:354–358.
13. Nishida M, Yasuda S, Murakami K, Yamamura I, Nagata Y, Iizuka T. Retropharyngeal lymph node metastases from oral cancer: a report of 2 patients. *J Oral Maxillofac Surg* 2005;63:410–412.
14. Umeda M, Shigeta T, Takahashi H, et al. Metastasis to the lateral retropharyngeal lymph node from squamous cell carcinoma of the oral cavity: report of three cases. *Int J Oral Maxillofac Surg* 2009;38:1004–1008.
15. Pisani P, Krengli M, Ramponi A, Guglielmetti R, Pia F. Metastases to parotid gland from cancers of the upper airway and digestive tract. *Br J Oral Maxillofac Surg* 1998;36:54–57.
16. Olsen SM, Moore EJ, Koch CA, Kasperbauer JL, Olsen KD. Oral cavity and oropharynx squamous cell carcinoma with metastasis to the parotid lymph nodes. *Oral Oncol* 2011;47:142–144.
17. Fisch UP. Cervical lymph flow in man following radiation and surgery. *Trans Am Acad Ophthalmol Otolaryngol* 1965;69:846–868.