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Total lesion glycolysis as a predictor of clinical T3–4a laryngeal cancer with laryngectomy or nonlaryngectomy

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Abstract

The purpose of the present study is to investigate whether the ^{18}F-fluorodeoxyglucose (^{18}F-FDG) uptake parameter is related to survival outcomes for patients with clinical T3–T4a laryngeal cancer with various definitive treatments including total laryngectomy (TL). Parameters of ^{18}F-FDG uptake in the primary tumors of 46 cases which were assessed by positron emission tomography with computed tomography were enrolled in the present observation study. Monovariate or multivariate survival analyses were performed with log-rank test or Cox regression model, with the hazard ratio (HR) and 95% confidence interval (CI), respectively. Cutoff values of the ^{18}F-FDG uptake parameters were determined by the lowest *P*-value for monovariate overall survival. In the monovariate analysis, both metabolic tumor volume ≥13.1 and total lesion glycolysis (TLG) ≥46.5 were significantly associated with shorter overall survival, and TLG ≥46.5 was also related to a reduction in distant metastasis-free survival. In the multivariate analysis adjusting for clinical T classification (cT4/cT3) and treatment group (TL/non-TL), TLG (≥46.5/<46.5) was associated with both poorer overall (HR: 3.16, 95% CI: 1.10–9.49) and distant metastasis-free (HR: 8.91, 95% CI: 1.93–62.6) survival. In conclusion, TLG is a predictor for survival in laryngeal cancer.

Abbreviations: ^{18}F-FDG = ^{18}F-fluorodeoxyglucose, CI = confidence interval, CRT = chemoradiotherapy, CT = computed tomography, DMFS = distant metastasis-free survival, HR = hazard ratio, LALSCC = locally-advanced laryngeal squamous cell carcinoma, LRRFS = locoregional recurrence-free survival, MTV = metabolic tumor volume, OS = overall survival, PET = positron emission tomography, RT = radiotherapy, SCC = squamous cell carcinoma, SUVmax = maximum standardised uptake value, SUVpeak = peak standardised uptake value, TL = total laryngectomy, TLG = total lesion glycolysis, VOIs = volumetric region of interests.

Keywords: distant metastasis, laryngeal squamous cell carcinoma, metabolic tumor volume, overall survival, total lesion glycolysis

1. Introduction

Positron emission tomography (PET) fused with computed tomography (CT) using ^{18}F-fluorodeoxyglucose (^{18}F-FDG) has been widely used in head and neck imaging for the initial staging of cancers.[1]^{18}F-FDG uptake parameters such as the maximum standardised uptake value (SUVmax) have been evaluated as a noninvasive predictor of survival in patients with squamous cell carcinoma (SCC) of the head and neck who were treated mainly with radiotherapy (RT) or chemoradiotherapy (CRT).[2–4] However the relationship between ^{18}F-FDG uptake parameters and survival outcomes after various definitive treatments in laryngeal cancer has not fully been investigated.

Total laryngectomy (TL) with survival benefit in various definitive treatments is mostly preferred for locally-advanced laryngeal SCC (LALSCC) of clinical T3–T4a tumors.[5] Cases with LALSCC have also been treated by various laryngeal-preserving treatments including RT, CRT, partial laryngectomy, chemoselection based on induction chemotherapy, and alternating CRT based on early assessment with salvage surgery after induction CRT.[6,7] While we recently reported in patient with LALSCC who received TL or laryngeal-preserving treatments that the treatment package time predicts both LALSCC-specific survival and distant metastasis-free survival (DMFS), although the time does not predict overall survival (OS).[8]

In the present study, we researched whether ^{18}F-FDG uptake parameters are associated with survival outcomes for patients with LALSCC who are treated with TL or laryngeal-preserving treatments.

2. Materials and methods

2.1. Study population

A total of 100 patients who were newly diagnosed with LALSCC underwent definitive treatment at the Department of Head and

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Neck Surgery, Aichi Cancer Center Hospital, from June 2004 to October 2016.[8] Among these 100 patients, we investigated 46 patients with a serum glucose level less than 200 mg/mL who underwent pretreatment ^{18}F-FDG PET/CT at the Nagoya Radiological Diagnosis Foundation. This retrospective investigation was conducted in accordance with the Declaration of Helsinki and approved by the Aichi Cancer Center Review Board, and all patients provided informed consent for treatment and examination.

2.2. Clinical parameters

Staging was determined based on the tumor–node-metastasis classification was determined according to the seventh edition of the International Union Against Cancer.[9] Vocal cord fixation was diagnosed by flexible laryngoscope. The primary tumor subsites were the glottis (n = 31) and supraglottis (n = 15). Initial treatment of the primary tumor consisted of TL ± RT with or without chemotherapy (n = 13), partial laryngectomy (n = 1), concurrent CRT (n = 8), alternating CRT (n = 14), chemoselection (n = 9), and RT alone (n = 1). Initial treatment selection first recommended TL, and all patients were grouped by initial treatment as follows: TL ± RT with or without chemotherapy (TL group: n = 13) and laryngeal-preserving treatment (non-TL group: n = 33). Adjuvant treatment consisted of postoperative RT with/without chemotherapy based on postoperative pathologic examination and salvage surgery for patients who did not respond to induction therapy or residual tumor. The other methods of clinical staging, treatment, initial treatment selection, adjuvant treatment, and follow-up have been described elsewhere.[8] Charlson comorbidity index and treatment package time were calculated from 19 comorbid conditions and days between the beginning of any treatment and the finish of all treatments, respectively.

2.3. ^{18}F-FDG uptake parameters

We conducted a semiquantitative evaluation of the ^{18}F-FDG uptake parameters (Advantage Workstation 4.6 software program PET VCAR, GE Healthcare, Chalfont, UK) to the volumetric region of interests (VOIs) from the ^{18}F-FDG-PET/CT scanning (Biograph True Point PET/CT/40 with True V, Siemens Health Medical Solution Inc., Malven, PA).[10] The means ± standard deviations duration between ^{18}F-FDG-PET/CT and the beginning to any treatment and the blood glucose level at the staging were 19.8 ± 20.2 days and 106 ± 22.0 mg/dL, respectively. The threshold fraction of SUVmax for computing the metabolic tumor volume (MTV) and total lesion glycolysis (TLG) from the VOI was 45%. The definition of the peak standardised uptake value (SUVpeak) was the maximum average standardised uptake value within a 1-mL sphere VOI.

2.4. Statistical analysis

Relationships between clinical parameters (clinical T and N classification, clinical stage, subsites, vocal cord fixation, Charlson comorbidity index, gender, age, treatment group, adjuvant treatment, treatment package time) and ^{18}F-FDG-uptake parameters (SUVmax, SUVpeak, MTV, TLG) were compared using the Mann–Whitney *U* test. We used the Kaplan–Meier method to compute the survival days from the beginning of any treatment to the last contact or a marked event. The marked event was death for OS, distant metastasis for DMFS and local or regional recurrence for locoregional recurrence-free survival (LRRFS). The cutoff values for the versatile ^{18}F-FDG-uptake parameters were assessed by using univariate OS analysis on log-rank test. For the univariate survival analysis, patients were separated into groups based on SUVmax (≥28.9 or <28.9), SUVpeak (≥12.3 or <12.3), MTV (≥13.1 or <13.1), and TLG (≥46.5 or <46.5). Survival outcomes (OS, LRRFS, DMFS) between 2 groups which were/not received by chemotherapy (presence: n = 32/absence: n = 14) were compared by log-rank test. Multivariate survival analyses, which were adjusted based on classification (cT4/cT3) and treatment group (non-TL/TL), used 3 models of Cox regression with hazard ratio (HR) and 95% confidence interval (CI). Model 1 for OS was adjusted with MTV (≥13.1/<13.1). Model 2 for OS was adjusted with TLG (≥46.5/<46.5). Model 3 for DMFS was adjusted with TLG (≥46.5/<46.5). All statistical analyses were performed using JMP software, version 9 (SAS, Cary, NC). *P*-values less than .05 were considered significant.

3. Results

3.1. ^{18}F-FDG-uptake parameters and clinical parameters

The means ± standard deviations of SUVmax, SUVpeak, MTV, and TLG of the primary tumours in all 46 patients were 19.5 ± 6.63, 4.84 ± 4.78, 13.4 ± 5.01 and 62.8 ± 68.9, respectively. Table 1 presents the association between ^{18}F-FDG-uptake parameters and clinical parameters. The levels of both MTV ($P < .01$) and TLG ($P < .01$) were higher for patients with clinical T4 classification than clinical T3 classification. Higher levels of SUVmax ($P = .04$), SUVpeak ($P < .01$), MTV ($P < .01$) and TLG ($P < .01$) were noted among those with a clinical N2–3 classification in comparison with patients with a clinical N0–1 classification. Patients with clinical stage III had lower levels of SUVpeak ($P = .04$), MTV ($P < .01$) and TLG ($P < .01$) than those with clinical stage IV. The presence of vocal cord fixation was associated with higher levels of both MTV ($P = .01$) and TLG ($P = .02$) than the absence of vocal cord fixation.

3.2. Clinical course

At the end of the study, the means ± standard deviations for follow-up duration were 4.65 ± 2.87 years among all patients, 5.92 ± 2.15 years for the 27 patients who were alive and 2.85 ± 2.84 years for the 19 patients who died. Distant metastasis and locoregional recurrence developed for 8 and 11 patients, respectively. Four-year rates of OS, DMFS, and LRRFS were 69.0%, 80.4%, and 72.9%, respectively.

3.3. Cutoff values of ^{18}F-FDG-uptake parameters

Based on the lowest *P*-value of the log-rank test for OS, the cutoff values were SUVmax = 28.9 ($P = .15$), SUVpeak = 12.3 ($P = .13$), MTV = 13.1 ($P < .01$), and TLG = 46.5 ($P < .01$). Figure 1 shows the *P*-values of the log-rank test at different cutoff values of both MTV and TLG.

3.4. Univariate survival analyses

Table 2 shows the results of univariate survival analyses. Cases with MTV ≥13.1 were associated with shorter OS than those

Table 1

Association between ^{18}F-FDG parameters and clinical characteristics in laryngeal squamous cell carcinoma.

Clinical characteristic		n	Mean ± standard deviation			
			SUVmax	SUVpeak	MTV	TLG
Whole		46	19.5±6.63	4.84±4.78	13.4±5.01	62.8±68.9
cT classification	cT3	36	19.5±7.17	13.2±5.30	3.18±2.35	42.0±41.9
	cT4	10	19.4±4.44	14.2±3.94	10.8±6.48	138±94.4
cN classification	*P*-value		.77	.52	<.01	<.01
	cN0–1	33	18.2±6.55	12.1±4.79	2.99±2.44	36.4±38.4
	cN2–3	13	22.8±5.84	16.6±4.18	9.54±6.02	130±84.1
cStage	*P*-value		.04	<.01	<.01	<.01
	cStageIII	28	18.3±6.85	12.2±4.91	2.56±1.43	30.7±23.4
	cStageIV	18	21.4±5.97	15.3±4.68	8.38±5.94	113±85.8
	P-value		.18	.04	<.01	<.01
Subsite	Glottis	31	19.8±6.61	13.6±4.78	4.93±4.08	63.2±60.8
	Supraglottis	15	18.8±6.87	13.0±5.61	4.65±6.14	62.1±85.7
	P-value		.72	.55	.31	.27
Vocal cord	Presence	26	19.7±6.63	14.1±4.78	6.28±5.52	80.6±77.0
fixation	Absence	20	19.2±6.79	12.6±5.30	2.96±2.73	39.7±49.4
	P-value		.86	.28	.01	.02
Charlson comorbidity index	0	18	20.9±5.56	14.6±3.84	5.27±4.47	68.4±59.0
	≥1	28	18.6±7.18	12.6±5.57	4.56±5.02	59.2±75.4
	P-value		.30	.16	.33	.16
Gender	Male	45	19.4±6.70	13.3±5.03	4.83±4.83	62.6±69.7
	Female	1	21.6	17.7	5.13	73.8
	P-value		.79	.31	.52	.31
Age	<68 years old	23	19.7±6.21	13.4±4.66	5.22±4.76	66.6±69.5
	≥68 years old	23	19.3±7.16	13.5±5.45	4.46±4.87	59.1±69.7
Treatment	*P*-value		.82	.90	.75	.73
group	Total laryngectomy	13	19.8±7.54	13.8±5.31	6.85±6.61	86.5±91.9
	Nontotal laryngectomy	33	19.4±6.36	13.2±4.97	4.04±3.66	53.5±56.5
	P-value		.76	.72	.14	.23
Adjuvant	Presence	10	19.5±5.62	13.6±4.01	5.12±3.94	61.1±47.2
treatment	Absence	36	19.5±6.96	13.4±5.31	4.76±5.03	63.3±74.4
	P-value		.96	.77	.32	.39
Treatment	<68 days	31	18.6±7.14	13.1±5.25	5.45±5.24	69.6±76.7
package time	≥68 days	15	21.3±5.17	14.1±4.60	3.57±3.47	48.8±48.4
	P-value		.39	.49	.14	.50

Statistical analysis was used by Mann–Whitney *U* test. MTV = metabolic tumor volume, SUVmax = maximum standardized uptake value, SUVpeak = peak standardized uptake value, TLG = total lesion glycolysis.

with MTV < 13.1 ($P < .01$). Cases with TLG ≥46.5 were related to both shorter OS ($P < .01$) and shorter DMFS ($P = .01$) than those with TLG < 46.5. Figure 2 shows the Kaplan–Meier curves of OS for the 2 groups of MTV (≥13.1 or <13.1), OS and DMFS of the 2 groups for TLG (≥46.5 or <46.5). No significant differences between 2 groups of chemotherapy (presence/absence) were observed in OS ($P = .14$), LRRFS ($P = .31$), and DMFS ($P = .63$).

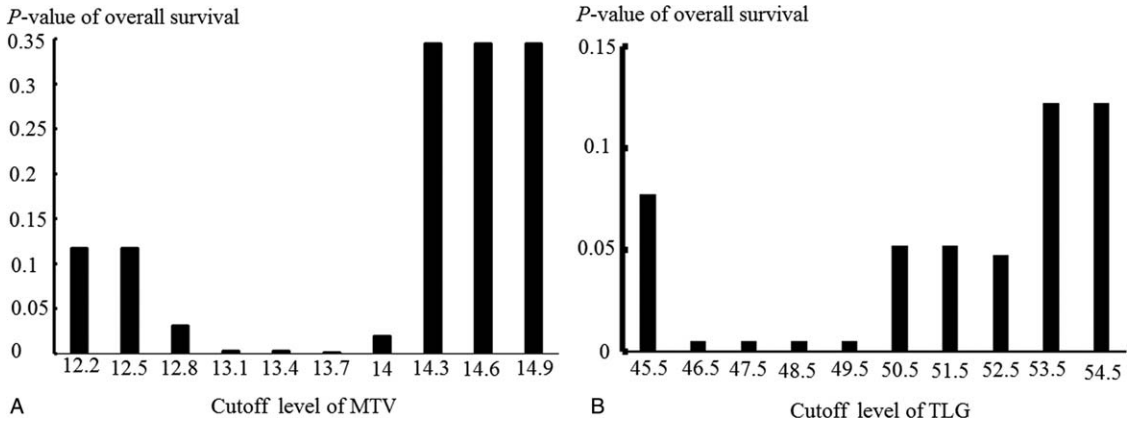

Figure 1. *P*-values of the log-rank test for OS applying dissimilar cutoff levels of MTV (A) and TLG (B) in 46 patients with LALSCC. LALSCC = locally-advanced laryngeal squamous cell carcinoma, MTV = metabolic tumor volume, OS = overall survival, TLG = total lesion glycolysis.

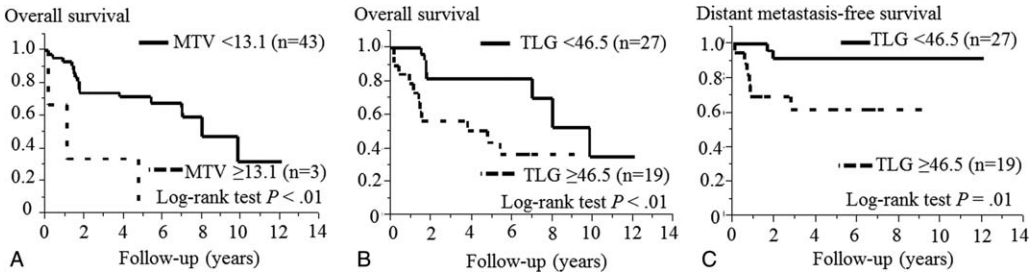

Figure 2. Comparison with 2 groups of MTV ≥13.1 vs MTV <13.1 for OS (A), TLG ≥46.5 vs TLG <46.5 for OS (B), TLG ≥46.5 vs TLG <46.5 for DMFS, and (C) for 46 patients of LALSCC. The statistical analysis from the survival calculation based on the Kaplan–Meier method was compared by log-rank test. DMFS = distant metastasis-free survival, LALSCC = locally-advanced laryngeal squamous cell carcinoma, MTV = metabolic tumor volume, OS = overall survival, TLG = total lesion glycolysis.

Table 2

Univariate survival analysis in laryngeal squamous cell carcinoma by log-rank test.

^{18}F-FDG uptake parameter	Patient number	4-year OS, %	*P*-value	4-year LRRFS, %	*P*-value	4-year DMFS, %	*P*-value
SUVmax							
≥28.9	4	100		100		100	
<28.9	42	66.0	.15	69.7	.23	78.2	.32
SUVpeak							
≥12.3	21	62.7		71.6		77.4	
<12.3	25	76.2	.13	74.7	.75	84.1	.52
MTV							
≥13.1	3	33.3		100		66.7	
<13.1	43	71.5	<.01	71.7	.46	81.5	.27
TLG							
≥46.5	19	50.5		59.1		61.8	
<46.5	27	81.5	<.01	80.8	.1	91.6	.01

^{18}F-FDG = ^{18}F-fluorodeoxyglucose, DMFS = distant metastasis–free survival, LRRFS = locoregional recurrence-free survival, MTV = metabolic tumor volume, OS = overall survival, SUVmax = maximum standardized uptake value, SUVpeak = peak standardized uptake value, TLG = total lesion glycolysis.

3.5. Multivariate survival analyses

Table 3 presents the results of multivariate survival analyses. In the model 1, no significant associations were found between MTV (≥13.1/<13.1) and OS. In the model 2, there was a significant association between TLG (≥46.5/<46.5) and poorer OS was significant (HR = 3.16, 95% CI = 1.10–9.49, *P* = .03). In the model 3, the relationship between TLG (≥46.5/<46.5) and poorer DMFS was significant (HR = 8.91, 95% CI = 1.93–62.6, *P* < .01).

Representative images were shown in Figure 3 as an example.

4. Discussion

In the present study, we demonstrated that among 46 cases with LALSCC treated by either TL or non-TL, a TLG ≥46.5 is associated with a shorter OS and DMFS in both the monovariate and multivariate survival analysis after adjusting for clinical T classification and treatment group.

Table 3

Multivariate analysis in laryngeal squamous cell carcinoma by Cox proportional hazards model.

Model	Adjustment	Hazard ratio	95% confidence interval	*P*-value
Model 1 for OS				
	cT (cT4/cT3)	1.12	0.24 to 3.80	.87
	Treatment group (non-TL/TL)	0.54	0.17 to 2.06	.34
	MTV (≥13.1/<13.1)	3.79	0.50 to 30.6	.19
Model 2 for OS				
	cT (cT4/cT3)	1.12	0.36 to 3.18	.84
	Treatment group (non-TL/TL)	0.46	0.17 to 1.32	.14
	TLG (≥46.5/<46.5)	3.16	1.10 to 9.49	.03
Model 3 for DMFS				
	cT (cT4/cT3)	0.27	0.01 to 1.64	.17
	Treatment group (non-TL/TL)	1.44	0.33 to 9.94	.65
	TLG (≥46.5/<46.5)	8.91	1.93 to 62.6	<.01

DMFS = distant metastasis-free survival, MTV = metabolic tumor volume, OS = overall survival, TL = total laryngectomy, TLG = total lesion glycolysis.

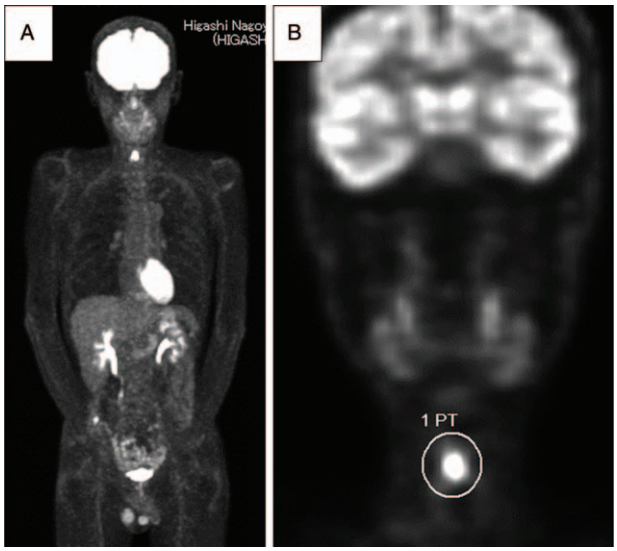

Figure 3. ^{18}F-2-fluorodeoxyglucose positron emission tomography combined computed tomography images (A: whole body, B: volume of interest) of a 66-year-old man with laryngeal squamous cell carcinomas.

Several meta-analyses regarding for SCC of the head and neck had been investigated TLG as a volumetric metabolic predictor of survival outcomes mostly in patients receiving nonsurgical treatments.[2–4] While recently, in 2020, Creff et al[11] systemically reviewed 3585 patients with surgically treated head and neck cancer and found that ^{18}F-FDG uptake parameters such as TLG predict survival outcomes. We also showed that in 53 patients with hypopharyngeal SCC, TLG ≥42 is a significant predictor of OS and DMFS in univariate and multivariate analysis after adjusting for clinical T category and treatment group (surgery/RT).[10] The present results that demonstrate a significant association between higher TLG and shorter survivals (OS and DMFS) are in agreement with these previous results.[2–4,10,11]

By focusing on laryngeal cancer as a single organ, both TLG and MTV predict pathological invasion of the thyroid cartilage from 50 primary tumors.[12] SUVmax was a significant predictor for both recurrence and disease-specific survival in 42 patients with supracricoid partial laryngectomy; however, other volumetric parameters such as MTV and TLG were not investigated.[13] Yabuki et al[14] reported that MTV was a significant predictor after RT or CRT in 118 laryngeal cancer, and that surgery was associated with better relapse-free survival and OS than RT-based treatments in 63 laryngeal cancers with a high MTV (≥4.9 mL).[15] However, TLG was not investigated in either of these studies.[9,15] To the best of our knowledge, the association between ^{18}F-FDG uptake parameters and survival outcomes of laryngeal cancer in multivariate analysis after adjusting for treatment group and clinical T classification has not yet been investigated. Therefore, we believe there was a need for the present study.

To determine the cutoff value of the ^{18}F-FDG-uptake parameters had been used by various methods including median value, receiver-operating curve analysis and lowest *P*-value.[2] Although the lowest *P*-value is associated with the possibility of a false-positive,[2] we used this measure in the same manner as in previous studies of ^{18}F-FDG-up parameters for hypopharyngeal SCC.[10]

Larger VOI was selected manually from the information for the presence of primary tumor. Because SUVmax, TLG, and MTV from the VOI was automatically assessed by workstation, we considered that there were scarcely any intra-observer variation. Although there was a possibility of any variation in TLG values with different PET/CT analysis software as described by Pierce et al.[16] TLG value in the present study was assessed by 1 software for PET/CT analysis.

There are several limitations of the present study, including its retrospective nature and relatively small number of participants. Future analysis of data from prospective studies with a larger number of cases will lead to more precise and useful results.

In conclusion, the present study demonstrated that a higher TLG is a predictor of OS and DMFS in patients with LALSCC who were treated by various definitive treatments, including TL and non-TL.

Author contributions

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References

[1] Strohl MP, Ha PK, Flavell RR, Yom SS. PET/CT in surgical planning for head and neck cancer. Semin Nucl Med 2021;51:50–8.
[2] Pak K, Cheon GJ, Nam HY, et al. Prognostic value of metabolic tumor volume and total lesion glycolysis in head and neck cancer: asystematic review and meta-analysis. J Nucl Med 2014;55:884–90.
[3] Wang L, Bai J, Duan P. Prognostic value of 18F-FDG PET/CT functional parameters in patients with head and neck cancer: a meta-analysis. Nucl Med Commun 2019;40:361–9.
[4] Rijo-Cedeño J, Mucientes J, Álvarez O, et al. Metabolic tumor volume and total lesion glycolysis as prognostic factors in head and neck cancer: systematic review and meta-analysis. Head Neck 2020;42:3744–54.
[5] Forastiere AA, Ismaila N, Lewin JS, et al. Use of larynx-preservation strategies in the treatment of laryngeal cancer: American Society of Clinical Oncology Clinical Practice Guideline update. J Clin Oncol 2018;36:1143–69.
[6] Sanabria A, Chaves ALF, Kowalski LP, et al. Organ preservation with chemoradiation in advanced laryngeal cancer: the problem of generalizing results from randomized controlled trials. Auris Nasus Larynx 2017;44:18–25.
[7] Nakata Y, Ijichi K, Hanai N, et al. Treatment results of alternating chemoradiotherapy with early assessment for advanced laryngeal cancer: a multi-institutional phase II study. Auris Nasus Larynx 2017;44:104–10.
[8] Suzuki H, Terada H, Hanai N, et al. Treatment package time predicts cancer-specific survival and distant metastasis in laryngeal cancer. Oncol Lett 2019;17:1384–90.
[9] Sobin LH, Gospodarowicz MK, Wittekind C. TNM classification of malignant tumours. 7th ed2009;Wiley-Blackwell, Oxford,
[10] Suzuki H, Nishio M, Nakanishi H, et al. Impact of total lesion glycolysis measured by 18F-FDG-PET/CT on overall survival and distant metastasis in hypopharyngeal cancer. Oncol Lett 2016;12:1493–500.
[11] Creff G, Devillers A, Depeursinge A, et al. Evaluation of the prognostic value of FDG PET/CT parameters for patients with surgically treated head and neck cancer: a systematic review. JAMA Otolaryngol Head Neck Surg 2020;146:471–9.

[12] Kendi AT, Corey A, Magliocca KR, et al. Is there a role for PET/CT parameters to differentiate thyroid cartilage invasion from penetration? Eur J Radiol 2016;85:319–23.
[13] Joo YH, Yoo IeR, Cho KJ, et al. Utility of 18F-FDG PET/CT in supracricoid partial laryngectomy. Acta Otolaryngol 2013;133: 1207–12.
[14] Yabuki K, Shiono O, Komatsu M, et al. Predictive and prognostic value of metabolic tumor volume (MTV) in patients with laryngeal carcinoma treated by radiotherapy (RT) /concurrent chemoradiotherapy (CCRT). PLoS One 2015;10:e0117924.
[15] Yabuki K, Sano D, Shiono O, et al. Surgery-based versus radiation-based treatment strategy for a high metabolic volume laryngeal cancer. Laryngoscope 2017;127:862–7.
[16] Pierce LA2nd, Elston BF, Clunie DA, Nelson D, Kinahan PE. A digital reference object to analyze calculation accuracy of PET standardized uptake value. Radiology 2015;277:538–45.