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Original Article

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Predictors of Distant Metastasis after Radical Surgery Followed by Postoperative Radiotherapy with or without Chemotherapy for Oropharyngeal Cancer

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Purpose

We investigated the prognostic factors for distant metastasis (DM) in patients with locally advanced oropharyngeal cancer (OPC) treated with surgery and adjuvant radiotherapy with or without concurrent chemotherapy.

Materials and Methods

Eighty-five patients treated between January 1995 and August 2014 were evaluated retrospectively. Data regarding the pathological tumour and nodal status, human papillomavirus (HPV) status, treatment characteristics, and pretreatment maximum standardized uptake value (SUVmax) of 18-fluoro-2-deoxyglucose positron emission tomography–computed tomography scan (^{18}F-FDG PET-CT) were evaluated, and their influence on DM and survival outcomes were analyzed.

Results

Median follow-up period was 48.0 months. Recurrence was observed in 20 patients, including locoregional recurrence and DM. DM was observed in 13 patients. A multivariate analysis confirmed that the presence of lymphovascular invasion (p=0.031), lower neck lymph node (LN) involvement (p=0.006), SUVmax ≥ 9.7 (p=0.014), and tumour size ≥ 3 cm (p=0.037) significantly affected DM. HPV status was not associated with DM. Perineural invasion (p=0.048), lower neck LN involvement (p=0.008), SUVmax ≥ 9.7 (p=0.019), and tumour size ≥ 3 cm (p=0.033) were also significant factors for the DM-free survival rate.

Conclusion

Lower neck LN involvement, high SUVmax in pretreatment ^{18}F-FDG PET-CT, and large tumour size were predictive factors for DM in patients of OPC.

Key words
Oropharyngeal neoplasms, Distant metastasis, Lower neck involvement, Radiotherapy, SUVmax, Pretreatment ^{18}F-FDG PET-CT scan

Introduction

The incidence of oropharyngeal cancer (OPC) has increased over the past few years in Western countries as well as in Asia including Korea [1].

Numerous trials have recommended primary resection followed by radiotherapy (RT) with or without concurrent chemotherapy for locally advanced OPC with high-risk features, including extra-capsular nodal extension (ECE), positive resection margins (RM), pT3 or pT4, N2, or N3 nodal disease and perineural invasion (PNI) [2,3]. These studies demonstrated a significant benefit from adjuvant concurrent chemoradiotherapy (CRT) on locoregional (LR) control and overall survival (OS). Most recent studies reported improved LR control but failed to show a significant reduction in distant metastasis (DM). The RTOG 9501 study reported a DM rate of 19.3%-21.2% in patients treated for high-risk head and neck squamous cell carcinoma. Addition of postoperative concurrent chemotherapy to RT did not significantly reduce

the DM rate. The chance of cure is very low when DM occurs, and OS decreases dramatically [4]. Although several studies have focused on LR control for head and neck cancers, few of these studies determined the prognostic factors for DM in patients with OPC treated with primary resection followed by RT with or without concurrent chemotherapy [5,6]. We could identify strategies that would reduce DM risk using accurate tools to predict the risk. Use of appropriate strategies can lead to decreased rates of distant failure and ultimately help improve OS for patients with high-risk OPC after adjuvant RT with or without concurrent chemotherapy. Thus, the aim of this study was to investigate prognostic factors for DM in patients who undergo primary resection with adjuvant RT with or without concurrent chemotherapy for locally advanced OPC.

Materials and Methods

1. Patients

We reviewed the medical records of patients with locally advanced OPC treated with curative resection followed by RT with or without concurrent chemotherapy between January 1995 and August 2014. The inclusion criteria for this study were (1) histologically proven squamous cell carcinoma of OPC; (2) Eastern Cooperative Oncology Group (ECOG) performance status 0-2; (3) pT3 or pT4a and any nodal stage; (4) any T stage and N2-3; and (5) pT2 and N0 or N1 with unfavourable pathological findings, including ECE, positive RM, PNI, or lymphovascular invasion (LVI). Patients with DM of OPC at diagnosis were excluded. Finally, 85 patients were eligible. The TNM stages of the patients were re-classified according to the seventh edition of the American Joint Committee on Cancer staging system. All medical records were reviewed, including radiological images, pathology, including immunohistochemistry of Ki-67, p53, and human papillomavirus (HPV) status, surgery, chemotherapy, and RT. Institutional review board approval was obtained prior to the study.

2. Treatment

1) Surgery

The pretreatment evaluation included history and physical examination; renal, hepatic, and bone marrow function tests; computed tomography (CT) or magnetic resonance imaging (MRI) of the head and neck and chest imaging, as clinically indicated. All patients underwent surgery with curative intent by two highly specialised head and neck surgeons. Neck dissections were performed in 85 patients at the time of surgery. Bilateral modified radical neck node dissection (MRND) was performed in 12 patients, ipsilateral MRND and contralateral selective neck dissection (SND) in 52 patients, ipsilateral MRND in 11 patients, ipsilateral SND in five patients, and bilateral SND in five patients.

2) Radiation therapy

Patients received two-dimensional RT between 1995 and 2000 and three-dimensional conformal RT or intensity-modulated RT (IMRT) was performed after 2000. A total dose of 54-66 Gy with conventional fractionation (1.8-2.12 Gy daily) was planned for all patients. The clinical target volumes (CTV) were classified according to three groups; high-risk CTV was defined as the primary tumour bed and pathologically positive lymph node (LN) stations, intermediate-risk CTV was defined as ipsilateral neck LNs and occasionally the contralateral level II LN area, and low-risk CTV was defined as the contralateral pathologically negative LN levels. CTV was expanded to consider setup uncertainty, and the appropriate planning target volume was designed with an additional 0.3-0.5 cm from CTV. Cases of involved RM and ECE were boosted up to 66 Gy. All patients who underwent IMRT were treated after daily verification with volumetric image-guided RT.

3) Chemotherapy

Before making a decision of postoperative adjuvant treatment modality, the patient's age, performance status, co-morbidity, and pathology were evaluated by our multidisciplinary team. Adjuvant concurrent CRT was recommended to the patients of involved RM or ECE of LN. However, adjuvant concurrent CRT was considered in patients with other multiple risk factors including advanced T stage, multiple LN involvements, PNI, or LVI. Adjuvant therapy to decide RT or CRT was discussed considering high risk pathological features, patient's performance status, and co-morbidity together. In spite of involved RM or ECE, chemotherapy could not be given to old or co-morbid patients.

The chemotherapy regimen consisted of weekly doses of 30 mg cisplatin/m^2 body surface area (BSA) and 400 mg 5-fluorouracil/m^2 BSA by continuous intravenous infusion for 1 week in 43 of the 52 patients who received CRT. Besides these regimens, docetaxel, cisplatin, and 5-fluorouracil were administered to seven patients, and two patients received cetuximab and cisplatin. Chemotherapy was withheld in patients who developed grade 3 or higher neutropenia, thrombocytopenia, liver, or renal toxicity.

3. Follow-up

Patients were evaluated weekly by physical examination and appropriate blood tests during treatment. The patients were followed by all members of a multidisciplinary team at 1- to 3-month intervals for the first 2 years, and then every 6 months thereafter until 5 years after surgery. Thorough physical examination and imaging studies (neck CT and/or neck MRI, 18-fluoro-2-deoxyglucose positron emission tomography–computed tomography [PET-CT] and chest CT scans) were performed at each follow-up visit.

4. Statistical analysis

Distant metastasis-free survival (DMFS) was defined as time from operation date to DM, which ever occurred first. OS was defined as time from operation date to any cause of death or end of follow-up. DMFS and OS rates were estimated by using the Kaplan-Meier method. The log-rank test and Cox proportional hazards model were applied for identification of prognostic factors independently associated with DM and to estimate the hazard ratio (HR). Factors with p-values of < 0.25 in a univariate analysis were included in a multivariate analysis. Two-sided p-values of < 0.05 were considered significant. Correlation with HPV status and Ki-67, smoking, and p53 mutation was also analyzed using the chi-square test. All analyses were performed using SPSS ver. 12.0 (SPSS Inc., Chicago, IL).

Results

1. Patient characteristics

The patient characteristics are described in Table 1. The study cohort consisted of 81 men and four women with a median age of 58 years (range, 31 to 88 years). Of the 85 patients, 46 were current smokers, of whom 38 had a smoking history of ≥ 10 pack-years. Eighty-four patients (98.8%) had an ECOG performance status of 0-1. The primary tumour sites were the tonsils in 63 patients (74.1%), the base of the tongue in 19 (22.4%), and the soft palate in three (3.5%). Tumour stages were pT1-2 in 67 patients (78.8%) and pT3-4 in 18 (21.2%). Pathological LN stages were N0-2a in 32 patients (37.6%) and N2b-3 in 53 (62.4%). Seventy-five patients (88.3%) had well and moderately differentiated tumours.

LVI and ECE were observed in 52 (61.2%) and 38 (44.7%) patients, respectively. Surgical RM involvement was observed in 37 of the 85 patients (43.5%). The presence of PNI was observed in six patients (7.1%). HPV positivity was observed in 37 patients (43.5%). HPV-positive tumours were defined as specific *in situ* hybridization staining of tumour cell nuclei for HPV or positive p16 expression in an immunochemical analysis before 2013 and detection of HPV DNA by polymerase chain reaction after 2013. Lower neck LN (level IV and VB) involvement was observed in 17 patients (20.0%). Ki-67 index > 50% was observed in 32 patients (37.6%), p53 mutation was observed in 21 patients (24.7%). The median pretreatment maximum standardized uptake value (SUVmax) of primary tumours was 9.7, and a SUVmax ≥ 9.7 was observed in 30 patients (35.3%). Tumour size ≥ 3 cm was observed in 48 patients (56.5%).

2. Prognostic factors affecting DM

After a median follow-up period of 48.0 months (range, 5.3 to 189.2 months), recurrence was observed in 20 patients, including LR recurrence and DM. LR recurrence was observed in seven patients (8.2%). DM was observed in 13 patients (15.3%; lungs in eight patients, liver and bone in four, and peritoneal seeding in one). Most DM (76.9% of patients) occurred within 1 year after treatment, and the median time of DM was 9.43 months (range, 2.5 to 51.0 months). The result of univariate analysis for factors associated with DM is shown in Table 2. Three factors showed correlation with DM in the univariate analysis, including lower neck LN involvement, SUVmax ≥ 9.7, and tumour size ≥ 3 cm. No significant association was found between any other factor and DM. The multivariate logistic regression analysis showed that all the three factors in univariate analysis, lower neck LN involvement (HR, 77.394; 95% confidence interval [CI], 3.506 to 1,708.536; p=0.006), SUVmax ≥ 9.7 (HR, 57.713; 95% CI, 2.24 to 1,484.920; p=0.014), tumour size ≥ 3 cm (HR, 41.604; 95% CI, 1.261 to 1,372.724; p=0.037), and the presence of LVI (HR, 26.441; 95% CI, 1.339 to 522.179; p=0.031) were significant adverse factors affecting DM (Table 3). HPV status was not associated with DM.

3. Survival outcomes

The 5-year DMFS and OS rates are summarized in Table 4. The presence of PNI (p=0.048), lower neck LN involvement (p=0.008), SUVmax ≥ 9.7 (p=0.019), and tumour size more than 3 cm (p=0.033) were significant prognostic factors for DMFS (Fig. 1). The presence of PNI (p=0.001) and lower neck LN involvement (p=0.028) were significant factors for OS.

4. Salvage therapy

Three of the seven patients with LR recurrence underwent

Table 1. Patients' characteristics

Characteristic	No. (%) (n=85)
Age (yr)	
≤ 58	43 (50.6)
> 58	42 (49.4)
Sex	
Male	81 (95.3)
Female	4 (4.7)
Smoking	
Non-smoker	39 (45.9)
Current smoker	46 (54.1)
Smoking dose (pack-years)	
< 10, light	8 (9.4)
≥ 10, heavy	38 (44.7)
ECOG PS	
0	69 (81.2)
1	15 (17.6)
2	1 (1.2)
Disease site	
Tonsil	63 (74.1)
Base of tongue	19 (22.4)
Soft palate	3 (3.5)
Pathologic T stage	
T1	25 (29.4)
T2	42 (49.4)
T3	14 (16.5)
T4	4 (4.7)
Pathologic N stage	
N0	11 (12.9)
N1	13 (15.3)
N2a	8 (9.4)
N2b	45 (52.9)
N2c	6 (7.1)
N3	2 (2.4)
Tumor size (cm)	
< 3	37 (43.5)
≥ 3	48 (56.5)
Tumor differentiation	
Well and moderate	75 (88.3)
Poor	10 (11.8)
Lymphovascular invasion	
No	33 (38.8)
Yes	52 (61.2)
Extracapsular spread	
No	47 (55.3)
Yes	38 (44.7)
Surgical margin involvement	
No	48 (56.5)
Yes	37 (43.5)
Perineural involvement	
No	79 (92.9)
Yes	6 (7.1)
HPV status	
Negative	48 (56.5)
Positive	37 (43.5)
Lower neck involvement	
No	68 (80.0)
Yes	17 (20.0)
SUVmax	
< 9.7	37 (43.5)
≥ 9.7	30 (35.3)
Unknown	18 (21.2)
Adjuvant therapy	
CCRT	52 (61.2)
RT alone	33 (38.8)

ECOG PS, Eastern Cooperative Oncology Group performance status; HPV, human papillomavirus; SUVmax, maximum standardized uptake value; CCRT, concurrent chemoradiotherapy.

salvage RT. One patient received chemotherapy, one underwent salvage surgery, and the remaining patient refused additional therapy. Four of the 13 patients with DM underwent metastasectomy of the lungs or liver. Six patients underwent systemic chemotherapy, and one patient underwent palliative RT. Two patients did not undergo additional therapy because of relatively poor tolerance. Correlation with HPV status and Ki-67, smoking, and p53 mutation, HPV-positive tumour showed high Ki-67 staining. The median Ki-67 index was 50 and 23 of 37 HPV-positive tumours (62.2%) showed a Ki-67 index > 50% compared with that of HPV-negative tumours ($p < 0.001$) (Table 5). The HPV-positive group showed a 27.0% rate of p53 mutations, and 48.6% of the patients having a heavy smoking history. No difference was detected between HPV status and p53 mutation and smoking history.

5. Characteristics according to adjuvant therapy

Results of univariate analysis according to adjuvant therapy are shown in Table 6. Age ($p=0.015$), pathologic N stage ($p=0.042$), the presence of ECE ($p < 0.001$), and number of positive LN ($p=0.023$) were significantly different between the postoperative CRT group and the postoperative RT group.

Table 2. Univariate analysis of factors associated with distant metastasis

Characteristic	Unadjusted hazard ratio (95% CI)	p-value
Pathologic T stage		
T1-2	1	
T3-4	1.852 (0.569-6.027)	0.306
Pathologic N stage		
N0-2a	1	
N2b-3	3.929 (0.811-19.031)	0.089
Tumor differentiation		
Well and moderate	1	
Poor	1.455 (0.272-7.776)	0.661
Lymphovascular invasion		
No	1	
Yes	4.291 (0.926-19.891)	0.063
Extracapsular spread		
No	1	
Yes	1.860 (0.608-5.691)	0.277
Surgical margin involvement		
No	1	
Yes	1.013 (0.310-3.313)	0.983
Perineural involvement		
No	1	
Yes	4.219 (0.926-19.891)	0.063
HPV status		
Negative	1	
Positive	1.134 (0.346-3.712)	0.836
Lower neck involvement		
No	1	
Yes	3.739 (1.256-11.130)	0.018
Tumor size (cm)		
< 3	1	
≥ 3	5.500(1.138-26.592)	0.034
No. of positive lymph nodes		
< 4	1	
≥ 4	2.773 (0.820-9.379)	0.101
Depth of invasion (cm)		
< 1.23	1	
≥ 1.23	1.556 (0.469-5.160)	0.470
SUVmax		
< 9.7	1	
≥ 9.7	8.554 (1.027-71.226)	0.047
Age (yr)		
≤ 60	1	
> 60	0.397 (0.101-1.564)	0.187
Adjuvant therapy		
CCRT	1	
RT	0.982 (0.292-3.306)	0.977
RT duration (wk)		
< 9	1	
≥ 9	0.917 (0.101-8.311)	0.938
Duration between surgery and RT (wk)		
< 6	1	
≥ 6	0.659 (0.185-2.343)	0.519

Table 2. Continued

Characteristic	Unadjusted hazard ratio (95% CI)	p-value
No. of chemotherapy cycles		
5-7	1	
< 5	2.250 (0.243-20.837)	0.475
Smoking dose (pack-years)		
< 10, light	1	
≥ 10, heavy	3.724 (0.923-15.029)	0.065

CI, confidence interval; HPV, human papillomavirus; SUVmax, maximum standardized uptake value; CCRT, concurrent chemoradiotherapy; RT, radiotherapy.

Table 3. Multivariate analysis of factors associated with distant metastasis

Characteristic	Hazard ratio (95% CI)	p-value
Pathologic N stage		
N0-2a	1	
N2b-3	1.641 (0.113-23.748)	0.717
Lymphovascular invasion		
No	1	
Yes	26.441 (1.339-522.179)	0.031
Perineural involvement		
No	1	
Yes	1.662 (0.020-140.889)	0.822
Lower neck involvement		
No	1	
Yes	77.394 (3.506-1,708.536)	0.006
SUVmax		
< 9.7	1	
≥ 9.7	57.713 (2.243-1,484.920)	0.014
Tumor size (cm)		
< 3	1	
≥ 3	41.604 (1.261-1,372.724)	0.037

CI, confidence interval; SUVmax, maximum standardized uptake value.

Discussion

For high-risk patients with locally advanced OPC, including those with positive RM, the presence of ECE, and multiple LN metastasis, LR recurrence, and DM were common after primary surgery [2]. Therefore, postoperative CRT is necessary in these patients, with the expectation that it will provide improved LR control and a better OS rate. Previous studies have shown that postoperative CRT for locally advanced squamous cell carcinoma of the head and neck change LR control and OS rates. The RTOG 9501 and the EORTC 22931 trials demonstrated that postoperative CRT is a more effective treatment in terms of LR control and OS rate than that of adjuvant RT alone [2]. However, neither study showed any effect on distant control. Therefore, postoperative CRT does not reduce the probability of DM, despite use of high-dose cisplatin.

We analyzed only OPC patients who underwent surgery and adjuvant therapy in our hospital. And as possible prognostic factors for DM, we found that lower neck involvement, high SUVmax on pretreatment PET-CT, and large tumour size ≥ 3 cm were significant prognostic factors for DM. These findings suggest that further adjuvant chemotherapy or more effective novel chemotherapy regimens are needed to reduce DM in patients with high-risk OPC. Judicious use of adjuvant therapy could not only reduce the DM rate but also improve the OS rate in high-risk patients with

Table 4. Five-year Kaplan-Meier DMFS and OS according to the prognostic factors

Characteristic	No. of patients	5-Yr DMFS (%)	p-value	5-Yr OS (%)	p-value
Pathologic N stage					
N0-2a	32	93.7	0.078	68.4	0.796
N2b-3	53	74.0		68.7	
Lymphovascular invasion					
No	33	93.8	0.121	68.0	0.812
Yes	52	75.5		68.9	
Perineural involvement					
No	79	83.0	0.048	73.0	0.001
Yes	6	None		0.0	
Lower neck involvement					
No	68	88.3	0.008	70.3	0.028
Yes	17	54.1		60.3	
SUVmax					
< 9.7	37	96.4	0.019	71.6	0.967
≥ 9.7	30	78.8		71.5	
Tumor size (cm)					
< 3	37	94.0	0.033	75.5	0.562
≥ 3	48	72.7		63.7	

DMFS, distant metastasis-free survival; OS, overall survival; SUVmax, maximum standardized uptake value.

OPC.

In current T staging for OPC cancer, tumour size more than 2 cm and less than 4 cm is the same as T2. However, according to our result, tumour size more than 3 cm should be considered as a high-risk feature for DM. Likewise, in current N staging for OPC, LN size or ipsilateral/bilateral involvement is considered to decide N staging. However, according to our result, the level of involvement should be considered together to decide more aggressive adjuvant therapy.

Ono et al. [7] reported on the unfavourable effect of lower neck LN involvement in patients with head and neck carcinoma. In their study of 338 patients who underwent neck dissection for head and neck carcinoma, an extremely poor survival rate was clearly demonstrated when LN metastases were confined to level IV. Our results also demonstrate that lower neck LN involvement was significantly associated with a high incidence of DM and a poor OS rate. Kim et al. [8], who analyzed prognostic factors for DM after induction chemotherapy followed by CRT for head and neck cancer, reported that the 5-year DMFS rates according to lower neck LN involvement (positive vs. negative) were 34.3% versus 55.2%. Despite addition of induction chemotherapy prior to CRT to overcome DM, patients with lower neck LN involvement still showed a higher incidence of DM. Therefore, lower neck LN involvement might be regarded as a major factor when considering aggressive therapy.

Several studies have demonstrated that pretreatment SUVmax is a good predictor of OS and disease-free survival (DFS) in patients with head and neck cancer [9-11]. Xie et al. [10] conducted a meta-analysis of survival data to determine the prognostic value of pretreatment SUV for OS. In their study, the risk of death decreased by 76% in patients with a low SUV. In a univariate analysis, Suzuki et al. [9] found that patients with hypopharyngeal squamous cell carcinoma and pretreatment SUVmax ≥ 13 showed significantly shorter OS. We selected a SUVmax cut-off value of 9.7, which was the median pre-treatment SUVmax value. Although, SUVmax ≥ 9.7 was an independent predictor of DM, SUVmax ≥ 9.7 was not correlated with OS in our study. After 2004, 67 of 85 patients underwent PET-CT. We assumed that these small numbers prevented a statistically significant OS result.

Ang et al. [12] and the authors of several retrospective studies reported that patients with HPV-positive OPC cancer showed increased OS [13]. However, our results showed that HPV positivity was not significantly associated with higher OS or DFS, and the reason for this difference from previous studies is unclear.

In our study, 23 of 37 HPV-positive tumours (62.2%) showed a Ki-67 index > 50% compared with that of HPV-negative tumours ($p < 0.001$) (Table 5). A higher Ki-67 index in HPV-positive tumours was considered a confounding factor in our study.

Smoking and HPV are known major risk factors for OPC. Heavy smoking increases the frequency of p53 mutations, and the frequency of p53 mutations in smokers is twice as

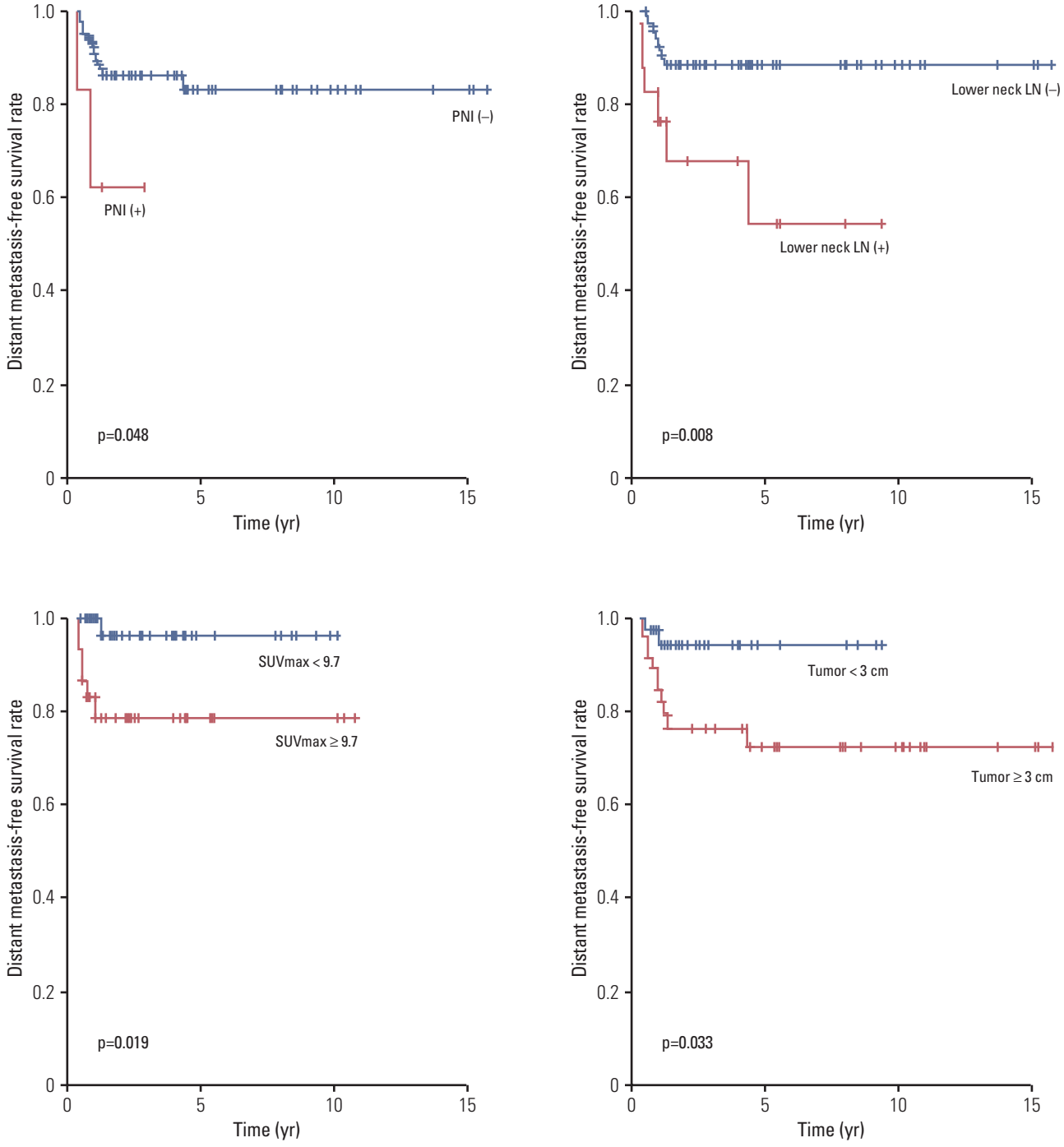

Fig. 1. Kaplan-Meier distant metastasis-free survival curve according to the prognostic factors. PNI, perineural invasion; LN, lymph node; SUVmax, maximum standardized uptake value.

high as that in non-smokers [14]. Previous studies have shown that patients with HPV-positive OPC are less likely to harbour p53 mutations compared to those with HPV-negative OPC [15]. Contrary to our expectation, the HPV-positive group showed a 27.0% rate of p53 mutations, and 48.6% of the patients having a heavy smoking history (Table 5). No difference was detected between HPV status and p53 and smoking. We tentatively assumed that the combination of

Table 5. Correlation with HPV status and Ki-67, smoking, and p53 mutation

Characteristic	HPV status		p-value
	No	Yes	
Ki-67 (%)			
≤ 50	39 (81.3)	14 (37.8)	< 0.001
> 50	9 (18.8)	23 (62.2)	
Smoking			
No	28 (58.3)	19 (51.4)	0.340
Yes	20 (41.7)	18 (48.6)	
p53 mutation			
No	37 (77.1)	27 (73.0)	0.801
Yes	11 (22.9)	10 (27.0)	

Values are presented as number (%). HPV, human papillomavirus.

Table 6. Characteristics according to adjuvant therapy

Characteristic	Adjuvant therapy		p-value
	CCRT	RT alone	
Age (yr)			
≤ 60	32 (61.5)	11 (33.3)	0.015
> 60	20 (38.5)	22 (66.7)	
Pathologic T stage			
T1-2	43 (82.7)	24 (72.7)	0.290
T3-4	9 (17.3)	9 (27.3)	
Pathologic N stage			
N0-2a	15 (28.8)	17 (51.5)	0.042
N2b-3	37 (71.2)	16 (48.5)	
Lymphovascular invasion			
No	19 (36.5)	13 (39.4)	0.821
Yes	33 (63.5)	20 (60.6)	
Extracapsular spread			
No	20 (38.5)	27 (81.8)	< 0.001
Yes	32 (61.5)	6 (18.2)	
Surgical margin involvement			
No	28 (53.8)	20 (60.6)	0.655
Yes	24 (46.2)	13 (39.4)	
Perineural involvement			
No	49 (94.2)	30 (90.9)	0.673
Yes	3 (5.8)	3 (9.1)	
No. of positive lymph nodes			
< 4	33 (63.5)	29 (87.9)	0.023
≥ 4	19 (36.5)	4 (12.1)	

Values are presented as number (%). CCRT, concurrent chemoradiotherapy; RT, radiotherapy.

HPV positivity and the intensity and duration of smoking played dual roles in the pathogenesis of OPC in the HPV-positive group. This assumption explains in part the lack of a significant difference in treatment outcomes between the HPV-positive and HPV-negative groups.

In the current study, we sought to identify factors to predict DM in patients with OPC. However, the study had some limitations. Sample size was limited to 85 patients. And the study was conducted retrospectively. The adjuvant treatment groups were divided into RT alone and CRT. Because we analyzed only resectable OPC, PNI (no 92.9% vs. yes 7.1%, p=0.063), lower neck LN involvement (no 80% vs. yes 20%, p=0.018) cases were relatively small in number and patient numbers with or without these risk factors were not well balanced. Despite these limitations, we identified meaningful prognostic factors regarding DM in OPC patients.

Conclusion

In conclusion, lower neck LN involvement, pretreatment SUVmax ≥ 9.7, and tumour size ≥ 3 cm were predictors for DM in a multivariate analysis of patients with OPC who underwent radical surgery followed by adjuvant RT with or without chemotherapy. The 5-year OS rate in patients with PNI and lower neck LN involvement was low; thus, further investigation of adjuvant therapies in prospective studies is needed for patients who are at high risk for DM.

Conflicts of Interest

Conflict of interest relevant to this article was not reported.

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