Prognostic Value of Preoperative Metabolic Tumor Volume and Total Lesion Glycolysis Measured by ^{18}F-FDG PET/CT in Salivary Gland Carcinomas

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Metabolic tumor volume (MTV) and total lesion glycolysis (TLG) from ^{18}F-FDG PET/CT are emerging prognostic biomarkers in various human cancers. This study examined the prognostic value of these metabolic tumor parameters measured by pretreatment ^{18}F-FDG PET/CT in patients with salivary gland carcinomas. **Methods:** Forty-nine patients with intermediate- or high-grade salivary gland carcinomas who underwent definitive surgery with or without radiotherapy or chemoradiotherapy were evaluated preoperatively by ^{18}F-FDG PET/CT. Maximum standardized uptake values (SUV_{max}), MTV, and TLG were measured for each patient. Univariate and multivariate analyses were used to identify clinicopathologic and imaging variables associated with progression-free survival (PFS) and overall survival (OS). Univariate analyses included the following variables: age, sex, pT and pN classifications, overall pTNM stage, histologic grade, resection margin, tumor lymphovascular invasion and perineural invasion, postoperative adjuvant therapy, gross total volume, SUV_{max}, MTV, and TLG. **Results:** The 3-y PFS and OS rates for all study patients were 66.9% and 81.6%, respectively. The median SUV_{max}, MTV, and TLG were 5.1 (range, 1.7–21.5), 16.2 mL (1.0–115.1 mL), and 24.4 g (2.1–224.4 g), respectively. Univariate analyses showed that there were significant correlations between pT classification, pN classification, MTV, and TLG and both PFS and OS ($P < 0.05$). However, SUV_{max} was not associated with either PFS ($P = 0.111$) or OS ($P = 0.316$). Multivariate analyses revealed that MTV ($P = 0.011$; hazard ratio, 11.50; 95% confidence interval, 1.45–91.01) and TLG ($P = 0.038$; hazard ratio, 3.55; 95% confidence interval, 1.07–11.76) were independent variables for PFS. **Conclusion:** Pretreatment values of MTV and TLG are independent prognostic factors in patients with intermediate or high-grade salivary gland carcinomas.

Key Words: salivary gland carcinomas; ^{18}F-FDG PET/CT; metabolic tumor volume; total lesion glycolysis; prognostic factors

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Salivary gland carcinoma is a rare neoplasm, accounting for 3%–5% of head and neck cancers and 0.3% of all human cancers (*1,2*). The histopathology of salivary gland tumors is extremely varied and complex, with at least 24 different types recognized by the World Health Organization (*3*). This diversity, combined with the rarity of many of the tumor types and unpredictable long-term outcomes, imposes a significant challenge in their management (*4*). Although various factors affect the prognosis of patients with salivary gland carcinomas, the most significant factors are histologic grade and clinical stage at diagnosis (*5,6*). It remains difficult for clinicians to select appropriate treatment strategies and make prognoses for these patients. Many additional clinicopathologic and biologic markers have been investigated for predicting outcomes and supplementing TNM stage (*4,7–9*).

^{18}F-FDG PET imaging is based on tumor glucose metabolism and serves as a marker of tumor metabolic activity such as cell viability and proliferative activity (*10,11*). Combining ^{18}F-FDG PET with CT provides useful functional and anatomic information and enables more accurate evaluation of initial staging, monitoring of treatment response, and posttreatment surveillance of patients with head and neck cancers (*12–15*). The maximum standardized uptake value (SUV_{max}), as an estimate of tumor metabolic activity, is the most commonly used parameter in ^{18}F-FDG PET/CT. However, SUV_{max} is measured by the most numerous pixels in a region of interest; it shows only the highest intensity of ^{18}F-FDG uptake in the tumor and cannot reflect the metabolic activity of the whole tumor.

Recently, ^{18}F-FDG metabolic tumor volume (MTV) and total lesion glycolysis (TLG), combining the tumor volume and metabolic activity of the entire tumor, have been introduced as prognostic biomarkers for various solid malignancies (*16–18*). To our knowledge, no reports have assessed the prognostic significance of MTV and TLG in patients with salivary gland carcinomas. Therefore, we evaluated the prognostic value of these metabolic parameters measured by pretreatment ^{18}F-FDG PET/CT in these patients in helping to identify a subgroup at high risk of disease progression after definitive treatment.

MATERIALS AND METHODS

Patient Population

We reviewed the records of 98 patients with newly diagnosed salivary gland carcinomas who underwent ^{18}F-FDG PET/CT imaging

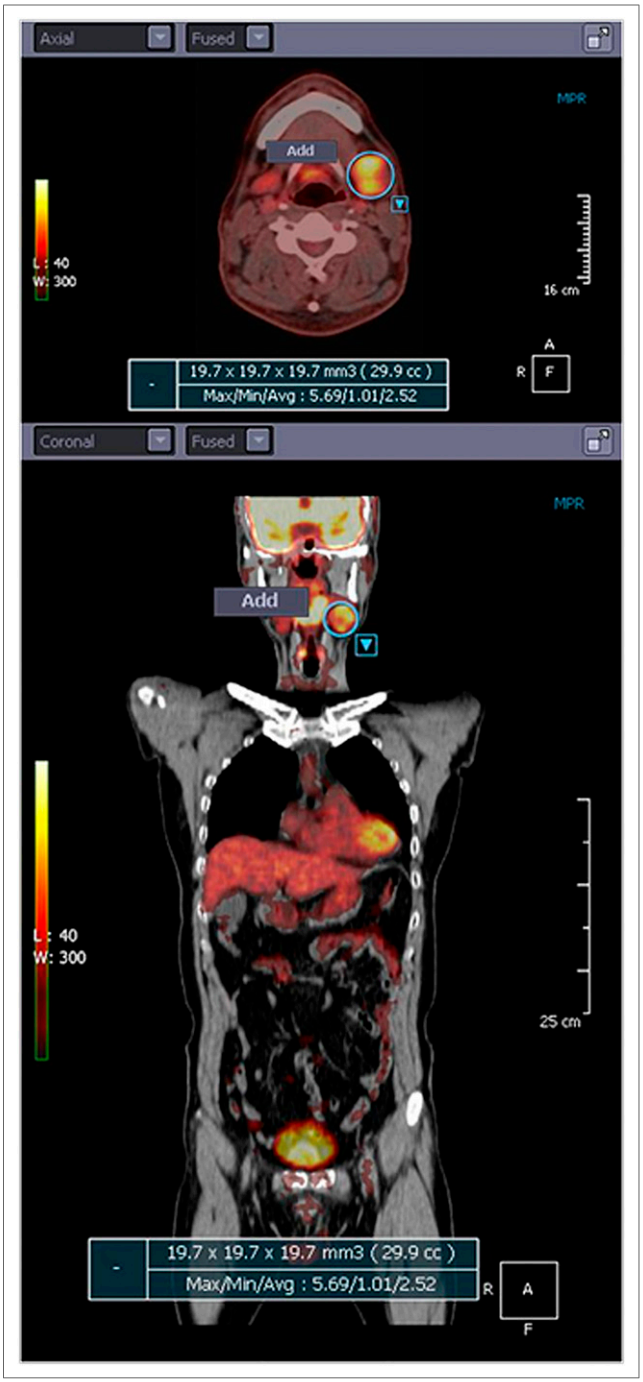

FIGURE 1. Measurement of MTV. Region of interest (circled) was set to include whole tumor or metastatic disease with metabolic activity, and software automatically calculated SUV_{max} and MTV.

for initial staging between January 2004 and August 2011. Exclusion criteria included low-grade salivary gland carcinoma ($n = 29$), because of its low probability of metastasizing or progressing; no pretreatment ^{18}F-FDG PET/CT ($n = 16$); incomplete treatment or clinical data ($n = 3$); and initial nonsurgical treatment by neoadjuvant chemotherapy ($n = 1$). All surviving patients were followed up for at least 12 mo. Forty-nine patients with pathologically confirmed intermediate- or high-grade salivary gland carcinomas were eligible for this study. The diagnosis was established by ultrasonography-guided fine-needle aspiration or core-needle biopsy and imaging work-ups including CT imaging of the head and neck. All included patients underwent ^{18}F-FDG PET/CT imaging within 2–4 wk before surgery.

Data were obtained from medical records, including clinicopathologic characteristics, treatment, and follow-up. Follow-up data were available for all patients, with recurrence and survival calculated from the date of initial surgery. Tumors were staged clinically according to the system of the American Joint Committee on Cancer (*19*). This study was approved by the Institutional Review Board of our hospital, and informed consent from patients was waived.

Treatments and Histopathology

All patients initially underwent surgery with curative intent for the primary tumor, and 43 patients underwent neck dissection. Patients with clinical nodal metastasis underwent modified radical ($n = 13$) or radical ($n = 4$) neck dissection, and 2 underwent bilateral dissection. Twenty-six patients with no clinical nodal metastasis (cN0) underwent selective neck dissection. Four patients received postoperative chemoradiation therapy, and 36 patients received postoperative radiotherapy with 59.4 Gy (range, 50.4–66.0 Gy) in a single daily fraction. Indications for postoperative adjuvant therapy relied on postoperative pathologic features such as positive surgical margins, advanced T3–T4 classification, intermediate or high histologic grades, extraparenchymal extension, lymphovascular invasion, and perineural invasion (*4,7–9*).

The tumor pathology of each patient was reviewed carefully to obtain detailed information on histologic subtype and grade, extraparenchymal extension, margin status, lymphovascular invasion, and microscopic perineural invasion. The histology of each tumor was graded according to the World Health Organization classification (*3*). The following histologic types were categorized as low, intermediate, or high: mucoepidermoid carcinoma, nonspecified adenocarcinoma, adenoid cystic

TABLE 1
Patient Characteristics

Characteristic	Data*
Age (y)	
Median	54
Range	16–79
Sex (*n*)	
Male	34 (69)
Female	15 (31)
Site of primary tumor (*n*)	
Parotid gland	27 (55)
Submandibular gland	14 (29)
Sublingual gland	2 (4)
Minor salivary gland	6 (12)
Size of primary tumor (cm)	
Median	2.5
Range	0.8–9.0
Histologic grade (*n*)	
Intermediate	23 (47)
High	26 (53)
pTNM stage (*n*) (*19*)	
T1/T2/T3/T4	7/17/15/10
N0/N1/N2/N3	30/3/16/0
M0/M1	47/2
Stage I/II/III/IV	4/13/11/21
Treatment (*n*)	
Surgery alone	9 (18)
Surgery + radiotherapy	36 (74)
Surgery + chemoradiotherapy	4 (8)
Disease progression (*n*)	13 (27)

*Values in parentheses are percentages.

carcinoma, carcinoma ex pleomorphic adenoma, and squamous cell carcinoma. All cases of some histologic types were considered high-grade, such as salivary duct carcinoma and poorly differentiated carcinoma.

^{18}F-FDG PET/CT and Contrast-Enhanced CT Imaging

^{18}F-FDG PET/CT scans were obtained with the Biograph Sensation 16 (Siemens Medical Systems), TruePoint 40 (Siemens Medical Systems), or Discovery STE 8 (GE Healthcare) PET/CT system equipped with 16-, 40- or 8-slice CT, respectively. All patients fasted for at least 6 h before ^{18}F-FDG PET. Their blood glucose concentrations were less than 150 mg/dL before the scan. Whole-body images were obtained approximately 60 min after intravenous injection of about 370–555 MBq of ^{18}F-FDG. A CT scan was obtained in spiral mode from the skull base to the proximal thigh at 100 mAs and 120 kV, with a section width of 5 mm and collimation of 0.75 mm. No oral or intravenous contrast medium was used. CT scanning data were obtained for attenuation correction and image fusion, followed by a 3-dimensional caudocranial PET emission scan with an acquisition time of 2.5 min per cradle position, using 8 bed positions. The PET data were reconstructed from the CT data, using a standard iterative algorithm.

For the purpose of defining anatomic tumor volume, contrast-enhanced CT of the head and neck was performed on all patients, using a Somatom Sensation 16 (Siemens Medical Solutions) with a slice thickness of 3 mm. For contrast enhancement, 90 mL of an iodinated contrast agent (Ultravist 300; Schering) was injected intravenously at 3 mL/s with an automated injector. The scan delay time was 35 s.

Image Interpretation

^{18}F-FDG PET/CT findings were reviewed on the workstation by a board-certified nuclear medicine physician with 15 y of clinical experience in head and neck PET or PET/CT, who identified visible lesions with high tracer uptake and then quantified the ^{18}F-FDG uptake. The maximum and average SUVs (SUV_{max} and SUV_{mean}, respectively) were used to determine ^{18}F-FDG PET activity. The SUV was analyzed using the equation SUV = A/(ID/BW), where A is the decay-corrected activity in tissue (in MBq/mL), ID is the injected dose of ^{18}F-FDG (in MBq), and BW is the patient's body weight (in g). Spheric regions of interest were placed over the lesions visible on PET images. The SUV_{max} and SUV_{mean} were calculated by automatically drawing a region of interest over the PET image slice on which the primary tumor and metastatic lymph nodes were visibly most intense.

MTVs were computed from attenuation-corrected PET data using a commercial software package (Infinitt PACS; Infinitt Healthcare Co. Ltd.) (Fig. 1). ^{18}F-FDG PET data were fed into the workstation in DICOM format, and intensity values were automatically converted to SUVs. Because salivary gland carcinomas have more varied and lower ^{18}F-FDG avidity than other head and neck cancers, the absolute values of tumor SUV could not be used to measure MTV (*13,17*). Therefore, in the absence of an established method for calculating MTV, it was taken as the tumor volume with ^{18}F-FDG uptake segmented by fixed threshold methods at 30%, 40%, 50%, and 60% of SUV_{max}, to determine whether these different values could predict survival rates. The contouring method using a fixed SUV_{max} threshold relied on including all voxels that were greater than a defined percentage of the maximum voxel within a sphere defined by the operator. Cross-sectional circles were displayed in all 3 projections (axial, sagittal, and coronal) to ensure 3-dimensional coverage of the entire hypermetabolic tumor lesion. Lymph nodes less than 1 cm in diameter were generally not included unless they showed abnormal uptake of ^{18}F-FDG on the corresponding PET images. The software program automatically calculated the volume of the tumor in each region of interest. The total metabolic volume of each tumor and cervical lymph node was then found (Fig. 1). The TLG was defined as (MTV) × (SUV_{mean}) (*20*).

The contrast-enhanced CT images were interpreted by a board-certified radiologist with 12 y of clinical experience in head and neck radiology. To calculate the gross tumor volume (GTV), the contours of the primary tumors and metastatic lymph nodes were found using axial CT images. The contrast uptake of lesions helped to differentiate tumors from surrounding structures. The software automatically calculated the areas of the lesions and the volume of tumor per slice from the thickness of the slice and the total volume of all the slices.

Statistical Analysis

Continuous variables were expressed as median and range, and categoric variables as numbers and percentage. The primary endpoint was to establish whether the exploratory imaging markers, MTV and TLG, added prognostic information about overall survival (OS) and progression-free survival (PFS). Time points were calculated from the date of surgery either to the date of death (or progression) or to the last clinical follow-up. Disease progression after achieving locoregional control by curative surgery was defined as the existence of histologically confirmed recurrent tumors at local, regional, or distant sites or as the progression of initial distant metastatic diseases according to the Response Evaluation Criteria in Solid Tumors (*21*).

The OS and PFS rates were calculated using the Kaplan–Meier method. The log-rank test was used to compare survival rates according to clinicopathologic factors and imaging parameters. Univariate analyses included the following variables: age, sex, pT and pN classifications, overall pTNM stage, histologic grade, resection margin, tumor lymphovascular invasion and perineural invasion, postoperative adjuvant therapy, GTV, SUV_{max}, MTV, and TLG. Variables with a P value of less than 0.05 on univariate analyses were selected for multivariate analyses. A Cox proportional hazard model was used to identify independent predictors of PFS or OS, and the estimated hazard ratio and 95% confidence interval (CI) were calculated. Analyses were also performed by a bootstrap method using 1,000 simple bootstrap samples. Multicolinearity between MTV and TLG was established using the Pearson correlation coefficient. Analysis of receiver-operating-characteristic curves was used to determine areas under the curve

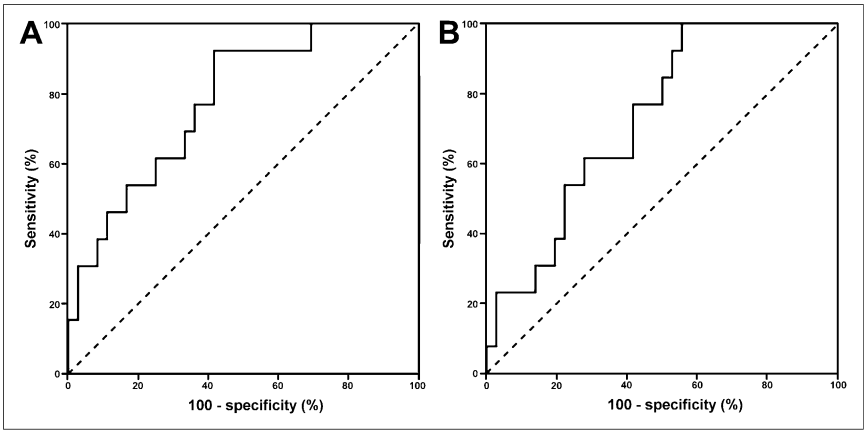

FIGURE 2. Receiver-operating-characteristic curves of disease progression according to MTV and TLG in 49 patients. (A) AUC was 0.817 (P = 0.003; 95% CI, 0.720–0.914), and 17.7 mL was chosen as MTV cutoff value. (B) AUC was 0.762 (P = 0.015; 95% CI, 0.644–0.879), and 56.3 g was chosen as TLG cutoff value.

TABLE 2
Univariate Analyses of Clinicopathologic and Imaging Variables on PFS and OS

Variable	*N*	3-y PFS (%)	*P**	3-y OS (%)	*P**
Age at diagnosis (y)			0.632		0.324
≤60	32 (65%)	67.4		87.1	
>60	17 (35%)	69.0		73.3	
Sex			0.212		0.207
Male	34 (69%)	64.0		77.1	
Female	15 (31%)	74.7		93.3	
pT classification			0.041		0.048
T1–T2	24 (49%)	82.8		88.9	
T3–T4	25 (51%)	52.9		65.2	
pN classification			0.043		0.009
N0	30 (61%)	76.2		87.7	
N1–N2	19 (39%)	55.1		73.3	
Overall pTNM stage			0.018		0.069
I–II	17 (35%)	77.3		88.3	
III–IV	32 (65%)	54.2		74.6	
Histologic grade			0.440		0.131
Intermediate	23 (47%)	75.8		88.9	
High	26 (53%)	67.7		76.3	
Resection margin			0.703		0.379
Not involved	29 (59%)	72.7		92.0	
Involved	20 (41%)	58.6		67.8	
Extraparenchymal extension			0.507		0.301
No	23 (47%)	77.9		74.4	
Yes	26 (53%)	66.8		68.8	
Lymphovascular invasion			0.022		0.164
No	32 (65%)	75.0		93.1	
Yes	17 (35%)	50.2		63.5	
Perineural invasion			0.037		0.144
No	29 (59%)	75.5		85.6	
Yes	20 (41%)	56.7		76.0	
Treatment			0.804		0.890
Surgery alone	9 (18%)	71.1		88.9	
Surgery + radiotherapy/chemoradiotherapy	40 (82%)	65.8		79.5	
GTV			0.067		0.012
≤22.7 mL	33 (67%)	74.7		93.1	
>22.7 mL	16 (33%)	53.0		60.8	
SUV_{max}			0.111		0.316
≤4.7	21 (43%)	79.1		94.1	
>4.7	28 (57%)	55.3		70.8	
MTV†			0.002		0.002
≤17.7 mL	22 (45%)	90.0		100	
>17.7 mL	27 (55%)	50.7		66.0	
TLG			0.008		0.020
≤56.3 g	31 (63%)	76.9		90.3	
>56.3 g	18 (37%)	55.6		67.9	

*Log-rank tests, $P < 0.05$.
†Total MTVs of primary tumors and metastatic neck nodes were added together.

(AUC) to estimate the accuracy and predictive value of various imaging biomarkers (*22*). The sensitivity and specificity depended on the cutoff values of MTV and TLG. All tests were 2-sided, and a probability of less than 0.05 was considered statistically significant. All statistical analyses were performed using SPSS software (version 18.0; SPSS Inc.).

RESULTS

Patient Characteristics

The 49 eligible patients consisted of 34 men and 15 women, with a median age of 54 y (range, 16–79 y). Their demographic and clinicopathologic characteristics are presented in Table 1. Cancer of the parotid gland was the most common, being present in 27 patients (55%), and high-grade tumors were observed in 26 patients (53%). Twelve patients (25%) had salivary duct carcinomas; 11 (22%), mucoepidermoid carcinomas; 11 (22%), adenoid cystic carcinomas; 9 (18%), carcinoma ex pleomorphic adenomas; 3 (6%), poorly differentiated carcinomas; 2 (4%), squamous cell carcinomas; and 1 (2%), a nonspecified adenocarcinoma. Twenty-five patients (51%) had advanced T-staged tumors, 19 (39%) had pathologically positive cervical lymph nodes, and 32 (65%) were in advanced overall stage III/IV. Two patients (4%) who had

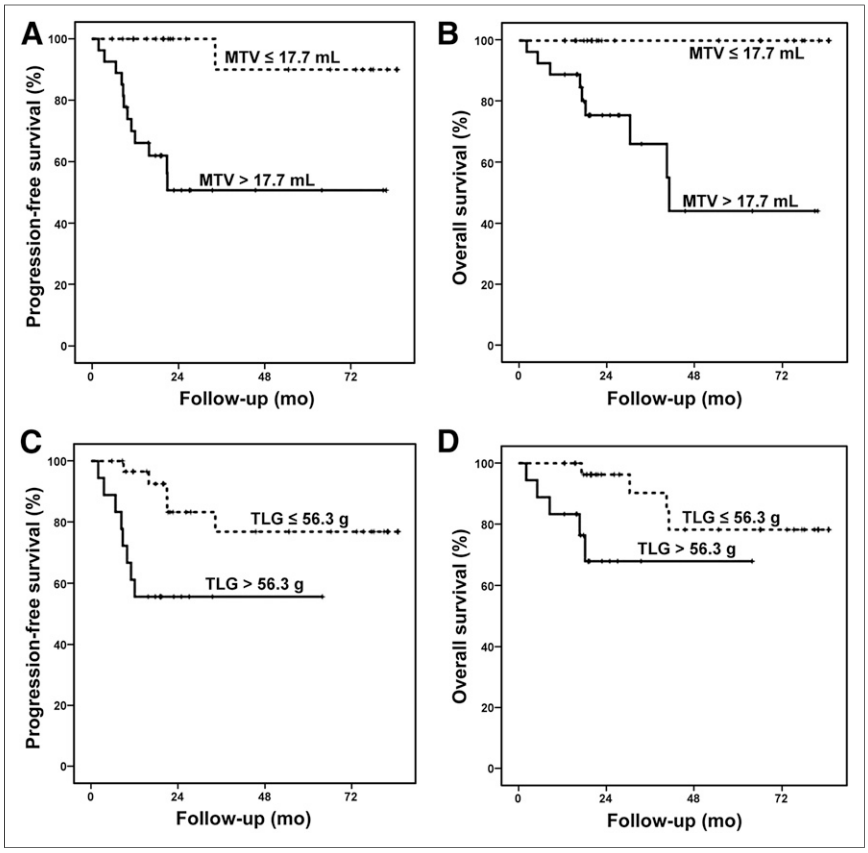

FIGURE 3. Kaplan–Meier curves of PFS (A and C) and OS (B and D) according to MTV and TLG in study population ($n = 49$). (A and B) Upper line, MTV ≤ 17.7 mL ($n = 22$); lower line, MTV > 17.7 mL ($n = 27$). $P = 0.002$ for PFS and $P = 0.002$ for OS. (C and D) Upper line, TLG ≤ 56.3 g ($n = 31$); lower line, TLG > 56.3 g ($n = 18$). $P = 0.008$ for PFS and $P = 0.020$ for OS.

adenoid cystic carcinoma metastatic to the lung at initial diagnosis underwent surgery for their locoregional disease. The median follow-up for surviving patients was 29 mo (range, 13–85 mo). During follow-up after complete locoregional control by surgery, 13 patients (27%) had disease progression and 9 (18%) died of their disease. No patients died from other causes. The median time to disease progression was 21 mo (range, 2–85 mo) after surgery. The Kaplan–Meier estimates of 3-y PFS and OS rates for all patients were 66.9% and 81.6%, respectively.

Determination of the Cutoff Values of Imaging Parameters

The AUCs for predicting PFS with MTV calculation at 30%, 40%, 50%, and 60% of SUV_{max} were 0.81 ($P = 0.011$), 0.75 ($P = 0.020$), 0.73 ($P = 0.028$), and 0.74 ($P = 0.025$), respectively. The AUCs for predicting OS with MTV calculated at 30%, 40%, 50%, and 60% of SUV_{max} were 0.85 ($P = 0.010$), 0.79 ($P = 0.020$), 0.79 ($P = 0.028$), and 0.80 ($P = 0.025$), respectively. Therefore, we used the 30% of SUV_{max} showing the lowest P value and the highest AUC as the optimal fixed threshold for MTV.

The median GTV, SUV_{max}, MTV, and TLG were 12.5 mL (range, 1.4–142.6 mL), 5.1 (1.7–21.5), 16.2 mL (1.0–115.1 mL), and 24.4 g (2.1–224.4 g) (Supplemental Table 1 and Fig. 1; supplemental materials are available online at http://jnm.snmjournals.org). From the receiver-operating-characteristic curve analyses, the MTV cutoff value was 17.7 mL with a sensitivity of 97.3% and a specificity of 61.2% ($P = 0.003$; AUC, 0.817; 95% CI, 0.720–0.914), and the TLG cutoff value was 56.3 g with a sensitivity of 86.6% and a specificity of 71.1% ($P = 0.015$; AUC, 0.762; 95% CI, 0.644–0.879) (Fig. 2). The SUV_{max} and GTV cutoff values, respectively, were 4.7 ($P = 0.667$; AUC, 0.541; 95% CI, 0.368–0.713) and 22.7 mL ($P = 0.182$; AUC, 0.612; 95% CI, 0.433–0.791) and were shown to be insignificant. In addition, dichotomization analyses of patient survival validated the cutoff points defined from the receiver-operating-characteristic curve analyses.

Univariate and Multivariate Analyses for Identifying Significant Prognostic Variables

Univariate analyses for PFS showed that pT classification, pN classification, overall pTNM stage, lymphovascular invasion, perineural invasion, MTV, and TLG were significantly associated with decreased PFS ($P < 0.05$ each). Univariate analyses for OS revealed that pT classification, pN classification, GTV, MTV, and TLG were significantly associated with decreased OS ($P < 0.05$ each) (Table 2). The patients with an MTV greater than 17.7 mL had significantly lower PFS rates (50.7% vs. 90.9%, $P = 0.002$) and OS rates (66.0% vs. 100%, $P = 0.002$) than those with an MTV of 17.7 mL or less (Figs. 3A and 3B). The patients with a TLG greater than 56.3 g also had significantly lower PFS rates (55.6% vs. 76.9%, $P = 0.008$) and OS rates (67.9% vs. 90.3%, $P = 0.020$) than those with a TLG of 56.3 g or less (Figs. 3C and 3D). However, SUV_{max} was not a significant variable for either PFS ($P = 0.111$) or OS ($P = 0.316$).

As expected, there was a significant correlation between MTV and TLG (calculated by multiplying MTV by SUV_{mean}) ($r = 0.902$, $P < 0.001$). Therefore, 2 different models including MTV or TLG separately were used for multivariate analyses. Multivariate analyses for PFS showed that MTV ($P = 0.011$; hazard ratio, 11.50; 95% CI, 1.45–91.01) and TLG ($P = 0.038$; hazard ratio, 3.55; 95% CI, 1.07–11.76) were the only independent prognostic factors for PFS (Table 3). Because the overall OS rate of patients with an MTV of 17.7 mL or less reached 100%, the Cox proportional hazard model could not be used for multivariate analysis for OS.

DISCUSSION

Because of the histologic and prognostic variability of salivary gland carcinomas, it is still unclear whether the results of studies on the prognostic significance of ^{18}F-FDG PET or PET/CT in patients with head and neck squamous cell carcinomas can be applied directly to patients with salivary gland carcinomas (*23–25*). Recent studies have shown that ^{18}F-FDG PET and PET/CT are clinically useful imaging methods for distinguishing between

benign and malignant tumors, for initial staging, and for follow-up of patients with salivary malignancies (*13,26–28*).

In the present study, we examined the utility of the ^{18}F-FDG metabolic parameters for predicting clinical outcomes in patients with salivary gland carcinomas. We found a significant association between metabolic tumor burden defined by ^{18}F-FDG PET/CT and PFS: to our knowledge, ours is the first study to suggest that the pretreatment values of MTV and TLG can serve as prognostic imaging biomarkers in patients with salivary gland carcinomas. This capability may provide more advanced, clinically useful information comparable to that in a recent report that showed that MTV and TLG were able to differentiate between benign and malignant tumors in 49 patients with increased ^{18}F-FDG uptake in the parotid gland (*29*).

Various ^{18}F-FDG PET parameters have been explored by researchers in a variety of solid tumors (*15–18*). MTV, the volume of the tumor displaying ^{18}F-FDG uptake and indicating the distribution of metabolic activity, has proved to be a better prognostic guide than SUV_{max} (*30*). TLG represents metabolic activity throughout the entire tumor above a minimum threshold designed to exclude background activity (*20*). Hence, a large TLG may reflect a small volume with high metabolic activity or a large volume with lower metabolic activity. Therefore, volume-based parameters such as MTV and TLG may reflect the metabolic burden of the active tumor more accurately and provide a potentially more sensitive method than SUV_{max} or tumor diameter. In the current study, multivariate analysis showed that MTV and TLG were independent prognostic factors for PFS. The risk of disease progression was more than 11 times higher for patients with an MTV greater than 17.7 mL than for those with an MTV of 17.7 mL or less, and the risk of disease progression was more than 3.5 times higher for patients with a TLG greater than 56.3 g than for those with a TLG of 56.3 g or less. High MTV or TLG were also significantly associated with reduced OS.

Histologic grades and TNM stage are known to be important prognostic factors for clinical outcome. Nevertheless, they were not prognostic factors of disease progression in the current study, perhaps because of the small number of patients. The lack of prognostic power for these factors in our study emphasizes the importance of preoperative MTV and TLG as strong predictive parameters. Interestingly, regression analysis revealed a significant association between TNM stage and increased MTV ($P < 0.001$) and TLG ($P = 0.001$) and between histologic grades and increased MTV ($P = 0.038$) and TLG ($P = 0.045$) (data not shown). This finding underlines the association between the metabolic parameters, TNM stage, and histologic grades.

Pretreatment SUV_{max} as a classic parameter for prognosis of head and neck cancer has been investigated in previous studies, many of which found a worse clinical course in patients with elevated SUV_{max} (*25,31,32*). However, both previous work and the present study have shown that high SUV_{max} is not a prognostic factor for survival of patients with salivary gland carcinomas (*27*). The present study also showed that SUV_{max} was not significantly correlated with either PFS or OS, possibly because salivary gland carcinomas are relatively rare and the various histologic subtypes differ in their ^{18}F-FDG avidities (*26,28*). MTV or TLG may be more reliable prognostic predictors than SUV_{max} in these patients.

Although volume-based parameters have advantages in measuring metabolic tumor burden, there is still debate about the most appropriate segmentation method for estimating MTV and TLG. Previous studies have generally used a fixed SUV of 2.5 for head and neck squamous carcinomas (*17,30*). However, salivary gland tumors differ in their metabolic activity depending on their histologic subtype, and they have lower ^{18}F-FDG avidities than squamous carcinomas (*26,28*). Therefore, we examined various fixed percentages of SUV_{max} thresholds. Although all the MTVs measured at the various fixed percentages correlated with both PFS and OS, we selected 30% of SUV_{max}—which was associated with the lowest *P* value and the highest AUC—as the optimal fixed threshold for MTV. There needs to be further discussion of the most appropriate segmentation method for validation.

Our study had several limitations, including its retrospective design, the small number of patients, the diverse pathologies of their tumors, and the inherent selection biases. Moreover, ^{18}F-FDG PET/CT was not performed on every patient before treatment, and the follow-up period was too short to determine long-term patient outcomes. Nevertheless, our findings are valuable and showed the prognostic value of pretreatment MTV and TLG in patients with salivary gland carcinomas.

TABLE 3
Multivariate Analyses of Clinicopathologic and Imaging Variables on PFS

Variable	Model A*		Model B*	
	Hazard ratio	*P*†	Hazard ratio	*P*†
Lymphovascular invasion, no vs. yes	2.87 (0.49–16.69)	0.239	2.23 (0.38–12.92)	0.372
Perineural invasion, no vs. yes	1.01 (0.171–5.50)	0.970	1.20 (0.21–6.97)	0.839
pT1–2 vs. pT3–4	1.10 (0.24–2.55)	0.551	1.69 (0.36–4.60)	0.872
pN0 vs. pN1–2	1.27 (0.38–4.46)	0.876	1.10 (0.25–4.61)	0.922
Overall pTNM stage I–II vs. III–IV	1.91 (0.38–9.51)	0.431	1.87 (0.67–10.10)	0.186
MTV ≤ 17.7 vs. > 17.7 mL	11.50 (1.45–91.01)	0.011	—	
TLG ≤ 56.3 vs. > 56.3 g	—		3.55 (1.07–11.76)	0.038

*Because of multicolinearity ($r = 0.902$) between MTV and TGA, TLG and MTV were not included in models A and B, respectively.

†Multivariate analysis using Cox-proportional hazards model. Variables with $P < 0.05$ in univariate analyses were selected for multivariate analysis.

Data in parentheses are 95% CIs.

CONCLUSION

Pretreatment MTV and TLG are independent prognostic factors for disease progression in patients with intermediate- or high-grade salivary gland carcinomas. Patients with high MTV or TLG have poor survival outcomes. Pretreatment MTV and TLG may be helpful in planning treatment and follow-up of these patients, but the present study needs to be validated by large-scale prospective trials with longer follow-up.

DISCLOSURE

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