Retention index of FDG-PET/CT SUVmax of the primary tumor in non-small cell lung cancer as a predictor of lymph node metastasis: a retrospective study

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Abstract

Background: Accurate staging of non-small cell lung cancer is key in treatment planning and prediction of prognosis. We investigated the correlation between the maximum standardized uptake value (SUVmax) retention index (RI) of the primary tumor and lymph node metastasis in non-small cell lung carcinoma. We also evaluated the tendencies according to the histological types.

Methods: We retrospectively evaluated 218 non-small cell lung cancer (NSCLC) tumors from 217 patients who underwent pre-operative fluorodeoxyglucose-positron emission tomography/computed tomography (PET/CT) followed by lung surgery and lymph node resection between July 2015 and August 2020. All primary tumors were calculated as the SUVmax at 50 min ($SUVmax_{early}$ [$SUVmax_e$]) and 120 min ($SUVmax_{delayed}$ [$SUVmax_d$]), and RI. The clinico-pathological factors of interest were compared based on lymph node metastasis status and NSCLC histo-pathological subtype.

Results: The median $SUVmax_e$ and $SUVmax_d$ of the primary tumor were 3.3 and 4.2, respectively, and the median RI was 0.25. The RI was significantly higher in the pN(+) (n = 44) group (0.30) compared to the pN0 (n = 174) group (0.24) (p = 0.01). In patients with adenocarcinoma (n = 145), the RI was also significantly higher in the pN(+) (n = 29) group (0.29) compared to the pN0 (n = 116) group (0.16) (p <0.01). A high RI of the primary tumor was an independent risk factor for lymph node metastasis, particularly in patients with adenocarcinoma (odds ratio: 12.30, p <0.05).

Conclusions: The RI of primary NSCLC tumors can help predict lymph node metastases, particularly in patients with adenocarcinoma.

Background

Accurate staging of non-small cell lung cancer (NSCLC), especially the pre-operative diagnosis of lymph node metastasis, plays a key role in planning treatment and guiding prognostication in affected patients [1]. Lymph node metastasis can be ascertained using invasive or non-invasive methods. Positron emission tomography/computed tomography (PET/CT) using 18F-fluorodeoxyglucose (18F-FDG), a glucose analog shown to be useful for detecting malignancy, is a non-invasive method widely used to help stage NSCLC. The maximum standardized uptake value (SUVmax) of the primary tumor is risk factor for nodal metastasis, and the typical SUVmax cut-off value is 2.5–4.0 [1–4]. Dual-time-PET/CT is also widely implemented, with scanning being performed for almost 1–2 h following injection to distinguish between malignancy and inflammation [5]. The effectiveness of the dual-time-point (DTP) PET/CT retention index (RI) as a predictor of lymph node metastasis has been described [5–7]. However, these studies reported that the SUV RI of the lymph node itself was effective for predicting lymph node metastasis. Indeed, no studies have examined the role of the primary tumor's SUVmax RI in the prediction of lymph node metastasis. In a real-world clinical settings, the SUVmax of hilar and mediastinal lymph nodes is often not calculated. In this study, we therefore explored the meaning of the primary tumor's RI as a predictor for lymph node metastasis in a real-world healthcare setting..This study therefore

investigated the correlations between the SUVmax RI of the primary tumor and lymph node metastasis in different histological subtypes of NSCLC.

Methods

Patients

In this observational study, we retrospectively evaluated 218 NSCLC tumors from 217 enrolled patients who underwent a pre-operative FDG-PET evaluation and subsequent surgical resection (lobectomy, bilobectomy, pneumonectomy, or segmentectomy) and lymphadenectomy of ND1a-ND2a-2 between July 2015 and August 2020.

One of the male patients had two evaluable tumors, although the regional lymph node of each tumor was separated. We enrolled consecutive operative cases in that period that were clinically diagnosed as resectable lung cancer with clinical staging cN0–2. We excluded patients who underwent wedge resection with no lymph node dissection, and those who received neoadjuvant chemotherapy. Among the cases with adenocarcinoma, we excluded patients with adenocarcinoma in situ (AIS), minimally invasive adenocarcinoma (MIA), and former bronchioloalveolar carcinoma (BAC). Tumor size, lymph node metastasis, and histological types were all determined using surgically resected specimens. Pathological staging of all the patients was performed according to the 7th edition of the International Union Against Cancer and the American Joint Committee on Cancer TNM staging system for lung cancer [8]. The SUVmax was calculated for the primary tumor only. The study protocol was reviewed and approved by the institutional review board.

Nuclear imaging and analysis

Patients were asked to fast for at least 5 h before the examination, after which blood glucose levels were determined. The patients then received an intravenous injection of 185 MBq/body (at the time of inspection) of 18F-FDG and rested for approximately 50 min before scanning. PET/CT was performed for all the patients at Heisei-Memorial Medical Center (Fujieda, Japan) using a multidetector CT integrated high-resolution PET/CT scanner (Aquiduo PCA-7000B system, Canon Medical Systems Corporation, Otawara, Tochigi, Japan). Image acquisition started 50 min after FDG (early-phase) injection and 2 h after the injection (delayed-phase) in a relaxed supine position.

An unenhanced CT scan was performed first, from the inguinal region of the thigh to the head, with the following settings: 120 kV, 80 mA (average, max 110 mA), helical pitch 15, and section thickness of 4 mm, which matched the PET section thickness. A PET scan was performed that covered the identical transverse field of view immediately after the CT scan. The acquisition time for the PET scan was 2 min. Patients were in normal shallow respiration during image acquisition. The PET datasets were reconstructed iteratively using the CT data for attenuation correction, and co-registered images were displayed on a workstation (Aquiduo Vox-Base Managaser 2.8, J-MAC System).

Two experienced nuclear physicians blinded to the histologic results interpreted all 18F-FDG PET/CT findings. For the semi-quantitative analysis of FDG uptakes, the SUV was adopted. The SUVs were calculated using lean body mass according to the following formula:

$$\mathrm{SUV} = \frac{\text{radioactivity in regions of interest (ROI) (MBq/mL)} \times \text{body weight(k)}}{\text{injected FDG radioactivity (MBq)}}$$

Circular regions-of-interest were drawn to encompass primary lung tumor contours on the attenuation corrected PET/CT images.

The SUVmax RI was calculated using the following formula:

$$\mathrm{RI} = \frac{\text{SUVmax delayed point} - \text{SUVmax early point}}{\text{SUVmax early point}}$$

The SUVmax and RI were calculated for the primary tumor only.

Statistical analyses

Statistical analyses were performed using the EZR software package (version 1.40; Saitama Medical Center, Jichi Medical University, Saitama, Japan) [9], a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). The EZR software is a modified version of the R commander designed to facilitate the addition of statistical functions frequently used in biostatistics. Categorical data were presented as frequencies and compared between patient groups using Fisher's exact test. Data which fit normal distribution assumptions were described as the mean ± standard deviation. Non-normal data were described as the median and interquartile range. Parametric and non-parametric data were analyzed using an unpaired Student's *t*-test and the Mann–Whitney U test, respectively. The receiver operating characteristic (ROC) curve was used to analyze diagnostic efficacy, sensitivity, and specificity for NSCLC lymph node metastasis, and the cut-off point was calculated using the Youden index. The linear correlations between the pathological T size and RI were calculated using Pearson's correlation coefficients. Logistic regression analyses were performed to identify independent predictors of risk for pathological lymph node metastasis. All *p*-values were nominal, and a two-sided p-value < 0.05 was considered statistically significant.

Results

Patient characteristics

In total, data relevant to 218 NSCLC tumors from 217 patients were retrospectively reviewed. The patient characteristics are summarized in Table 1. This study included 139 men and 78 women (mean age, 69.6 ± 9.5 years). One of the male patients had two evaluable tumors, and the regional lymph node of each tumor was separated. In all cases, a pre-operative clinical stage of N0–N2 was considered inidcative of

curative resection. We diagnosed clinical lymph node metastasis when the short axis of the node was larger than 1 cm on CT, or when the lymph node had high FDG accumulation.

Table 1
Characteristics of the patients and tumors included in this study.

Characteristics	N (%)
Sex	
Male	139 (64.0%)
Female	78 (35.9%)
Lobe	
RU	67 (30.7%)
RM	13 (6.0%)
RL	51 (23.4%)
LU	41 (18.8%)
LL	46 (21.1%)
Histological type	
Adenocarcinoma	145 (66.5%)
Squamous	53 (24.3%)
Other	20 (9.2%)
cN	
0	187 (85.8%)
1	26 (11.9%)
2	5 (2.3%)
pN	
0	174 (79.8%)
1	27 (12.4%)
2	17 (7.8%)
pN	

[a]n = 218 for all characteristics, except sex (n = 217). Data are presented as n (%), mean ± standard deviations, or median [inter-quartile ranges].

pN, pathological lymph node metastasis; RU, right upper lung lobe; RL, right lower lung lobe; RM, right middle lung lobe; LU, left upper lung lobe; LL left lower lung lobe; $SUVmax_{early}$, early maximum standardized uptake value; $SUVmax_{delayed}$, delayed maximum standardized uptake value; RI, retention index; pT, pathological tumor size

Characteristics	N (%)
0	174 (79.8%)
1 or 2	44 (20.2%)
Age, years	69.6 ± 9.5
$SUVmax_{early}$	3.3 [1.73, 6.58]
$SUVmax_{delayed}$	4.2 [2.0, 8.68]
RI	0.25 [0.08, 0.37]
pT (mm)	22.0 [15.8, 30.0]
[a]n = 218 for all characteristics, except sex (n = 217). Data are presented as n (%), mean ± standard deviations, or median [inter-quartile ranges].	
pN, pathological lymph node metastasis; RU, right upper lung lobe; RL, right lower lung lobe; RM, right middle lung lobe; LU, left upper lung lobe; LL left lower lung lobe; $SUVmax_{early}$, early maximum standardized uptake value; $SUVmax_{delayed}$, delayed maximum standardized uptake value; RI, retention index; pT, pathological tumor size	

All lesions were surgically resected via lobectomy, segmentectomy, bilobectomy, or pneumonectomy accompanied by lymph node dissection of ND1a-ND2a-2. Table 1 summarizes the tumor characteristics. Histo-pathological examination revealed 145 (66.5%) adenocarcinomas, 53 (24.3%) squamous cell carcinomas, and 20 (9.2%) carcinomas of other NSCLC subtypes, including adenosquamous carcinoma, pleomorphic carcinoma, large cell carcinoma, large cell neuroendocrine carcinoma, carcinoid tumor, lymphoepithelioma-like carcinoma, and mucoepidermoid carcinoma. The median pathological tumor size (pT) was 22.0 (15.8–30.0) mm; the median $SUVmax_e$ and $SUVmax_d$ of the primary tumor were 3.3 (1.73–6.58) and 4.2 (2.0–8.68), respectively, whereas the median RI was 0.25 (0.08–0.37).

Clinico-pathological differences between the cohorts according to lymph node status

The clinico-pathological characteristics of the patients were compared based on the presence or absence of lymph node metastases (Table 2). In total, 44 patients were pathological lymph node (pN) positive (+), while 174 patients were pN negative (0).

Table 2
Clinicopathologic characteristics based on pathological N factor

Characteristics	Overall (n = 218)	pN 0 (n = 174)	pN 1 or 2 (n = 44)	*p*-value
Sex				
Male	140	108	32	0.22*
Female	78	66	12	
Lobe				
RU	67	56	11	0.17*
RM	13	9	4	
RL	51	45	6	
LU	41	31	10	
LL	46	33	13	
Histological type				
Adenocarcinoma	145	116	29	0.43*
Squamous cell	53	44	9	
Other	20	14	6	
Clinical N stage				
cN0	187	160	27	< 0.001*
cN1or2	31	14	17	
Age, years	69.6 ± 9.5	69.5 ± 9.7	70.0 ± 8.5	0.73**
$SUVmax_{early}$	3.3 [1.73–6.58]	2.9 [1.40–5.78]	5.7 [3.6–7.68]	< 0.001***
$SUVmax_{delayed}$	4.2 [2.0– 8.68]	3.5[1.45–7.70]	7.4 [4.35–10.58]	< 0.001***
RI	0.25 [0.08–0.37]	0.24 [0.01–0.36]	0.30 [0.23–0.39]	0.01***
pT, mm	22.0 [15.8–30.0]	21.0 [15.0–29.0]	25.5 [22.0–38.8]	< 0.001***

[a]Data are presented as n (%), mean ± standard deviation, or median [inter-quartile ranges].

*Fisher's exact test; **unpaired *t*-test; ***Mann–Whitney U test

pN, pathological lymph node metastasis; RU, right upper lung lobe; RL, right lower lung lobe; RM, right middle lung lobe; LU, left upper lung lobe; LL left lower lung lobe; $SUVmax_{early}$, early maximum standardized uptake value; $SUVmax_{delayed}$, delayed maximum standardized uptake value; RI, retention index; pT, pathological tumor size

Lymph node metastasis was confirmed in 44 tumors. The median RI was significantly higher in the pN0 (n = 174) group (0.24, 0.01–0.36) compared to the pN(+) (n = 44) group (0.30, 0.23–0.39) (p = 0.01) Fig. 1).

The area under the ROC curve (AUC) values for $SUVmax_e$ and $SUVmax_d$ as diagnostic markers of nodal metastasis were 0.73 (95% confidence intervals [CIs], 0.66–0.80) and 0.73 (95% CI, 0.66–0.78), respectively. The $SUVmax_e$ and $SUVmax_d$ thresholds were 2.80 and 3.70, respectively. The AUC for RI in the diagnosis of nodal metastasis was 0.62 (95% CI, 0.54–0.71), and the RI threshold was 0.276 (Fig. 2).

Histo-pathological analysis

In patients with adenocarcinoma (n = 145), the median RI values of the pN0 (n = 116) and pN(+) (n = 29) groups were 0.16 (0.0–0.30) and 0.29 (0.17–0.40), respectively. The RI of the primary tumor was significantly higher in the pN + group compared to the pN0 group (p < 0.01). In patients with squamous cell carcinoma (n = 53), median RI values did not differ significantly between the pN0 group (0.33, IQR 0.25–0.45) and the pN(+) group (0.33, IQR 0.28–0.44) (p = 0.62). In patients with other NSCLC subtypes (n = 20), there was also no significant differnce in median RI between the pN0 group (0.23, IQR 0.17–0.38) and the pN(+) group (0.29, IQR 0.26–0.30) (p = 0.34) (Table 3).

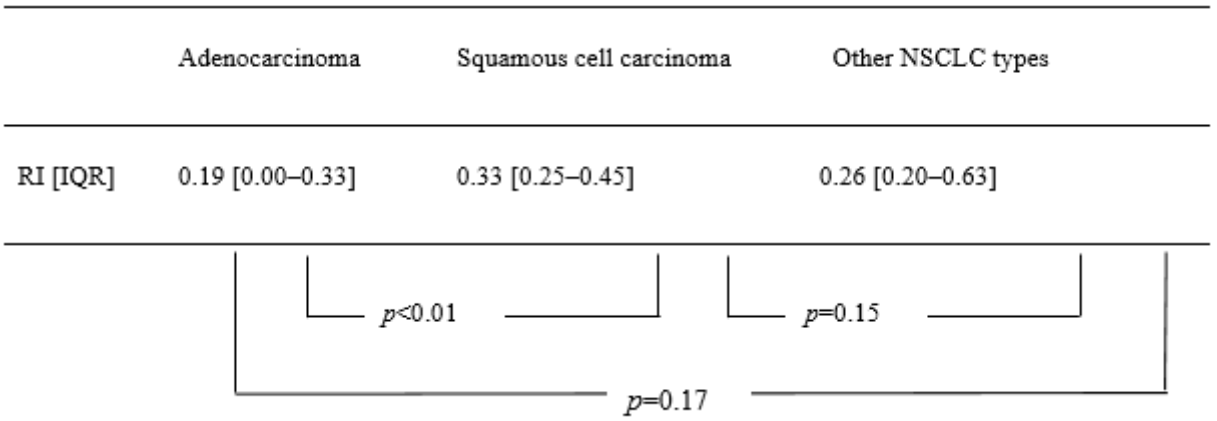
Table 3
Clinicopathologic characteristics based on pathological tumor stage and histo-pathological subtype.

Histo-pathological subtype	Value	pN0	pN(+)	*p*-value
Adenocarcinoma (n = 145)	SUVmax(e)	(n = 116)	(n = 29)	< 0.001
	SUVmax(d)	2.1 [1.08–3.38]	4.3 [3.0–7.2]	< 0.001
	RI	2.6 [1.2–4.7]	5.9 [4.1–8.9]	< 0.01
	pT	0.16 [0.0–0.30]	0.29 [0.17–0.40]	< 0.01
		19 [14–25]	25 [21–30]	
Squamous cell carcinoma (n = 53)	SUVmax(e)	(n = 44)	(n = 9)	0.02
	SUVmax(d)	5.9 [3.77–8.55]	9.3 [6.60–14.20]	0.03
	RI	8.1 [4.58–11.95]	13.4 [9.4–18.5]	0.62
	pT	0.33 [0.25–0.45]	0.33 [0.28–0.44]	0.05
		27 [19.8–32.0]	33 [32–42]	
Other (n = 20)	SUVmax(e)	(n = 14)	(n = 6)	0.39
	SUVmax(d)	5.3 [2.28–8.28],	7.0 [6.65–7.43]	0.39
	RI	6.5 [2.88–11.10]	9.1[8.53–9.75],	0.34
	pT	0.23 [0.17–0.38]	0.29 [0.26–0.30]	0.23
		21.5 [12.3–27.0]	27.0 [24.8–44.3]	

RI, retention index; SUVmax(e), early maximum standardized uptake value; SUVmax(d),delayed maximum standardized uptake value; pT, pathological tumor size

Figure 3 shows the ROC curves for RI as a diagnostic marker of nodal metastasis in patients with adenocarcinoma. The RI value of the primary tumor was statistically significant only in the pN0 and pN(+) groups among pathological subgroups. The AUC for lymph node metastasis diagnosis in adenocarcinoma was 0.67 (95% CI, 0.56–0.78), and the threshold of the RI was 0.167; sensitivity was 0.500, and specificity was 0.793 (Fig. 3). Table 4 shows a comparison of RI values between different histological subtypes. RI values were significantly higher in squamous cell carcinoma than adenocarcinoma.

Table 4. Comparison of retention index values by cell carcinoma histological type.



RI, retention index; NSCLC, non-small cell lung cancer; IQR, interquartile range

Correlation between tumor size and retention index

Since RI was significantly positively correlated with overall tumor since (Table 3), we further investigated the correlation between tumor size and RI in different histological subtypes of NSCLC.In the adenocarcinoma group (n = 145), the correlations between the primary tumor size and the RI was 0.34 (95% CI, 0.18–0.47, p < 0.01); in the squamous cell carcinoma group (n = 53), the correlation was 0.21 (95% CI, -0.07–0.45, p = 0.14); and for the other histological subtypes, the correlation was 0.63 (95% CI, 0.23–0.83, p < 0.01) (Table 5). In the squamous cell carcinoma group (n =), there was no positive correlation between tumor size and RI.

Table 5
Correlation coefficient values between RI and pT by histological type.

Histological type	Correlation coefficient	95% CI	*p*-value
All (n = 218)	0.35	0.23–0.46	< 0.01
Adenocarcinoma (n = 145)	0.34	0.18–0.47	< 0.01
Squamous cell carcinoma (n = 53)	0.21	-0.07–0.45	0.14
Other (n = 20)	0.63	0.23–0.83	< 0.01
CI, confidence interval; RI, retention index; pT pathological tumor size			

Multivariable analysis

We used a multivariable logistic regression to adjust for the potentially confounding roles of RI and tumor size on lymph node metastasis (Table 6). In a multivariable analysis, primary tumor RI was not an independent risk factor for lymph node metastasis (odds ratio [OR]: 2.53, 95% CI, 0.47–13.50, p = 0.28) in all histo-pathological subtypes. However, in the adenocarcinoma group, a higher RI value of the primary

tumor was associated with an increased risk fir lymph node metastasis (OR: 12.3, 95% CI, 1.11–135.0, p < 0.05).

Table 6
Multivariable analyses of predictors of lymph node metastasis in patients.

Histological type	Variable	OR	95% CI	*p*-value
All (n = 218)	pT	1.03	1.01–1.05	0.01
	RI	2.53	0.47–13.50	0.28
Adenocarcinoma	pT	1.02	1.00–1.05	0.11
(n = 145)	RI	12.3	1.11–135.0	0.04
Squamous cell carcinoma	pT	1.07	1.01–1.13	0.03
(n = 53)	RI	0.8	0.04–17.6	0.89
Other	pT	1.03	0.96–1.11	0.38
(n = 20)	RI	0.34	0.00–988.0	0.79

OR, odds ratio; CI, confidence interval; RI, retention index; pT pathological tumor size

Discussion

In this study, we examined the implications of the RI of the primary tumor as a predictor of lymph node metastasis in patients NSCLC. Several studies have examinde the role of tumor SUVmax as a risk marker for nodal metastasis [1–4]. The RI of the lymph node is also a predictor of lymph node metastasis in NSCLC, while higher RI of primary tumor is known to predict risk for distant metastasis and poor recurrence-free survival [5–7, 10, 11]. However, the role of the RI of the primary tumor as a predictor of lymph node metastasis in NSCLC remains unclear. To the best of our knowledge, no studies have been conducted in an attempt to compare the of primary tumor RI as a predictor of lymph node metastasis between different histological subtypes of NSCLC.

We found that the RI of the primary tumor predicted lymph node metastasis in patients with NSCLC across all histological subtypes. Furethermore, we demonstrated that, in patients with adenocarcinoma, the RI of the primary tumor was a significant predictor of lymph node metastasis; however, in patients with squamous cell carcinoma, and those with other NSCLC types, the RI of the primary tumor was not a significant predictor of lymph node metastasis.

RI values were higher in patients with squamous cell carcinoma than in those with adenocarcinoma. However, the RI was a reliable predictor of lymph node metastasis only in the adenocarcinoma group. We also demonstrated a correlation between the RI value and tumor size across all NSCLC types. Multivariable analysis demonstrated that, based on histology, the RI of the primary tumor was an independent risk factor for lymph node metastasis, but only in the adenocarcinoma group. The RI of the

primary tumor was therefore a reliable predictor of lymph node metastasis in patients with adenocarcinoma.

Similar histo-pathological tendencies of the FDG-PET/CT SUVmax have been reported in other studies. The single-time-point FDG-PET/CT SUVmax of the primary tumor was significantly higher in squamous cell carcinoma than in adenocarcinoma. However, the significance of the SUVmax as a prognostic factor was stronger in adenocarcinoma and weaker in squamous epithelial carcinoma [12, 13]. Glucose metabolism abnormalities might explain the differences in the role of the SUVmax between adenocarcinoma and squamous cell carcinoma [12, 13]. Tumor glucose transporter (GLUT)-1 overexpression is associated with high FDG uptake. GLUT-1 is fully (100%) expressed in squamous cell carcinoma, but only partially (58%) expressed in adenocarcinoma [12, 13]. GLUT-1 expression could explain the variable significance of SUVs as a predictor of lymph node metastasis in different histological subtypes evident in our study. This biological difference likely modified the effect of the RI as a risk factor among different histo-pathological subtypes.

We investigated the DTP SUVmax, $SUVmax_e$ at 50 min, and $SUVmax_d$ at 120 min. In accordance with previous reports, both the $SUVmax_e$ and $SUVmax_d$ were higher in squamous cell carcinoma and other NSCLC subtypes than in adenocarcinoma. The RI is calculated using both the $SUVmax_e$ and $SUVmax_d$. Therefore, we believe that there is a close histological link between the SUVmax and RI for different NSCLC subtypes.

The SUVmax and related indices (including the RI) are sensitive indicators of malignant potential in patients with adenocarcinoma. To the best of our knowledge, no prior studies have comprehensively investigated the clinical features and SUVmax or RI in detail in other patient samples with NSCLC. Furthermore,since number of the patients with other NSCLC subtypes was small, we could not determine the clinical behavior of those subgroups.

Numerous studies have mentioned that a high SUVmax of the primary tumor is a risk factor for lymph node metastasis, and the cut-off SUVmax of the primary tumor ranges from 2.5 to 4.0 [1, 3, 4, 14–18]. SUVmax data at the 60-min time-point following F18-FDG administration in many studies of single-time-point 18F-PET-CT examination are similar to the $SUVmax_e$ demonstrated in this study, showing that an $SUVmax_e$ cut-off of 2.8 was a predictor of nodal metastasis.

SUVmax values vary between facilities, and variations of up to 30% across three institutions have been reported [19]. We consider the RI using DTP PET-CT a reliable assessment tool that does not require standardization, since it is the ratio of the two SUVmax values. The RI is a simple value that can be widely used in many facilities with DTP PET-CT scanning data. Additionary, in the real world, the SUVmax of hilum and mediastinum lymph nodes is often not calculated. We used our simple parameter for predicting metastasis in the real world. Therefore the primary tumor's RI could help nodal metastasis widely in the real world.

This study had some limitations, including a retrospective, single-center design. Excluding the AIS, MIA, and old BAC categories from pathologic diagnoses constituted another limitation. This decision was motivated by our focus on targeting clear invasive adenocarcinoma. We thus did not formally consider the differences between the Union for International Cancer Control TNM 7th and 8th edition guidelines on adenocarcinoma in our study. Furthermore, the number of cases of other NSCLC types was small, which may have affected our results.

Conclusions

This study demonstrated that the RI of DTP FDG-PET imaging in the primary tumors of patients with NSCLC could be a useful predictor of lymph node metastasis. The RI was a more significant predictor of lymph node metastasis in patients with adenocarcinoma compared to other cancer subtypes.

Abbreviations

18F-FDG: 18F-fluorodeoxyglucose

AIS: Adenocarcinoma in situ

BAC: Bronchioloalveolar carcinoma

CI: Confidence index

CT: Computed tomography

DTP: Dual time-point

MIA: Minimally invasive adenocarcinoma

NSCLC: Non small-cell lung cancer

OR: Odds ratio

PET: Positron emission tomography

pT: Pathological tumor size

RI: Retention index

ROC: Receiver operating curve

SUVmax: Maximum standardized uptake value

Declarations

Ethics approval and consent to participate

The study received approval from the institutional review board of Fujieda Municipal General Hospital (R02-29, 2020.12.22).

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during this study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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None.

Authors' contributions

TE acquired the data and wrote the manuscript. HK contributed to the study design. SM and HT contributed to the study design and revised the PET/CT scan protocol. MO and HN performed data acquisition. KF and NS substantively revised the manuscript and supervised the experimental process. All authors read and approved the final manuscript.

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Figures

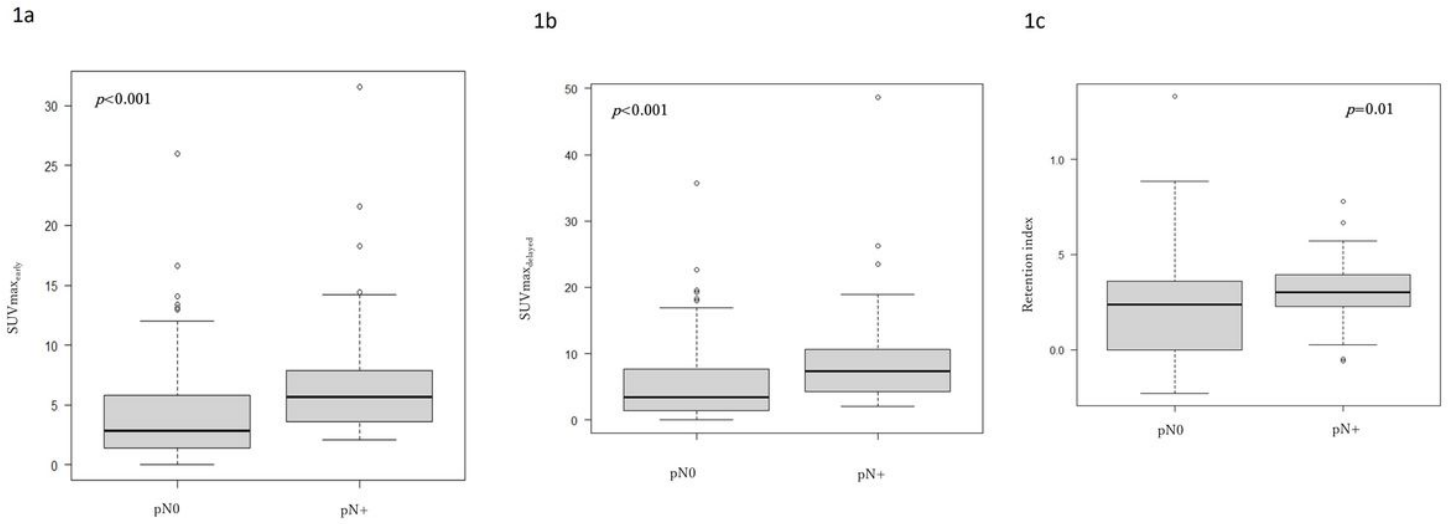

Figure 1

The **(A)** early maximum standardized uptake value ($SUVmax_e$), **(B)** delayed maximum standardized uptake value ($SUVmax_d$), and **(C)** retention index values were compared based on the presence of lymph node metastasis.

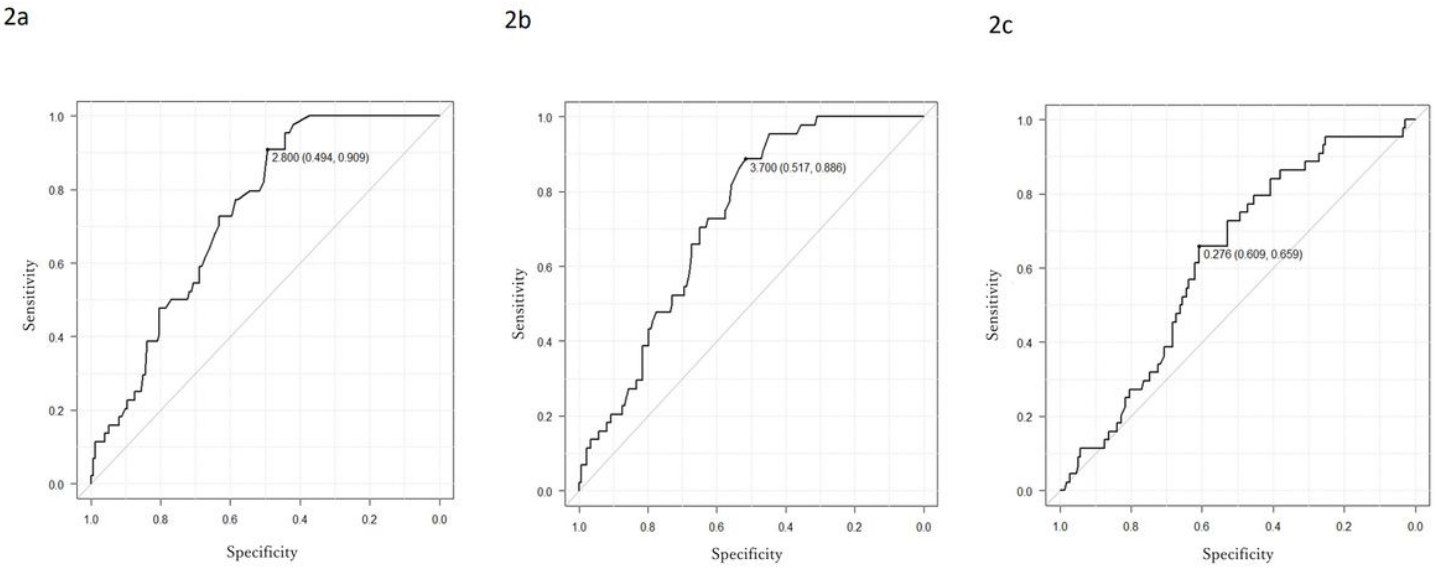

Figure 2

(A) Receiver-operating characteristic (ROC) curve for early maximum standardized uptake value ($SUVmax_e$) as a predictor of lymph node metastasis. The area under the ROC curve (AUC) was 0.73 with an $SUVmax_e$ of 2.80 as the threshold; the sensitivity and specificity were 0.494 and 0.909, respectively. **(B)** ROC curve for delayed maximum standardized uptake value ($SUVmax_d$) as a predictor of lymph node metastasis. The AUC was 0.73, with an $SUVmax_d$ of 3.70 as the threshold, and the sensitivity and specificity were 0.517 and 0.886, respectively. **(C)** ROC curve for the retention index (RI) as a predictor of lymph node metastasis. The AUC of the RI was 0.62 (95% CI, 0.54–0.71), and the threshold of the RI was 0.276; the sensitivity and specificity were 0.609 and 0.659, respectively.

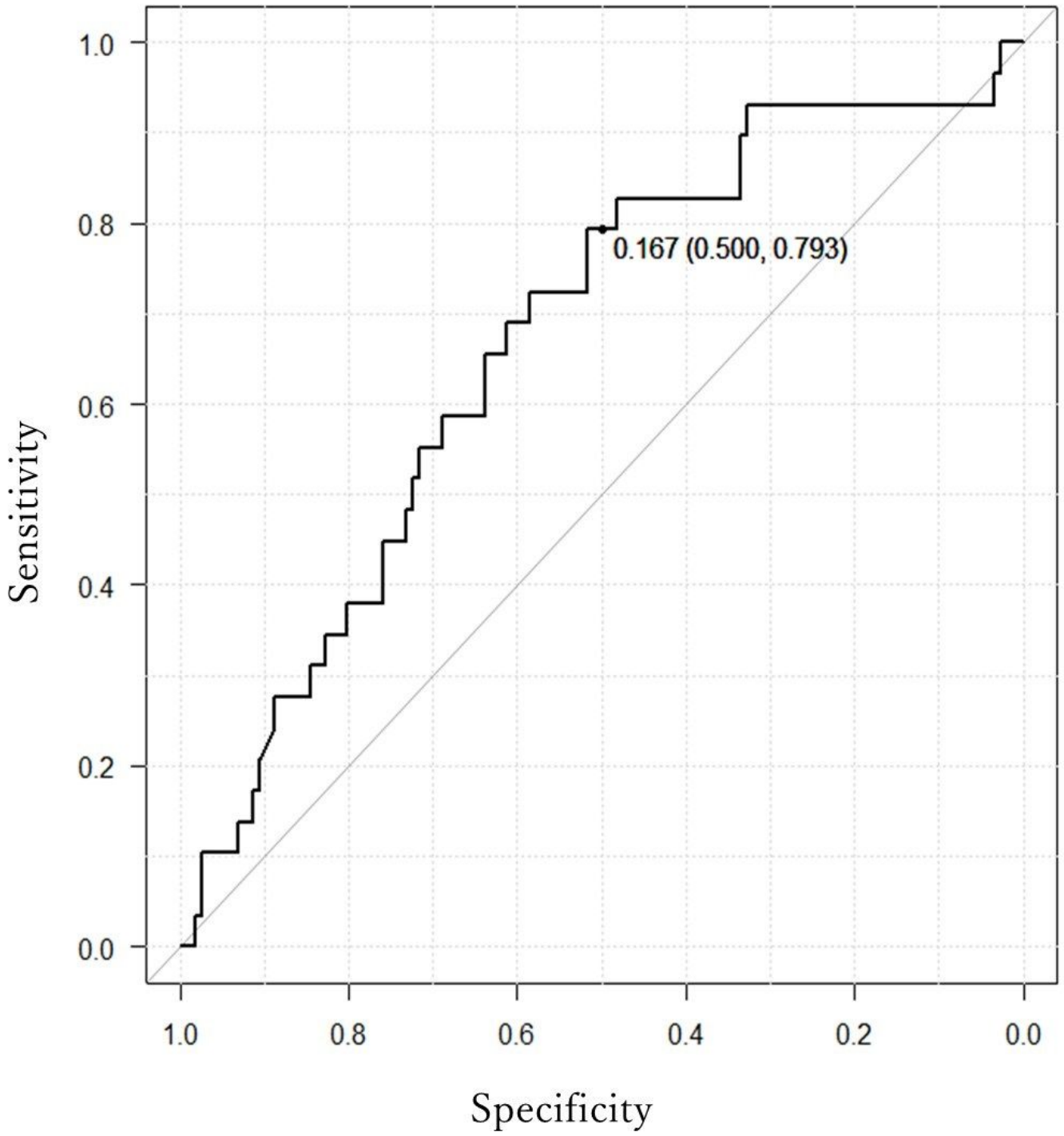

Figure 3

Receiver-operating characteristic (ROC) curve for the retention index (RI) in the adenocarcinoma for lymph node metastasis. The area under the ROC curve (AUC) of the RI was 0.67 (95% CI, 0.56–0.78), the threshold of RI for the nodal metastasis was 0.167, and the sensitivity and specificity were 0.500 and 0.793, respectively.

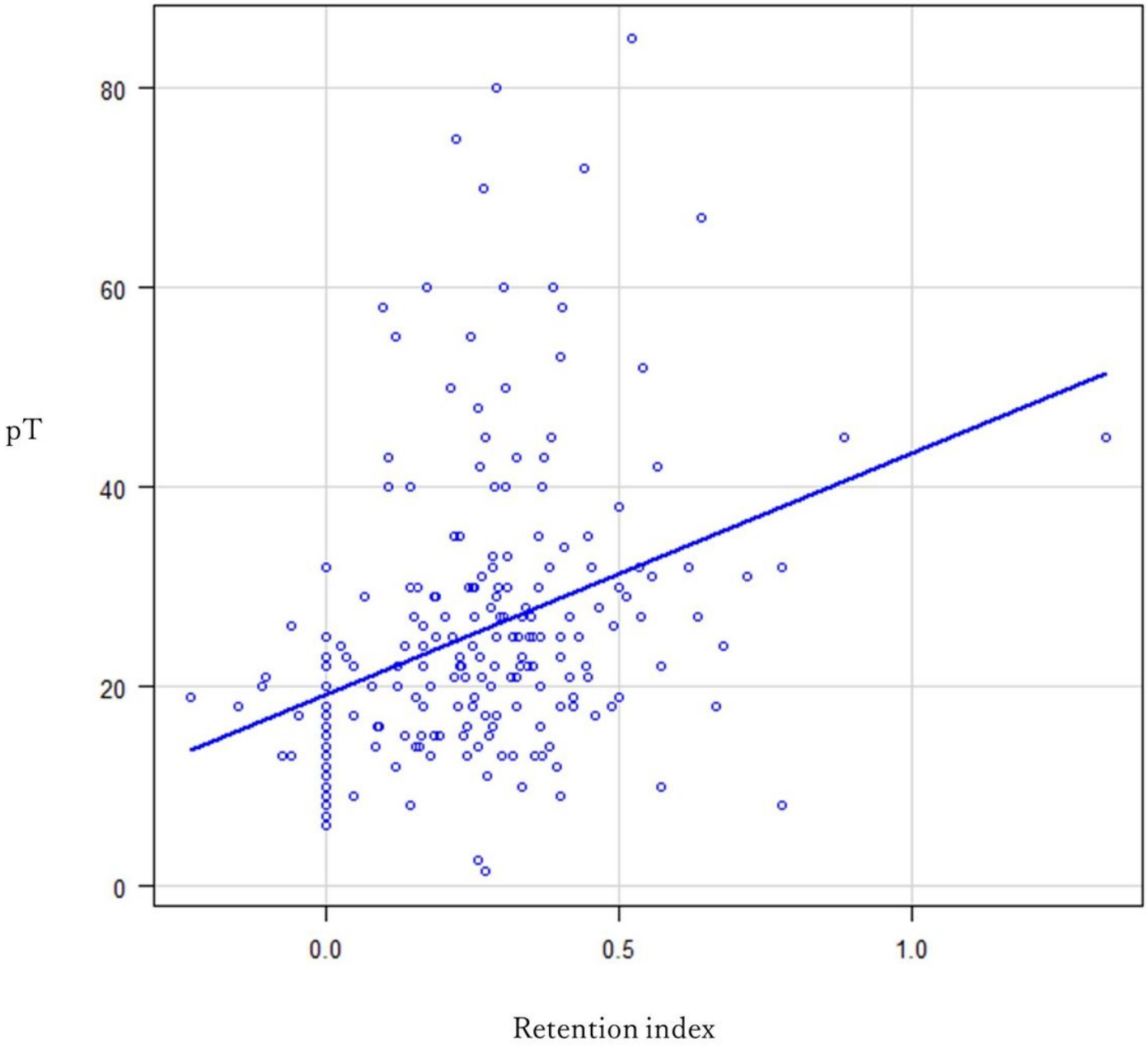

Figure 4

Correlation coefficient value between the retention index and pathological tumor size in all the histological types was 0.35 (95% CI 0.23–0.46; p <0.01)