

Quantitative analysis of metabolic parameters at ^{18}F -fluorodeoxyglucose positron emission tomography in predicting malignant potential of anterior mediastinal tumors

TOSHIKI YAJIMA¹, AKIRA MOGI¹, KIMIHIRO SHIMIZU¹, TAKAYUKI KOSAKA¹, YOICHI OHTAKI¹, KAI OBAYASHI¹, SESHIRU NAKAZAWA¹, TAKAHITO NAKAJIMA², YOSHITO TSUSHIMA² and KEN SHIRABE¹

Departments of ¹General Surgical Science, and ²Diagnostic Radiology and Nuclear Medicine, Gunma University Graduate School of Medicine, Maebashi, Gunma 371-8511, Japan

Received March 30, 2019; Accepted October 7, 2019

DOI: 10.3892/ol.2020.11276

Abstract. To evaluate the utility of ^{18}F -fluorodeoxyglucose (FDG)-positron emission tomography (PET) for predicting the malignancy of anterior mediastinal tumors, the present study retrospectively examined a total of 105 consecutive patients who underwent surgical resection of anterior mediastinal tumors at Gunma University Hospital after undergoing a preoperative FDG-PET scan. Patients were divided into benign and malignant groups in accordance with the following three classification systems: i) Clinical classification, benign or malignant (thymoma and carcinoma); ii) recurrence-based classification, low-risk recurrence (benign and low-risk thymoma) or high-risk recurrence (high-risk thymoma and carcinoma); and iii) pathological classification, benign (benign and thymoma) or malignant (carcinoma). The present study analyzed the differences between the benign and malignant groups in terms of FDG-PET parameters, including maximum standardized uptake value (SUVmax), metabolic tumor volume (MTV) and total lesion glycolysis (TLG). The malignant group exhibited a significantly greater SUVmax than the benign group according to all classification systems. By contrast, there was only a slight difference between groups in volume-based metabolic parameters (MTV and TLG) using the clinical classification, and no intergroup differences using the recurrence-based and pathological classifications. The area under the curve in receiver-operating characteristic curve analysis for predicting malignancy was significantly greater for SUVmax than for volume-based metabolic parameters using all classification methods. The respective optimal cut-off

value, sensitivity and specificity of SUVmax to predict malignancy were 1.77, 92.0 and 87.0% for the clinical classification, 2.54, 93.6 and 60.3% for the recurrence-based classification, and 5.15, 78.9 and 90.7% for the pathological classification. SUVmax was the most useful parameter for predicting the malignancy of anterior mediastinal tumors.

Introduction

The preoperative diagnosis of anterior mediastinal tumors is comprehensively determined by their clinical presentation and several imaging modalities, as the anatomical location usually makes it difficult to perform needle biopsy for pathologic diagnosis. Although computed tomography (CT) is essential for detecting anterior mediastinal tumors, it can be difficult to differentiate between benign and malignant tumors using CT (1,2). To improve the accuracy of preoperative diagnosis, magnetic resonance imaging (MRI) and/or positron emission tomography (PET) are additionally performed at the attending surgeon's discretion. Besides tumor detection, MRI can also be useful for qualitative assessment of the tumor in some conditions, such as hemorrhagic or inflammatory thymic cysts that mimic a solid tumor, despite low enhancement (3,4). Accurate evaluation of malignant potential may aid in the decision-making process regarding the management of anterior mediastinal tumors, i.e., either monitoring or surgical resection.

Many small sample-sized studies have reported that ^{18}F -fluorodeoxyglucose (FDG)-PET was useful for definitively diagnosing anterior mediastinal tumors. The differentiation of benign vs. malignant tumors in the anterior mediastinum is reportedly aided by analysis of the maximum standardized uptake value (SUVmax) of FDG-PET (5-7). Studies on thymic epithelial tumors have shown that SUVmax is greater in high-risk thymoma, particularly in thymic cancer, than in low-risk thymoma (8-15); however, other studies report that SUVmax is similar in low-risk thymoma and high-risk thymoma (16-20). In addition, the tumor to mediastinal (T/M) ratio, which is a semiquantitative parameter defined as the ratio of the SUVmax of the tumor to the aorta, has been proposed for differentiating high-risk thymoma from low-risk thymoma in thymic epithelial tumors (21-23). Recently, several studies

Correspondence to: Dr Toshiki Yajima, Department of General Surgical Science, Gunma University Graduate School of Medicine, 3-39-22 Showa, Maebashi, Gunma 371-8511, Japan
E-mail: yajimato@gunma-u.ac.jp

Key words: anterior mediastinal tumor, positron emission tomography, maximum standardized uptake value, metabolic tumor volume, total lesion glycolysis

have reported that volume-based metabolic parameters, including metabolic tumor volume (MTV) and total lesion glycolysis (TLG), are useful in predicting malignant potential of anterior mediastinal tumors (7,24,25). However, it is still unclear which PET parameters (including SUVmax, T/M ratio, and volume-based metabolic parameters) are most useful for screening the malignant potential of anterior mediastinal tumors, as all of these studies were small-scale studies that investigated patients with thymic epithelial tumors, and there have been no reported comparisons of the predictive value of these parameters.

In general, tumors are categorized pathologically as either benign or malignant in accordance with their histological features. Although thymoma was classically classified as a pathological benign tumor based on its histological features, it is classified clinically as a malignant tumor when there is invasion into a neighboring organ, dissemination, or metastasis. Furthermore, the WHO classifies thymomas into five types (A, AB, B1, B2, and B3), and further divides these types into two groups: Low-risk thymoma (A, AB, and B1) and high-risk thymoma (B2 and B3) (15,26), as patients with low-risk thymoma rarely experience recurrence after complete resection. Therefore, in the clinical situation, we considered that anterior mediastinal tumors should be classified into four groups in accordance with their malignant potential: Benign, low-risk thymoma, high-risk thymoma, and malignant.

In the present study, we aimed to elucidate the utility of several metabolic parameters, including SUVmax and volume-based metabolic parameters (MTV and TLG), in predicting the malignant potential of anterior mediastinal tumors.

Patients and methods

Population. The present study included 132 consecutive patients with an anterior mediastinal tumor who had undergone surgery at Gunma University between January 2007 and December 2017 after preoperative FDG-PET examination. Preoperative PET examination was conducted at one of three institutions: 105 were performed in our institution, and 27 were performed in the other institutions. To reduce interinstitutional variability, the main analyses were conducted only for the 105 patients (55 males and 50 females; mean age 58.1 years, range 15-90 years) who underwent preoperative PET at our institution. The present study was approved by the ethics committee of Gunma University Hospital (approval no. 1575). Anterior mediastinal tumors were independently divided into two groups in accordance with three different classification systems: Clinical (c) classification [c-benign (benign) or c-malignant (thymoma and carcinoma)]; recurrence-based classification [low-risk recurrence (LRR) (benign and low-risk thymoma) or high-risk recurrence (HRR) (high-risk thymoma and carcinoma)]; pathological (p) classification [p-benign (benign and thymoma) or p-malignant (carcinoma)].

¹⁸F-fluorodeoxyglucose-PET imaging. Patients fasted for at least 6 h before FDG-PET examination. Intravenous ¹⁸F-FDG was administered at a dose of 5 MBq/kg. Sixty minutes after the injection, data was acquired using a Discovery STE PET/CT scanner (GE Healthcare) or a Biograph 16 PET/CT

scanner (Siemens). Three-dimensional emission scanning was performed from the groin area to the top of the skull. The FDG uptake in the anterior mediastinal tumor was recorded.

¹⁸F-fluorodeoxyglucose-PET analysis. The FDG-PET images were reviewed independently by two experienced physicians. The data obtained were reconstructed by iterative ordered subset expectation maximization. To evaluate the metabolic parameters in each anterior mediastinal tumor, SUVmax, MTV, and TLG were obtained for the primary tumor using a previously described method (7,24,25). In brief, SUVmax represented the greatest activity of a single pixel within the tumor, while MTV was calculated as the volume of the FDG-avid area with a threshold of more than 40% of the SUVmax. TLG was defined as the multiplication of the MTV and the mean SUV within the area of the MTV, which signified the overall tumor burden. The T/M ratio for each patient was calculated as the ratio of the tumor SUVmax to the background mediastinum SUVmax. The region of interest was placed in the aortic arch as the reference area for mediastinal activity (21-23). The metabolic parameters were compared with the clinical features based on each classification system.

Statistical analysis. Mean SUVmax, T/M ratio, MTV, and TLG were compared between the benign and the malignant groups using the Students' t-test. In addition, receiver-operating characteristic (ROC) analysis was used to identify the cut-off values for the PET parameters that accurately differentiated the malignant group from the benign group. Sensitivity, specificity, accuracy, positive predictive values (PPV), and negative predictive values (NPV) were calculated for each threshold value. Differences in the area under the ROC curve (AUC) for SUVmax, T/M ratio, MTV, and TLG were assessed using comparison models created the logistic regression models. All P values were two-sided, and P<0.05 was considered to indicate a statistically significant difference. JMP 12 (SAS Institute) was used for the statistical analyses.

Results

Pathological diagnoses of anterior mediastinal tumors. Among the 105 included patients, 30 (28.6%) had benign lesions, including thymic cyst (n=18), mature teratoma (n=6), pericardial cyst (n=1), bronchogenic cyst (n=1), and others (n=4, i.e., schwannoma, lymphangioma, cavernous hemangioma, and parathyroid cyst; Table I). Fifty-six patients (53.3%) had thymoma, including 28 patients with low-risk thymoma (A: n=7, AB: n=10, B1: n=9, micronodular thymoma with lymphoid stroma: n=2), and 28 patients with high risk-thymoma (B2: n=13, B3: n=15). The remaining 19 (18.1%) patients had malignant tumors, including thymic cancer (n=7), germinoma (n=3), metastatic lymph node from other carcinoma (n=3), mucosa associated lymphoid tissue lymphoma (n=2), thymic carcinoid (n=1), and others (n=3, i.e., malignant meningioma, rhabdomyosarcoma, and solitary fibrous tumor). The three metastatic lymph nodes originated from the stomach in one case, and the thyroid in two cases.

Comparison of the FDG-PET parameters in the benign and malignant groups. The characteristics of these 105 patients in accordance with the three classification systems are shown

Table I. Pathological diagnoses of anterior mediastinal tumors, and division into benign vs. malignant lesions in accordance with three classification systems.

Type (n=105)	Pathological diagnosis	Patients, n (%)	Clinical classification	Recurrence-based classification	Pathological classification
Benign (n=30)	Thymic cyst	18 (17.1)	c-benign (n=30)	LRR (n=58)	p-benign (n=86)
	Mature teratoma	6 (5.7)			
	Pericardial cyst	1 (1.0)			
	Bronchogenic cyst	1 (1.0)			
	Lymphangioma	1 (1.0)			
	Schwannoma	1 (1.0)			
	Cavernous hemangioma	1 (1.0)			
	Parathyroid cyst	1 (1.0)			
Thymoma (n=56)	Low-risk thymoma		c-malignant (n=75)	HRR (n=47)	
	A	7 (6.7)			
	AB	10 (9.5)			
	B1	9 (8.6)			
	MNT	2 (1.9)			
	High-risk thymoma				
Malignant (n=19)	B2	13 (12.4)			
	B3	15 (14.3)			
	Thymic cancer	7 (6.7)			p-malignant (n=19)
	Germinoma	3 (2.9)			
	Metastatic tumor	3 (2.9)			
	MALT lymphoma	2 (1.9)			
	Carcinoid	1 (1.0)			
	Meningioma	1 (1.0)			
Rabdomiosarcoma	1 (1.0)				
Solitary fibrous tumor	1 (1.0)				

c-, clinical; LRR, low-risk recurrence; HRR, high-risk recurrence; p-, pathological; MNT, micronodular thymoma with lymphoid stroma; MALT lymphoma, mucosa associated lymphoid tissue lymphoma.

in Table I. Mean age, sex, and mean tumor diameter were comparable between the c-benign and c-malignant groups, LRR and HRR groups, and p-benign and p-malignant groups (Table SI). Mean SUVmax was significantly greater in the malignant group than the benign group for all classifications: c-benign and c-malignant (1.52 vs. 4.51, P<0.0001), LRR and HRR (2.60 vs. 4.96, P<0.0001), p-benign and p-malignant (3.06 vs. 6.35, P<0.0001; Fig. 1 and Table II). Mean T/M ratios were also significantly greater in the malignant group than the benign group using all three classification systems (Table SII). Although the volume-based metabolic parameters (TLG and MTV) were both slightly but significantly greater in the c-malignant group than the c-benign group, there were no significant differences between the benign and malignant groups in accordance with the recurrence-based and pathological classification systems (Table II).

ROC analysis for FDG-PET parameters in predicting the malignant groups. The AUC of SUVmax was significantly greater than that of MTV or TLG for predicting c-malignant (0.9347, 0.8342 and 0.7080, respectively, SUVmax vs. TLG P=0.0009. SUVmax vs. MTV P<0.0001) or p-malignant

lesions (0.8562, 0.6616, and 0.4691, respectively, SUVmax vs. TLG P=0.0002. SUVmax vs. MTV P<0.0001; Fig. 2). For predicting HRR lesions, the AUC of SUVmax was also significantly greater than MTG or TLG (0.8140, 0.7190, and 0.6315, respectively, SUVmax vs. TLG P=0.0145. SUVmax vs. MTV P=0.0006). Similar trends to the ROC analysis of SUVmax were found for the ROC analysis of T/M ratio. The AUC of the T/M ratio was comparable to the AUC of SUVmax for predicting c-malignant, HRR, and p-malignant lesions (0.9300, 0.8424 and 0.8693, respectively; Fig. S1).

Optimal cut-off value of FDG-PET parameters in predicting the malignant groups. The optimal cut-off values of SUVmax for predicting c-malignant, HRR, and p-malignant lesions were 1.77, 2.54 and 5.15, respectively (Table III and Fig. 1). The optimal cut-off value of 1.77 for SUVmax in predicting c-malignant lesions had a specificity, sensitivity, and accuracy of 92.0, 87.0 and 93.3%, respectively. The PPV for predicting c-malignant lesions was very high (94.7%), indicating that almost all clinically malignant mediastinal tumors had a SUVmax greater than 1.77. In contrast, a cut-off value of 5.15 for SUVmax in predicting p-malignant lesions had a

Table II. Comparison of the SUVmax, TLG and MTV of anterior mediastinal tumors in the benign and malignant groups created in accordance with three classification systems.

Variable	c-benign (n=30)	c-malignant (n=75)	LRR (n=58)	HRR (n=47)	p-benign (n=86)	p-malignant (n=19)	P-value
SUVmax, mean ± SD (range)	1.52±0.81 (0.75-4.18)	4.51±2.41 (1.09-12.88)	2.60±1.99 (0.75-12.88)	4.96±2.42 (1.81-11.51)	3.06±2.01 (0.75-12.88)	6.35±2.64 (2.19-11.51)	<0.0001
TLG (g), mean ± SD (range)	27.0±46.1 (0.9-214.7)	164.7±244.2 (3.0-1396.6)	89.9±201.7 (0.9-1396.6)	169.2±228.3 (3.0-861.6)	112.6±210.3 (0.9-1396.6)	183.3±240.8 (3.0-823.3)	0.0028
MTV (ml), mean ± SD (range)	22.4±25.6 (1.7-99.0)	57.4±84.4 (2.2-526.9)	41.8±75.9 (1.7-526.9)	54.3±72.1 (2.2-418.6)	47.6±77.7 (1.7-526.9)	46.3±57.1 (2.2-236.7)	0.0283

c-, clinical; LRR, low-risk recurrence; HRR, high-risk recurrence; p, pathological; SUVmax, maximum standardized uptake value; TLG, total lesion glycolysis; MTV, metabolic tumor volume.

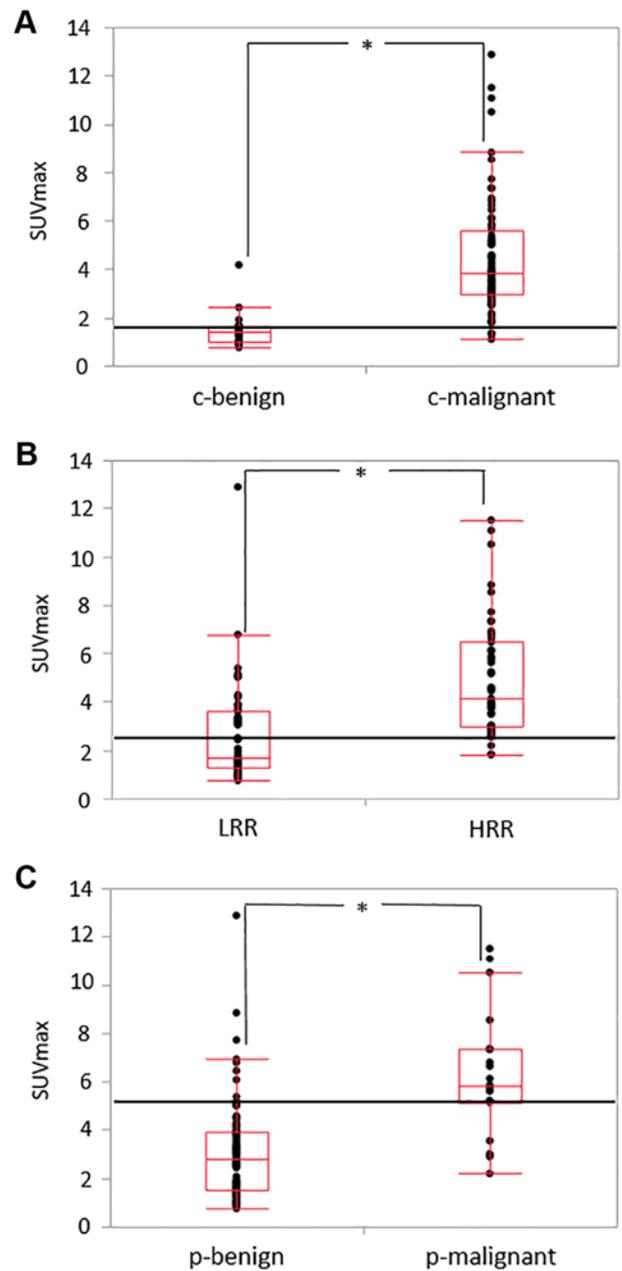


Figure 1. Box and whisker plots comparing the mean SUVmax values of two groups. (A) c-classification: c-benign (benign) or c-malignant (thymoma and carcinoma). (B) Recurrence-based classification: LRR (benign and low-risk thymoma) or HRR (high-risk thymoma and carcinoma). (C) p-classification: p-benign (benign and thymoma) or p-malignant (carcinoma). The horizontal line in the middle of each box indicates the median, the top and bottom borders of the box mark the 75 and 25th percentiles, respectively, and the whiskers mark the 90th and 10th percentiles. The horizontal lines indicate the optimal cut-off values of SUVmax for predicting c-malignant, HRR and p-malignant lesions, which were (A) 1.77, (B) 2.54 and (C) 5.15, respectively. *P<0.05. SUVmax, maximum standardized uptake value; p-, pathological; c-, clinical; LRR, low-risk recurrence; HRR, high-risk recurrence.

specificity, sensitivity, and accuracy of 78.9, 90.7 and 88.6%, respectively. The NPV for detecting p-malignant lesions was also very high (95.1%), indicating that almost all pathologically benign mediastinal tumors had a SUVmax of less than 5.15. In predicting HRR lesions, the cut-off value of 2.54 for SUVmax had a specificity, sensitivity, and accuracy of 93.6, 60.3 and 75.2%, respectively. SUVmax was less accurate in

Table III. Optimal cut-off value of SUVmax for predicting c-malignant, HRR and p-malignant anterior mediastinal tumors.

SUVmax	AUC	Optimal cut-off	Sensitivity	Specificity	PPV	NPV	Accuracy
c-malignant	0.9347	1.77	92.0	87.0	94.7	89.7	93.3
HRR	0.8140	2.54	93.6	60.3	65.7	92.1	75.2
p-malignant	0.8562	5.15	78.9	90.7	65.2	95.1	88.6

c-, clinical; HRR, high-risk recurrence; p-, pathological; AUC, area under the curve; PPV, positive predictive value; NPV, negative predictive value; SUVmax, maximum standardized uptake value.

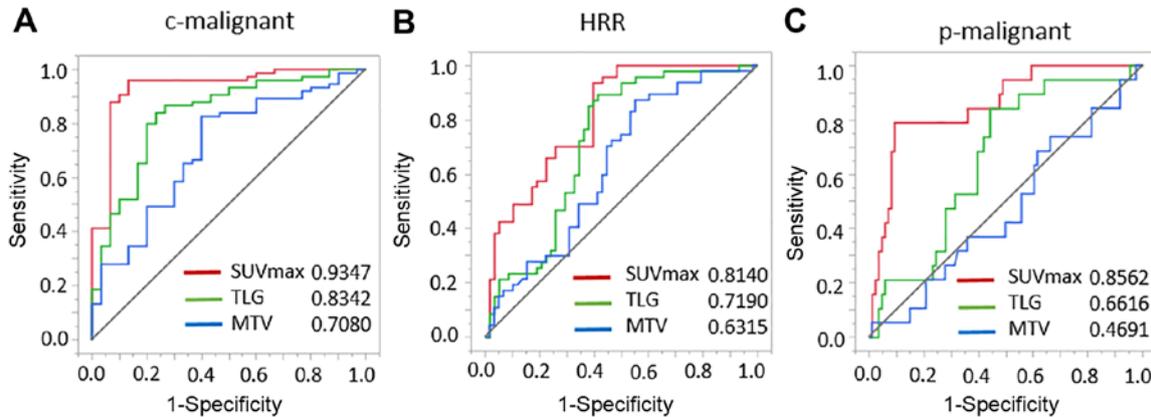


Figure 2. Receiver-operating characteristic curve analysis for SUVmax, TLG and MTV in predicting (A) c-malignant, (B) HRR or (C) p-malignant anterior mediastinal tumors. Area under the curve of each PET parameter was indicated in three classification, respectively. (A) c-malignant: = SUVmax vs. TLG (P=0.0009); SUVmax vs. MTV (P<0.0001). (B) HRR: SUVmax vs. TLG (P=0.0146); SUVmax vs. MTV (P=0.0006). (C) p-malignant: SUVmax vs. TLG (P=0.0002); SUVmax vs. MTV (P<0.0001). SUVmax, maximum standardized uptake value; TLG, total lesion glycolysis; MTV, metabolic tumor volume; c-, clinical; HRR, high-risk recurrence; PET, positron emission tomography; p-, pathological.

predicting HRR lesions than in predicting c- and p-malignant lesions. The optimal cut-off values of the T/M ratio for predicting c-malignant, HRR, and p-malignant lesions were 1.14, 1.46 and 2.18, respectively (Table SIII).

Discussion

The present study revealed that the SUVmax in PET was useful for predicting the malignant potential of anterior mediastinal tumors, especially in accordance with the clinical and pathological malignant classifications. In contrast, although the volume-based metabolic parameters of PET were slightly greater in c-malignant than in c-benign anterior mediastinal tumors, these parameters were not very useful for predicting malignant potential. Therefore, SUVmax may be a critical parameter for screening the malignant potential of anterior mediastinal tumors.

No previous study has evaluated more than 100 cases to verify the utility of PET parameters including SUVmax, T/M ratio, MTV, and TLG to diagnose anterior mediastinal tumors in a single institution. Several studies have reported that the SUVmax of FDG-PET is useful for predicting malignant and high-risk thymoma in selected thymic epithelial tumors, but the sample sizes of these previous studies were limited to only a few dozen cases (8-20). As anterior mediastinal tumors are relatively rare, it is difficult to collect data from sufficient numbers of patients with these tumors during

short periods. Moreover, although CT was always performed during preoperative examination of patients with an anterior mediastinal tumor, PET examination was not performed in all patients with an anterior mediastinal tumor. In our institution, FDG-PET was performed during preoperative examination as often as possible, and we retrospectively examined the data from a long-term period of more than 10 years. Therefore, we were able to collect sufficient data to verify the utility of PET parameters for predicting malignant potential in all anterior mediastinal tumors, not just in thymic epithelial tumors.

In general, most tumors are categorized as either benign or malignant in accordance with their histological features. Although thymomas have been classically classified as pathologically benign tumors in accordance with their histological features, they can be clinically classified as malignant tumors because of invasion into a neighboring organ, dissemination, or metastasis. In addition, although the WHO classified thymomas into five types (A, AB, B1, B2 and B3), they were further divided into two groups in accordance with the risk of recurrence: Low-risk thymoma (A, AB and B1) and high-risk thymoma (B2 and B3) (26). Therefore, we considered that the cut-off points of several PET parameters were necessary to screen the malignant potential of anterior mediastinal tumors in various clinical situations. We thus divided patients into two groups in accordance with three classification systems: c-benign and c-malignant, LRR and HRR, and p-benign and p-malignant.

In comparison with c-benign lesions, we found that an optimal cut-off value of 1.77 for SUVmax in predicting c-malignant lesions had a specificity, sensitivity, and accuracy of 92.0, 87.0 and 93.3% respectively. There were only four false positive results: Infectious thymic cyst (n=1), schwannoma (n=1), and mature teratoma (n=2). The patients with a mature teratoma obtained an adequate diagnosis via CT alone. The case of schwannoma in the anterior mediastinum was quite rare, and this lesion usually mimics a malignant tumor because of the large amount of FDG accumulation. Therefore, we believe that almost all clinically malignant tumors (including thymomas) could be detected by performing PET in addition to CT. Although we usually perform surgical resection for growing cystic lesions because of the possibility of cystic thymoma and risk of rupture, all thymic cysts except the infectious lesion showed no FDG accumulation, regardless of tumor growth. Therefore, we may recommend monitoring of anterior mediastinal tumors with no accumulation of FDG, and thus avoid unnecessary open thoracotomy.

Several studies have reported that SUVmax may be useful for differentiating high-risk thymoma from low-risk thymoma in those with thymic epithelial tumors, but these results were controversial (8-20). We found that the SUVmax and T/M ratio were significantly greater in high-risk thymomas than in low-risk thymomas. However, an optimal AUC value for predicting a HRR lesion was not obtained using ROC analysis of SUVmax in anterior mediastinal tumors. The SUVmax of FDG-PET is reportedly useful for predicting the recurrence potential of thymic epithelial tumors (15). Therefore, SUVmax may be important for screening the recurrence potential of thymic epithelial tumors, rather than high-risk thymomas. Further data collections are necessary to clarify these possibilities.

Almost all previous studies showed that SUVmax was significantly greater in pathologically malignant tumors of the anterior mediastinum, including thymic cancer, than in benign tumors (8-20). We found that the optimal cut-off value of SUVmax was 5.15 for detecting p-malignant lesions, with a specificity, sensitivity, and accuracy of 78.9, 90.7 and 88.6%, respectively. The NPV of p-malignant lesions was very high (95.1%), indicating that the SUVmax of almost all benign lesion was less than 5.15. Similarly to our findings, Toba *et al* (14) reported an optimal cut-off value of 5.6 for SUVmax in predicting pathologically malignant lesions. A SUVmax value of more than 5.15 may indicate a need for a surgical approach for anterior mediastinal tumors, including open thoracotomy or video-assisted surgery.

Previous studies have reported that the T/M ratio of FDG-PET is useful in predicting the malignant potential of anterior mediastinal tumors (21-23). We found that the utility of the T/M ratio was comparable to that of the SUVmax for predicting c-malignant, HRR, and p-malignant lesions. This suggests that both the SUVmax and T/M ratio of PET were useful in predicting the malignant potential of anterior mediastinal tumors. The T/M ratio may be a useful parameter in cases where the preoperative PET examination is performed in a different institution using a different PET scanner. In fact, we obtained almost the same data concerning the usefulness of the T/M ratio when we extended the analysis to include 132 patients by adding the 27 patients for whom the PET

examination was conducted in another institution, but who underwent surgical resection in our institution (Fig. S2). Our data suggest that the T/M ratio may be used to screen the malignant potential of anterior mediastinal tumors in a general situation.

Volume-based metabolic parameters of PET, including TLG and MTV, are reportedly useful in differentiating benign and malignant lesions in the anterior mediastinum (7,24,25). In contrast, we found that the volume-based metabolic parameters of PET were not useful in predicting the malignant potential of anterior mediastinal tumors. Volume-based metabolic parameters were similar for LRR and HRR, or p-benign and p-malignant anterior mediastinal tumors. When comparing c-benign and c-malignant lesions, although the volume-based metabolic PET parameters were slightly but significantly greater in c-malignant than in c-benign lesions, these differences may result from the difference in tumor volume, as the c-malignant lesions had larger tumor diameters than the c-benign lesions. To define the contouring margins around the tumor, the defined threshold was considered to be 2.5, according to previous studies (24,25). Similar results were obtained using an SUV cut-off of 2.5 in both TLG and MTV in all classification systems. Therefore, the volume-based metabolic PET parameters may not be useful in predicting the malignant potential of anterior mediastinal tumors. It is difficult to use tumor size alone to screen for malignant potential, and it is important to detect the part with the highest metabolic activity, which probably correlates with the malignant part of tumor, but not the whole metabolic volume.

Our study had several limitations. First, it was a retrospective study with an insufficient-sized study population; although we included more than 100 patients, we plan to extend the study to a larger patient population. As anterior mediastinal tumors are relatively rare, a larger scale, prospective, multicenter study is needed to obtain a larger study population. It may be possible to conduct the validation study by this multicenter study to evaluate the diagnostic performance using the same cut-off values which were calculated at this study. Second, selection bias was inevitable, as we included only the patients who underwent surgical resection. Third, no validation studies were included in this report to strength our conclusion.

In conclusion, the SUVmax and T/M ratio of PET are useful for screening the malignant potential of anterior mediastinal tumors. Performing preoperative PET-CT may aid in the selection of either surgical resection or observation for anterior mediastinal tumors.

Acknowledgements

The authors would like to thank Dr Kelly Zammit for editing a draft of this manuscript.

Funding

No funding was received.

Availability of data and materials

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

Authors' contributions

TY, AM and KiS were involved in the study design. TY contributed to the preparation of the manuscript and data analysis. TK, YO, TN, YT and KeS contributed to data collection and data analysis. KO and SN contributed to the data analysis and prepared the figures and tables. All authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of Gunma University Hospital (approval no. 1575). All patients agreed to participate in the present study and provided written informed consent.

Patient consent for publication

Informed consent for publication was obtained from all participants.

Competing interests

The authors declare that they have no competing interests.

References

1. Tomiyama N, Honda O, Tsubamoto M, Inoue A, Sumikawa H, Kuriyama K, Kusumoto M, Johkoh T and Nakamura H: Anterior mediastinal tumors: Diagnostic accuracy of CT and MRI. *Eur J Radiol* 69: 280-288, 2009.
2. Sakai S, Murayama S, Soeda H, Matsuo Y, Ono M and Masuda K: Differential diagnosis between thymoma and non-thymoma by dynamic MR imaging. *Acta Radiol* 43: 262-268, 2002.
3. Usuda K, Maeda S, Motono N, Ueno M, Tanaka M, Machida Y, Matoba M, Watanabe N, Tonami H, Ueda Y and Sagawa M: Diffusion weighted imaging can distinguish benign from malignant mediastinal tumors and mass lesions: Comparison with positron emission tomography. *Asian Pac J Cancer Prev* 16: 6469-6475, 2015.
4. Yabuuchi H, Matsuo Y, Abe K, Baba S, Sunami S, Kamitani T, Yonezawa M, Yamasaki Y, Kawanami S, Nagao M, *et al*: Anterior mediastinal solid tumours in adults: Characterisation using dynamic contrast-enhanced MRI, diffusion-weighted MRI, and FDG-PET/CT. *Clin Radiol* 70: 1289-1298, 2015.
5. Kubota K, Yamada S, Kondo T, Yamada K, Fukuda H, Fujiwara T, Ito M and Ido T: PET imaging of primary mediastinal tumours. *Br J Cancer* 73: 882-886, 1996.
6. Kitami A, Sano F, Ohashi S, Suzuki K, Uematsu S, Suzuki T and Kadokura M: The usefulness of positron-emission tomography findings in the management of anterior mediastinal tumors. *Ann Thorac Cardiovasc Surg* 23: 26-30, 2017.
7. Morita T, Tatsumi M, Ishibashi M, Isohashi K, Kato H, Honda O, Shimosegawa E, Tomiyama N and Hatazawa J: Assessment of mediastinal tumors using SUV_{max} and volumetric parameters on FDG-PET/CT. *Asia Ocean J Nucl Med Biol* 5: 22-29, 2017.
8. Sung YM, Lee KS, Kim BT, Choi JY, Shim YM and Yi CA: 18F-FDG PET/CT of thymic epithelial tumors: Usefulness for distinguishing and staging tumor subgroups. *J Nucl Med* 47: 1628-1634, 2006.
9. Luzzi L, Campione A, Gorla A, Vassallo G, Bianchi A, Biggi A and Terzi A: Role of fluorine-fluorodeoxyglucose positron emission tomography/computed tomography in preoperative assessment of anterior mediastinal masses. *Eur J Cardiothorac Surg* 36: 475-479, 2009.
10. Igai H, Matsuura N, Tarumi S, Chang SS, Misaki N, Go T, Ishikawa S and Yokomise H: Usefulness of [18F]fluoro-2-deoxy-D-glucose positron emission tomography for predicting the world health organization malignancy grade of thymic epithelial tumors. *Eur J Cardiothorac Surg* 40: 143-145, 2011.
11. Lococo F, Cesario A, Okami J, Cardillo G, Cavuto S, Tokunaga T, Apolone G, Margaritora S and Granone P: Role of combined 18F-FDG-PET/CT for predicting the WHO malignancy grade of thymic epithelial tumors: A multicenter analysis. *Lung Cancer* 82: 245-251, 2013.
12. Purandare NC, Pramesh CS, Karimundackal G, Jiwnani S, Agrawal A, Shah S, Agarwal JP, Prabhaskar K, Noronha V, Joshi A, *et al*: Thymic epithelial tumors: Can fluorodeoxyglucose positron emission tomography help in predicting histologic type and stage? *Indian J Cancer* 53: 270-273, 2016.
13. Treglia G, Sadeghi R, Giovanella L, Cafarotti S, Filosso P and Lococo F: Is (18)F-FDG PET useful in predicting the WHO grade of malignancy in thymic epithelial tumors? A meta-analysis. *Lung Cancer* 86: 5-13, 2014.
14. Toba H, Kondo K, Sadohara Y, Otsuka H, Morimoto M, Kajiuira K, Nakagawa Y, Yoshida M, Kawakami Y, Takizawa H, *et al*: 18F-fluorodeoxyglucose positron emission tomography/computed tomography and the relationship between fluorodeoxyglucose uptake and the expression of hypoxia-inducible factor-1 α , glucose transporter-1 and vascular endothelial growth factor in thymic epithelial tumours. *Eur J Cardiothorac Surg* 44: e105-e112, 2013.
15. Seki N, Sakamoto S, Karube Y, Oyaizu T, Ishihama H and Chida M: 18F-fluorodeoxyglucose positron emission tomography for evaluation of thymic epithelial tumors: Utility for world health organization classification and predicting recurrence-free survival. *Ann Nucl Med* 28: 257-262, 2014.
16. Fukumoto K, Taniguchi T, Ishikawa Y, Kawaguchi K, Fukui T, Kato K, Matsuo K and Yokoi K: The utility of [18F]-fluorodeoxyglucose positron emission tomography-computed tomography in thymic epithelial tumours. *Eur J Cardiothorac Surg* 42: e152-e156, 2012.
17. Kaira K, Sunaga N, Ishizuka T, Shimizu K and Yamamoto N: The role of [18F] fluorodeoxyglucose positron emission tomography in thymic epithelial tumors. *Cancer Imaging* 11: 195-201, 2011.
18. Kumar A, Regmi SK, Dutta R, Kumar R, Gupta SD, Das P, Halanaik D and Jindal T: Characterization of thymic masses using (18)F-FDG PET-CT. *Ann Nucl Med* 23: 569-577, 2009.
19. Kim JY, Kim HO, Kim JS, Moon DH, Kim YH, Kim DK, Park SI, Park YS and Ryu JS: (18)F-FDG PET/CT is useful for pretreatment assessment of the histopathologic type of thymic epithelial tumors. *Nucl Med Mol Imaging* 44: 177-184, 2010.
20. Benveniste MF, Moran CA, Mawlawi O, Fox PS, Swisher SG, Munden RF and Marom EM: FDG PET-CT aids in the preoperative assessment of patients with newly diagnosed thymic epithelial malignancies. *J Thorac Oncol* 8: 502-510, 2013.
21. Shinya T, Tanaka T, Soh J, Matsushita T, Sato S, Toyooka S, Yoshino T, Miyoshi S and Kanazawa S: Diagnostic value of dual-time-point F-18 FDG PET/CT and chest CT for the prediction of thymic epithelial neoplasms. *Acta Med Okayama* 71: 105-112, 2017.
22. Endo M, Nakagawa K, Ohde Y, Okumura T, Kondo H, Igawa S, Nakamura Y, Tsuya A, Murakami H, Takahashi T, *et al*: Utility of 18FDG-PET for differentiating the grade of malignancy in thymic epithelial tumors. *Lung Cancer* 61: 350-355, 2008.
23. Terzi A, Bertolaccini L, Rizzardi G, Luzzi L, Bianchi A, Campione A, Comino A and Biggi A: Usefulness of 18-F FDG PET/CT in the pre-treatment evaluation of thymic epithelial neoplasms. *Lung Cancer* 74: 239-243, 2011.
24. Park SY, Cho A, Bae MK, Lee CY, Kim DJ, and Chung KY: Value of 18F-FDG PET/CT for predicting the world health organization malignant grade of thymic epithelial tumors: Focused in volume-dependent parameters. *Clin Nucl Med* 41: 15-20, 2016.
25. Scagliori E, Evangelista L, Panunzio A, Calabrese F, Nannini N, Polverosi R and Pommeri F: Conflicting or complementary role of computed tomography (CT) and positron emission tomography (PET)/CT in the assessment of thymic cancer and thymoma: Our experience and literature review. *Thorac Cancer* 6: 433-442, 2015.
26. Sandri A, Cusumano G, Lococo F, Alifano M, Granone P, Margaritora S, Cesario A, Oliaro A, Filosso P, Regnard JF and Ruffini E: Long-term results after treatment for recurrent thymoma: A multicenter analysis. *J Thorac Oncol* 9: 1796-1804, 2014.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International (CC BY-NC-ND 4.0) License.