Survival in Squamous Cell Carcinoma of the Oral Cavity

Differences Between pT4 N0 and Other Stage IVA Categories

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Received December 27, 2006; revision received April 9, 2007; accepted April 11, 2007.

BACKGROUND. According to the American Joint Commission on Cancer (AJCC, 5th edition) classification system, pT4 N0 oral cavity squamous cell carcinoma (OSCC) qualifies for stage IVA status, with its implied poor prognosis. However, preliminary observations suggested that patients with pT4 N0 OSCC might have better survival than other stage IVA categories. The authors sought to identify accurate prognosticators in patients with stage III/IVA OSCC.

METHODS. The authors retrospectively reviewed 513 consecutive patients with stage III/IVA OSCC who were undergoing radical surgery. Survival was plotted by Kaplan-Meier analysis.

RESULTS. One hundred seventy-eight patients were in stage III, and 335 were in stage IVA. The 335 stage IVA patients were divided into pT4 N0 (n = 105) and pT4 N1/TAny N2 (NO pT4 N0 M0, n = 230). By univariate analysis, 5-year neck control rates ($P < .0001$), distant metastases ($P < .0001$), disease-free survival rates ($P < .0001$), and overall survival rates ($P < .0001$) were significantly different in pT4 N0 compared with NO pT4 N0 patients. No significant difference in survival between pT4 N0 stage IVA and pstage III could be shown. Multivariate analysis for overall survival demonstrated that the following factors were independently associated with pT4 N0: tumor depth $\geq$35 mm, vessel invasion, lymph invasion, and perineural invasion. In contrast, tumor depth $\geq$25 mm, treatment with surgery alone, poor differentiation, extracapsular spread, and pathological nodal metastases ($\geq$8 lymph nodes) were independent predictors of overall survival in NO pT4 N0.

CONCLUSIONS. In patients with stage IVA OSCC (AJCC, 1997), the survival rates for pT4 N0 are better than those for NO pT4 N0 and similar to those of patients with pstage III. ***Cancer* 2007;110:564–71.** © *2007 American Cancer Society.*

KEYWORDS: squamous cell carcinoma, stage IVA, prognosis.

According to the staging system of the American Joint Committee on Cancer (AJCC), 5th edition,[1] pT4 N0 oral cavity squamous cell carcinoma (OSCC) qualifies for stage IVA status, with its implied poor prognosis. Invasion of neighboring tissues by the OSCC, mainly into cortical bone, the extrinsic muscle of the tongue, the maxillary sinus, or the skin of the face, denotes a cT4 lesion. Because histopathological examination of cT4 lesions may be performed only after surgical

DOI 10.1002/cncr.22814
Published online 18 June 2007 in Wiley InterScience (www.interscience.wiley.com).

resection, it is possible that some degree of misclassification in the assignment of tumor status may occur in this patient group. This phenomenon may have important implications, as it could affect survival statistics in clinical research. Because preliminary observations seem to suggest that patients with pT4 N0 OSCC may have better survival than patients with the other stage IVA categories, we sought to identify accurate prognosticators in patients with stage III to IVA OSCC. To accomplish this aim, we retrospectively reviewed 513 consecutive patients with stage III to IVA OSCC who underwent radical surgery in January 1996 through September 2004. Stage IVA patients were divided into pT4 N0 and pT4 N1/TAny N2 (NO pT4 N0).

In the present study, AJCC 1997 5th edition stating system was used for several reasons. First, some histopathological specimens collected before 2002 were not available for further review. Second, correct classification of the tumor infiltration into the masticatory space or the pterygoid plate according to AJCC 2002 criteria[2] was extremely troublesome. Third, some specimens were already sectioned according to previous criteria, rendering AJCC 2002 criteria unusable for the present investigation. Finally, pathologic status was a better predictor of survival than clinical status in our patient group.

MATERIALS AND METHODS

Study Patients

We retrospectively reviewed 513 consecutive patients with stage III/IVA OSCC who underwent radical surgery during the time period of January 1996 to September 2004. Patients in this series underwent an extensive presurgical evaluation. This evaluation included a medical history and complete physical examination, flexible fiberoptic pharyngoscopy, complete blood count and routine blood biochemistry, computed tomography (CT) or magnetic resonance imaging (MRI) scans of the head and neck, chest radiographs, bone scan, and liver ultrasound. Patients were staged according to the 1997 AJCC, 5th edition staging criteria.[1]

Surgery and Adjuvant Therapy

Primary tumors were excised with $\geq$1 cm safety margins (both peripheral and deep margins). Classic radical or modified neck dissections, levels I-V, were performed on patients with clinically positive nodal disease (by largest lymph node size >3 cm or outside level I-positive or level II-positive nodes). Supraomohyoid neck dissections (levels I-III) were performed in clinically lymph node-negative patients or in patients with level I-positive or level II-positive nodes (by largest lymph node size $\leq$3 cm) in the absence of extracapsular spread as determined by CT or MRI scans. Bilateral neck dissections were performed when the primary tumor contacted or crossed the midline sagittal plane of the oral cavity. On the basis of tumor extent and location, maxillectomy or mandibulectomy were performed to obtain adequate surgical margins.

Tumor margin tissue was cryogenically sectioned. If a margin was positive, then additional tissue was excised and cryogenically sectioned to ensure that the margin was free of tumor. The surgical defects were repaired with primary closure by head and neck surgeons or were reconstructed by free or local flaps immediately by plastic surgeons.

Postoperative radiotherapy (RT) was performed on patients with pT4 tumors, positive lymph nodes, or close margins ($\leq$4 mm). RT was scheduled within 4–8 weeks after the operation. The initial RT treatment field was to irradiate the entire tumor bed area with 1–2 cm margins and the regional lymphatics with 6 MV x-ray beams by means of bilaterally opposed fields with either a matched anterior supraclavicular field or the 3D conformal RT technique based on postoperative CT simulator imaging. The prescribed dose was 1.8–2 Gy per fraction per day, given 5 days per week. The total radiation dose was 66 Gy for patients with multiple positive neck lymph nodes and/or extracapsular spread and 60 Gy for the rest of the patients. Concomitant chemoradiotherapy (CCRT) with cisplatin-based agents was administered to those with extracapsular spread or pathological multiple nodal metastases. The cisplatin-based regimen[3] was either cisplatin 30 mg/m^2 weekly or a biweekly cisplatin/tegafur/leucovorin regimen.[4]

Data Analysis

Follow-ups were continued until September 2006. All patients received follow-up examinations for at least 24 months after surgical treatment or until death. Descriptive statistics were summarized by using frequencies, percentages, medians, standard deviations, and ranges. The Kaplan-Meier method was applied for survival analysis. The statistical significance was evaluated by using the log-rank test. Univariate and multivariate analyses were used to define independent risk factors. Multivariate analyses of prognostic factors were performed by using the Cox logistic regression method with forward selection. In all analyses, P values <.05 were considered to be statistically significant.

RESULTS

Patients

Table 1 shows the clinicopathological characteristics of the 513 study participants. The median age of the sample was 49 years (range, 25–82 years). In the entire study cohort, 178 patients were in stage III, and 335 were in stage IVA. Of the 178 stage III patients, stage disease was pT3 N0 in 90 patients and pT1-3 N1 in 88 patients. The 335 stage IVA patients were divided into pT4 N0 (n = 105), and pT4 N1/TAny N2a, TAny N2b, and TAny N2c (NO pT4 N0 M0, n = 230). Of the 513 patients, 502 (97.9%) received neck dissections. The neck dissections were ipsilateral in 404 (80.5%) patients and bilateral in 98 (19.5%) patients. Three hundred thirty-six (65.5%) patients had tumor excision along with mandibulectomy and/or maxillectomy, whereas 207 (40.4%) patients underwent tumor removal with facial skin excision. Four hundred eighty-eight (95.1%) patients received immediate free-flap reconstruction from a plastic surgeon. In 394 (76.5%) patients, surgery was followed by postoperative RT or CCRT. Of the 105 pT4 N0 patients, 6 had tongue extrinsic muscle involvement, 70 had bone marrow invasion, 22 had skin invasion, and 7 showed both bone marrow and skin invasion.

Clinical Course

pStage III

At the time of analyses, 118 (66.3%) of the 178 pstage III patients were alive, and 60 (33.7%) were dead. Twenty-five (14.0%) patients developed local recurrences, 18 (10.1%) had neck recurrences, and 19 (10.7%) patients had distant metastases.

Thirty-five (19.7%) patients presented a local and/or a neck recurrence of the tumor. Salvage therapy was carried out in 21 (60.0%) patients, consisting of surgery and RT or combined modalities. Of this patient group, 11 patients remained alive, and 24 patients died.

pT4 N0

At the time of analyses, 71 (67.6%) of the 105 pT4 N0 patients remained alive, and 34 (32.4%) had died. Seventeen patients (16.2%) developed local recurrences, 9 (8.6%) had neck recurrences, and 4 (3.8%) patients had distant metastases.

Twenty-one (20.0%) patients presented a local and/or a neck recurrence of the tumor. Salvage therapy was carried out in 10 (47.6%) patients. Of this patient group, 7 patients remained alive, and 14 patients died.

NO pT4 N0

At the time of analyses, 86 (37.4%) of the 230 NO pT4N0 patients remained alive, and 144 (62.6%) had dead. Forty patients (17.4%) developed local recurrences, 63 (27.4%) had neck recurrences, and 51 (22.2%) patients had distant metastases.

Eighty-one (35.2%) patients presented a local and/or a neck recurrence of the tumor. Salvage therapy was carried out in 32 (39.5%) patients. Of this patient group, 8 patients remained alive, and 73 patients died.

Independent prognosticators according to stage IVA status

Univariate and multivariate analyses were exploited to identify independent prognosticators in pT4 N0 versus NO pT4 N0 patients. The results of these analyses are shown in Tables 2 and 3. After we allowed for potential confounding variables, multivariate analyses (Table 3) demonstrated that tumor depth $\geq$35 mm, vessel invasion, lymph invasion, and perineural invasion were risk factors for pT4 N0 in 5-year overall survival. In contrast, tumor depth $\geq$25 mm, therapeutic modalities (surgery alone), poor differentiation, extracapsular spread, and pathological nodal metastases $\geq$8 lymph nodes were risk factors for NO pT4 N0 in 5-year overall survival.

Survival analyses

There were no significant differences between pT4 N0 and pstage III patients with respect to 5-year local control rates (81.9% vs 86.0%, $P = .4347$), neck control rates (90.8% vs 88.2%, $P = .7024$), locoregional control rates (78.0% vs 80.3%, $P = .7463$), distant metastases (4.2% vs 12.2%, $P = .0564$), disease-free survival rates (75.3% vs 74.7%, $P = .8696$), and overall survival rates (67.0% vs 65.6%, $P = .9987$). Also, no significant differences with respect to these parameters were evident between pT4 N0 and pT3 N0 (local control rates: 81.9% vs 88.9%, $P = .1261$; neck control rates: 90.8% vs 87.3%, $P = .6116$; locoregional control rates: 78.0% vs 83.3%, $P = 3038$; distant metastases: 4.2% vs 10.5%, $P = .1743$; disease-free survival rates: 75.3% vs 78.1%, $P = .5798$; and overall survival rates: 67.0% vs 67.3%, $P = .5729$), as well as between pT4 N0 and pT1-3N1, the only exception being distant metastases (4.2% vs 14.1%, $P = .0293$) (local control rates: 81.9% vs 82.7%, $P = .8024$; neck control rates: 90.8% vs 88.9%, $P = .8637$; locoregional control rates: 78.0% vs 76.6%, $P = .5991$; disease-free survival rates: 75.3% vs 70.9%, $P = .3791$; and overall survival rates: 67.0% vs 63.9%, $P = .5863$). However, statistically significant differences concerning these variables were evident when comparing pT4 N0 patients with NO pT4 N0 individuals, the only exception being local control (81.9% vs 75.4%, $P = .2084$) (neck control rates: 90.8% vs 67.4%, $P < .0001$; locoregional control rates: 78.0% vs 57.7%, $P = .0003$; distant metastases: 4.2% vs 26.2%, $P < .0001$; disease-free survival rates:

TABLE 1
Clinicopathological Characteristics of pT3N0 (n = 90), pT1-3N1 (n = 88), pT4N0 (n = 105), and NO pT4N0 pStage IVA (n = 230) Patients

Risk factors (No.)	pT3N0 No.	pT1-3N1 No.	pT4N0 No.	NO T4N0 No.	*P**	*P*†	*P*‡
Sex					.306	.025	.164
Men (485)	86	80	103	216			
Women (28)	4	8	2	14			
Age, y					.004	.009	<.001
≤40 (99)	20	18	8	53			
>40 (414)	70	70	97	177			
Tumor subsites					<.001	<.001	<.001
Tongue (170)	39	44	6	82			
Mouth floor (21)	2	5	2	11			
Lip (10)	1	1	2	6			
Buccal (180)	32	30	36	82			
Gum (80)	6	4	39	31			
Hard palate (20)	5	1	11	3			
Retromolar (32)	5	3	9	15			
Treatment mode					<.001	.008	<.001
OP (119)	57	10	28	24			
OP+RT/CCRT (394)	33	78	77	206			
Differentiation					.235	.348	.001
Well to moderate (463)	89	82	101	191			
Poor (50)	1	6	4	39			
Bone invasion							<.001
No (378)	90	88	28	171			
Yes (135)			77	59			
Skin invasion							<.001
No (458)	90	88	76	204			
Yes (55)			29	26			
Perineural invasion					.978	.229	<.001
No (353)	71	63	83	136			
Yes (160)	19	25	22	94			
Vessel invasion§					.061	.244	1.000
No (497)	90	87	101	219			
Yes (15)		1	4	10			
Lymph invasion§					.188	.088	<.001
No (451)	90	82	103	176			
Yes (61)		6	2	53			
Depth, mm§‖					<.001		
<25 (165)	85		80				
≥25 (28)	3		25				
Depth, mm§‖						<.001	
<8 (42)		29	13				
≥8 (149)		57	92				
Depth, mm‖							.034
<35 (317)			95	222			
≥35 (18)			10	8			
Close margin, mm§					.102	.625	.715
≤4 (52)	5	9	13	25			
>4 (447)	83	78	90	196			

OP indicates operation; RT, radiotherapy; CCRT, concurrent chemoradiation.

* Data between pT4N0 and pT3N0.

† Data between pT4N0 and pT1-3N1.

‡ Data between pT4N0 and NO pT4N0.

§ Unknown data: vessel invasion (n = 1), lymph invasion (n = 1), depth (n = 4), close margins (n = 14).

‖ Best cutoff tumor depth.

TABLE 2
Univariate Analyses of Risk Factors for 5-year Local Control, Neck Control, Locoregional Control, Distant Metastases, Disease-free Survival, and Overall Survival

	Local control	Neck control	Locoregional control	Distant metastases	Disease-free survival	Overall survival
pT3N0	tumor depth ≥8 mm (P = .0383)	tumor depth ≥8 mm (P = .0267)	tumor depth ≥8 mm (P = .0086) age >40 (P = .0357)		tumor depth ≥8 mm (P = .0022)	OP+RT/CCRT (P = .0202) poor differentiation (P = .0210)
pT1-3N1	tumor depth ≥8 mm (P = .0335) poor differentiation (P = .0170) lymph invasion (P = .0028)		poor differentiation (P = .0044) lymph invasion (P = .0389)		tumor depth ≥6 mm (P = .0305) poor differentiation (P = .0187)	
pT4N0	close margin ≤4 mm (P = .0253)	Woman (P = .0177) perineural invasion (P = .0086)	perineural invasion (P = .0298) close margin ≤4mm (P = .0148)	skin invasion (P = .0302) without bone invasion (P = .0188)	tumor depth ≥35 mm (P = .0485) close margin ≤4mm (P = .0395)	poor differentiation (P = .0472) perineural invasion (P = .0241) vessel invasion (P = .0009) lymph invasion (P = .0001) tumor depth ≥35 mm (P = .0007)
NO pT4N0	tumor depth ≥25 mm (P = .0114) close margin ≤4 mm (P = .0489) pT3-4 (P = .0196)	surgery alone (P = .0044) pN+ ≥8 nodes (P = .0024)	surgery alone (P = .0049) tumor depth ≥25 mm (P = .0142) close margin ≤4 mm (P = .0083) pN+ ≥8 nodes (P = .0225)	poor differentiation (P = .0001) perineural invasion (P = .0390) close margin ≥4mm (P = .0148) ECS (P = .0034) pN+ ≥8 nodes (P = .0001)	surgery alone (P = .0087) poor differentiation (P = .0269) perineural invasion (P = .0315) tumor depth ≥25 mm (P = .0014) close margin ≤4mm (P = .0022) ECS (P = .0200) pN+ ≥8 nodes (P = .0004)	surgery alone (P < .0001) poor differentiation (P = .0010) lymph invasion (P = .0462) tumor depth ≥25 mm (P = .0010) ECS (P = .0045) pT3-4 (P = .0080) pN+ ≥8 nodes (P = .0003)

ECS indicates extracapsular spread; OP, operation; RT, radiation therapy; CCRT, concurrent chemoradiation therapy; pN+, pathological nodal metastases.

75.3% vs 47.2%, $P < .0001$; and overall survival rates: 67.0% vs 36.1%, $P < .0001$) (Figs. 1–5).

Among the 4 pT4 N0 subgroups (namely tongue extrinsic muscle involvement, bone marrow invasion, skin invasion, and bone marrow and skin invasion), no statistical differences were found with respect to 5-year local control rates ($P = .4690$), neck control rates ($P = .0985$), locoregional control rates ($P = .2426$), distant metastases ($P = .0516$), disease-free survival rates ($P = .6634$), and overall survival rates ($P = .5025$).

Effect of adjuvant therapy in pStage IVA

In pT4 N0 patients, postoperative RT or CCRT did not significantly influence local control ($P = .3421$), neck control ($P = .3229$), locoregional control ($P = .1631$), distant metastases ($P = .9836$), disease-free survival rates ($P = .2313$), and overall survival rates ($P = .3823$). These parameters were not significantly influenced by the presence of bone invasion or skin invasion in pT4 N0 patients as well (data not shown).

In patients with NO pT4 N0, there was no difference of local control or distant metastases between patients with or without postoperative RT or CCRT. However, patients with or without postoperative RT or CCRT differed with regard to neck control (69.5% vs 37.3%, $P = .0044$), locoregional control (59.6% vs 32.7%, $P = .0049$), disease-free survival rates (48.8% vs 29.2%, $P = .0087$), and overall survival rates (38.8% vs 12.5%, $P < .0001$).

DISCUSSION

According to AJCC 5th edition criteria,[1] pT4 OSCC lesions are characterized by infiltration of neighboring tissues, mainly cortical bone, the extrinsic muscle

TABLE 3
Multivariate Analyses of Risk Factors for 5-year Local Control, Neck Control, Locoregional Control, Distant Metastases, Disease-free Survival, and Overall Survival

	Local control (*P*; HR; 95% CI)	Neck control (*P*; HR; 95% CI)	Locoregional control (*P*; HR; 95% CI)	Distant metastases (*P*; HR; 95% CI)	Disease-free survival (*P*; HR; 95% CI)	Overall survival (*P*; HR; 95% CI)
pT3N0						OP+RT/CCRT (.004; 1.004; 1.001–1.007) poor differentiation (.009; 1.138; 1.032–1.254)
pT1-3N1	tumor depth ≥8 mm (.012; 1.198; 1.041–1.379) poor differentiation (.007; 1.096; 1.026–1.170) lymph invasion (<.001; 19.204; 3.978–92.074) surgery alone (.045; 1.004; 1.000–1.009)		tumor depth ≥8 mm (.023; 1.142; 1.018–1.281) poor differentiation (.005; 1.076; 1.022–1.133) lymph invasion (.008; 6.027; 1.603–22.658)		tumor depth ≥6 mm (.012; 1.219; 1.044– 1.422) poor differentiation (.009; 1.070; 1.017–1.126)	ECS (.044; 2.066; 1.021–4.182)
pT4N0	close margin ≤4 mm (.036; 1.278; 1.016–1.607)	perineural invasion (.018; 4.917; 1.318–18.337)	perineural invasion (.010; 3.389; 1.338–8.581) close margin ≤4 mm (.011; 1.308; 1.063–1.609)		tumor depth ≥35 mm (.041; 1.033; 1.001–1.066)	perineural invasion (.032; 2.301; 1.075–4.925) vessel invasion (.004; 6.413; 1.815–22.652) lymph invasion (.018; 6.427; 1.378–29.987) tumor depth ≥35 mm (<.001; 1.045; 1.020–1.071)
NO pT4N0		surgery alone (.004; 1.004; 1.001–1.006) pN+ ≥8 nodes (.003; 2.998; 1.469–6.119)	surgery alone (.014; 1.003; 1.001–1.005) close margin ≤4 mm (.018; 1.157; 1.025–1.305) pN+ ≥8 nodes (.030; 2.272; 1.080–4.779)	poor differentiation (<.001; 1.052; 1.023–1.082) close margin ≤4 mm (.002; 3.244; 1.558–6.754) pN+ ≥8 nodes (.014; 1.193; 1.036–1.373)	surgery alone (.005; 1.003; 1.001–1.005) close margin ≤4 mm (.009; 1.147; 1.035–1.271) ECS (.019; 1.796; 1.101–2.931) tumor depth ≥25 mm (.014; 1.026; 1.005–1.047) pN+ ≥8 nodes (.028; 1.990; 1.075–3.682)	surgery alone (<.001; 1.005; 1.003–1.006) poor differentiation (.006; 1.027; 1.007–1.046) ECS (.007; 1.757; 1.166–2.649) tumor depth ≥25 mm (.004; 1.025; 1.008–1.042) pN+ ≥8 nodes (.034; 1.745; 1.043–2.917)

ECS indicates extracapsular spread; OP, operation; RT, radiation therapy; CCRT, concurrent chemoradiation therapy; pN+, pathological nodal metastases.

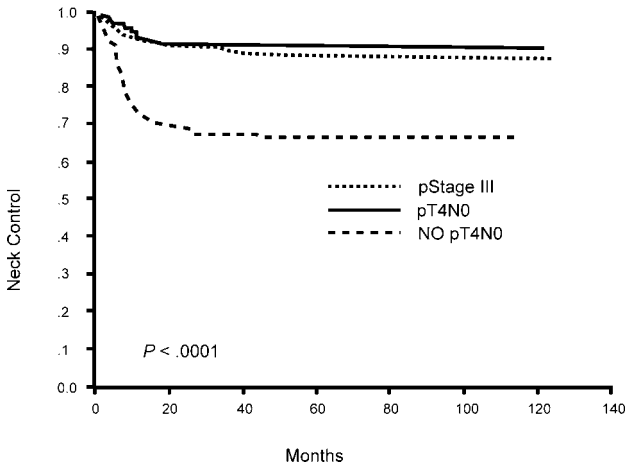

FIGURE 1. Neck control.

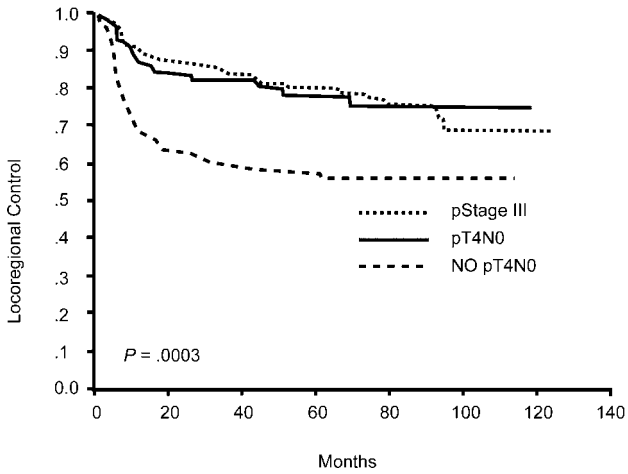

FIGURE 2. Locoregional control.

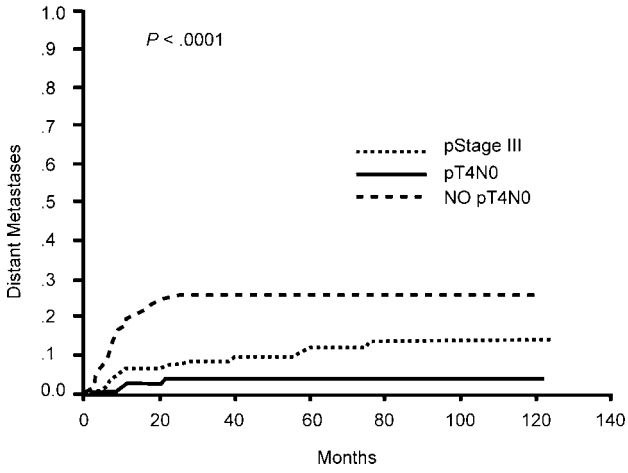

FIGURE 3. Distant metastases.

of the tongue, the maxillary sinus, or the skin of the face. Hence, it is worth noting that the AJCC 1997 criteria reflected primarily the extent of tumor invasion, rather than tumor size. This implies that aggressive, albeit small, tumors extending into the surrounding soft tissues are classified as T4 lesions. However, by the use of reconstructive surgery, it is nowadays possible to achieve adequate surgical margins regardless of tumor size. Despite the fact that pT4 N0 OSCC meets qualifications for stage IVA status in the 1997 AJCC classification, our data clearly indicate that survival rates for pT4N0 are better than NO pT4 N0 and similar to those of patients with pstage III. Specifically, we found similar 5-year local control rates, neck control rates, locoregional control rates, disease-free survival rates, and overall survival rates, although only distant metastatic rates were significantly different between pT4 N0 and pT1-3 N1 patients. Moreover, there were no significant differences with regard to these parameters between pT4 N0 patients and both pT3 N0 and pstage III patients. Significant differences, however, were evident between pT4 N0 and NO pT4 N0 (Figs. 1–5). Altogether these results suggest that patients with pT4 N0 tumors behaved as though they had pstage III disease and could be managed as pstage III patients. Of interest also is the observation that no statistical difference was observed with regard to patient outcome among the 4 pT4 N0 subgroups (namely tongue extrinsic muscle involvement, bone marrow invasion, skin invasion, and bone marrow and skin invasion).

Given the aggressive nature of OSCC pstage IVA tumors, postoperative adjuvant radiotherapy may be delivered with the goal to improve outcome. However, it should be kept in mind that adjuvant RT could also increase patient morbidity. It is, thus, crucial to establish whether RT could be of clinical aid in patients with pstage IVA. Our study demonstrated that 5-year local control rates, neck control rates, locoregional control rates, distant metastatic rates, disease-free survival rates, and overall survival rates were similar in pT4 N0 patients who received adjuvant RT or CCRT compared with those who did not. On the other hand, multivariate analyses showed that adjuvant RT or CCRT was beneficial in improving patients' outcome in NO pT4 N0 patients (Table 3). It is, thus, recommended that NO pT4 N0 patients should receive adjuvant RT or CCRT, whereas further studies are needed to draw firm conclusions about the potential usefulness of RT or CCRT in patients with pT4 N0 lesions. Our study confirms previous observations regarding the independent prognostic significance of lymph node metastases in OSCC

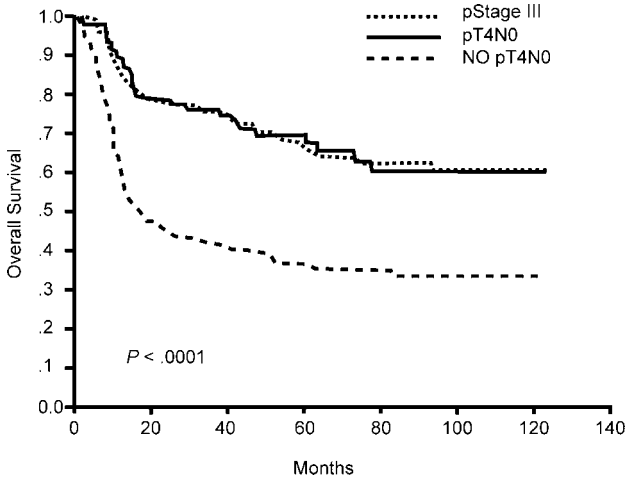

FIGURE 4. Overall survival.

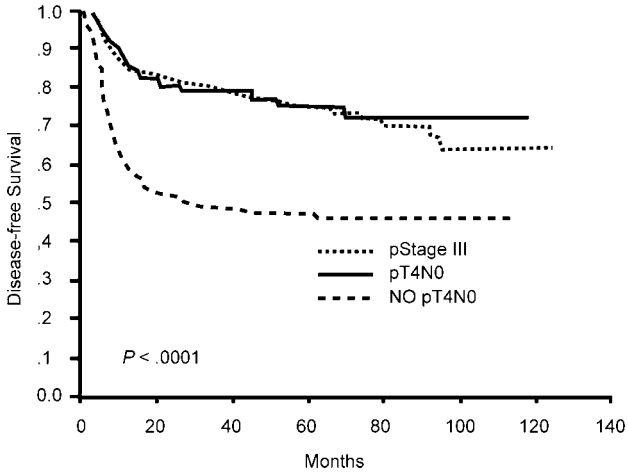

FIGURE 5. Disease-free survival.

patients.[5,6] However, the potential usefulness of adjuvant RT and/or CCRT in OSCC patients without nodal metastases and adequate safety margins requires further investigation in a prospective study.

The different survival rates observed for 2 pstage IVA subgroups (pT4 N0 compared with NO pT4 N0) may reflect an important difference in tumor biology between these patient groups. Accordingly, local tumor extension was an independent prognostic predictor in patients with pT4 N0 tumors, whereas regional and distant metastases should also be taken into account in NO pT4 N0 tumors. Hence, we found several differences in the relative weight of prognostic factors between the pT4 N0 and NO pT4 N0 stage IVA subgroups (Table 3).

Some qualifications to our report merit consideration. First, in the present study, AJCC 1997 5th edition staging system was used. Accordingly, patient data were collected between 1996 and 2004. In addition, we exploited only a pathologic staging system in our patient group. However, our study has some methodologic strengths that may make our results valid. Although it has previously been reported that similar survival rates in OSCC patients with pT4 N0 compared with pstage III patients,[7] our study comprised the largest series of OSCC individuals drawn from an endemic betel-chewing area. Moreover, it is important to emphasize that adequate surgical margins should be obtained in pT4 N0 patients to ensure good prognosis. In summary, we found that survival rates for pT4 N0 patients are better than those for pT4 N1/TAny N2 patients and similar to those for patients with pstage III.

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