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The Peak-Standardized Uptake Value (P-SUV) by Preoperative Positron Emission Tomography-Computed Tomography (PET-CT) is a Useful Indicator of Lymph Node Metastasis in Gastric Cancer

HYEON HWA OH, MD,[1] SANG EOK LEE, MD,[1]* IN SEOK CHOI, MD,[1] WON JUN CHOI, MD,[1] DAE SUNG YOON, MD,[1] HYUN SIK MIN, MD,[1] YU MI RA, MD,[1] JU IK MOON, MD,[1] AND YUN HEE KANG, MD[2]

[1]Department of Surgery, Konyang University Hospital, Daejeon, Korea
[2]Department of Nuclear Medicine, Konyang University Hospital, Daejeon, Korea

Background and objectives: Little data is currently available on the usefulness of peak-standardized uptake value (P-SUV) by positron emission tomography-computed tomography (PET-CT) in gastric cancer. The purpose of the present study was to evaluate the value of PET-CT for the preoperative evaluation of patients with gastric cancer. The aim of this study was to assess the relation of between primary tumor P-SUV, as determined by preoperative PET-CT, and lymph node metastasis in gastric cancer.

Methods: From December 2007 to March 2010, we analyzed the PET-CT of 147 patients that underwent gastrectomy for gastric cancer. P-SUV in PET-CT were measured by single nuclear medicine physician. Statistical analysis was performed to determine relations between clinicopathologic parameters including P-SUV and lymph node metastasis using the chi-square test, the independent *t*-test, and using logistic regression analysis.

Results: Age, tumor depth, tumor size, and lymph node metastasis were found to be associated with primary tumor P-SUV by PET-CT ($P = 0.009$, <0.001, <0.001, and <0.001, respectively). No association was found between P-SUV and tumor histology or tumor location ($P = 0.099$). Advanced gastric cancer was found to have a higher P-SUV than early gastric cancer, and a higher P-SUV was found to be associated with lymph node metastases by both univariate and multivariate analysis.

Conclusions: P-SUV of primary tumor could be an independent indicator of lymph node metastasis in gastric cancer. Gastric surgeons should pay more attention to the dissection of lymph nodes when primary tumors have higher P-SUV values by PET-CT.

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KEY WORDS: PET-CT; gastric cancer

INTRODUCTION

Gastric cancer is the commonest malignancy in Korea, and ranks second to lung cancer in terms of mortality [1,2]. Complete resection and lymph node dissection is the most important therapeutic strategy in gastric cancer. However, it is important to establish precisely local invasion, tumor size, lymph node involvement, and presence or absence of distant metastasis before operation [1,2]. During the course of surgery, lymph node metastasis is the most important determinator of the range of gastrectomy and lymphadenectomy [3,4].

Although preoperative computed tomography (CT) and endoscopic ultrasound (EUS) can detect lymph node metastasis with accuracy of 50–90%, additional methods, such as, sentinel node mapping are probably needed for a more precise understanding of lymph node status [5–8].

Positron emission tomography-computed tomography (PET-CT) is a comparatively recent modality, and is frequently used to understand distant metastasis and lymph node metastasis in various cancers, such as, those of the lung, esophagus, and colon [9–11]. PET-CT provides general metabolic information for the diagnosis of gastric cancer, based on the amount of glycogenolysis occurring in cancer cells [11–13].

The usefulness of PET-CT in gastric cancer is controversial in the context of lymph node metastasis, because physiologic uptake is high in gastric cancer, and when primary tumor uptake is low, the detection of lymph node metastasis is difficult [14,15]. In some studies, physiologic PET-CT uptake due to high blood flow in the normal stomach wall can produce regions of high uptake activity in the gastric wall, and produce false-positive findings [15].

Furthermore, few PET-CT studies have been undertaken to evaluate lymph node metastasis in gastric cancer. Yun et al. [12] compared PET-CT with CT and found that it had low sensitivity and produced a high level of false negative findings, but in another study, it was concluded that PET-CT is a useful tool for lymph node staging, since it has good specificity in terms of understanding lymph node metastasis in gastric cancer [12,15,16].

The purpose of this study was to evaluate the relation between primary tumor uptake using peak-standardized uptake value (P-SUV) and lymph node metastasis when a diagnosed patient undergoes preoperative PET-CT.

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*Correspondence to: Sang Eok Lee, MD, Department of Surgery, Konyang University Hospital, 685 Gasuwon-dong, Seo-gu, Daejeon 302-718, South Korea, Fax: +82-42-543-8956. E-mail: srglee@hanmail.net

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MATERIALS AND METHODS

One hundred and forty-seven patients with a diagnosis of gastric cancer that underwent gastrectomy from December 2007 to March 2010 were considered for this study. Preoperative PET-CT was conducted on all patients. PET-CT images and medical records were retrospective reviewed. Eleven patients with poor quality PET-CT images were excluded, and this, 136 patients were enrolled and these constituted the study cohort.

A primary tumor lesion P-SUV by PET-CT of $\geq$3.2 was defined as a cut-off value. When the P-SUV value of a primary tumor lesion was $<$3.2, the lesion is called undetectable, and when $\geq$3.2, were refer to it as a hypermetabolic lesion.

PET/CT Imaging Protocol

All examinations were performed using a Gemini TF PET-CT scanner (Philips Medical Systems, Cleveland, OH). PET-CT was performed 60 min after injecting of 7.4 MBq of fluorodeoxyglucose (FDG) per kilogram of body weight. A helical non-enhanced CT scan was acquired from the top of the skull base to the mid-thigh with normal breathing. Immediately after CT, PET was performed to cover the same axial field. PET emission data were acquired at 1 min per bed position. Blood glucose measurements were obtained before scanning and were $<$180 mg/dL in all cases. PET images were generated by using standard 3D RAMLA (Row Action Maximum Likelihood Algorithm) time-of-flight reconstruction algorithms with CT-based attenuation correction.

Image Interpretation

All PET-CT images were read directly from the screen of a computer workstation. A region of interest was drawn on the fused PET-CT image to measure the P-SUV values of gastric lesions: SUV was defined as peak kBq/mL in the region of interest divided by the injected activity/g of body weight.

Statistical Analysis

The statistical software package for social science (SPSS) version 15.0 for Windows (SPSS Inc., Chicago, IL) was used for all analyses. Clinical and pathological variables were analyzed using the chi-square test and the Student's *t*-test. Risk factors of lymph node metastasis were determined by logistic regression analyses. All *P*-values were two sided, and statistical significance was accepted for *P*-values of $<$0.05.

RESULTS

Patient Characteristics

Patient clinicopathologic variables are showed in Table I. A total of 136 consecutive patients with gastric cancer underwent gastrectomy. Average patient age was 64 years (range, 53–73 years), and there were 98 (72.1%) men and 38 (27.9%) women. 115 (84.6%) of the gastric cancer were located in the lower third of the stomach.

Relations Between Clinicopathologic Parameters and P-SUV

Of the 136 patients, 72 (53%) had a hypermetabolic tumor, and 64 (47%) had an undetectable tumor (Table II). For hypermetabolic tumors, mean tumor size was 5.1 $\pm$ 3.4 cm, and this was significantly larger than the sizes of undetectable tumors ($P < 0.001$). Hypermetabolic lesions than undetectable lesions were associated with lymph node metastasis (50, 69.4% vs. 13, 20.3%). Gender and histology were no different in the both groups.

TABLE I. Patient Characteristics

	Number(%)
Age (years)	64.4 $\pm$ 10.5
Gender	
Male	98 (72.1)
Female	38 (27.9)
Operating time (minutes)	290.3 $\pm$ 78.2
Operation	
Subtotal gastrectomy	110 (80.9)
Total gastrectomy	16 (11.8)
Segmental resection	5 (3.7)
Proximal gastrectomy	5 (3.7)
Tumor location	
Upper	14 (10.3)
Middle	7 (5.1)
Lower	115 (84.6)
Histology	
Differentiated	59 (43.4)
Undifferentiated	77 (56.6)
Tumor size (cm)	4.0 $\pm$ 3.1
Depth of invasion	
pT1	65 (47.8)
pT2	39 (28.7)
pT3	22 (16.2)
pT4	10 (7.4)
LN metastasis	
Negative	73 (53.7)
Positive	63 (46.3)

TABLE II. Relations Between Clinicopathologic Parameters and P-SUV Values

	Undetectable[a]	Hypermetabolism	*P*-value
Age (years)	62.0 $\pm$ 10.3	66.6 $\pm$ 10.3	0.009
Gender			0.062
Male	51 (79.7)	47 (65.3)	
Female	13 (20.3)	25 (34.7)	
BMI (kg/m^2)	23.2 $\pm$ 8.1	21.4 $\pm$ 7.3	0.196
Operating time (minutes)	62.0 $\pm$ 10.3	66.6 $\pm$ 10.3	0.398
Tumor size (cm)	2.89 $\pm$ 2.3	5.1 $\pm$ 3.4	$<$0.001
Ulcer			0.145
Absent	14 (21.9)	9 (12.5)	
Present	50 (78.1)	63 (87.5)	
Depth of invasion			$<$0.001
pT1	48 (75.0)	17 (23.6)	
pT2	10 (15.6)	29 (40.3)	
pT3	4 (6.3)	18 (25.0)	
pT4	2 (3.1)	8 (11.1)	
Lymph node metastasis			$<$0.001
Negative	51 (79.7)	22 (30.6)	
Positive	13 (20.3)	50 (69.4)	
Location			0.009
Upper	8 (12.5)	6 (8.3)	
Middle	7 (10.9)	0 (0)	
Lower	49 (76.6)	66 (91.7)	
Histology			0.099
Differentiated	23 (35.9)	36 (50.0)	
Undifferentiated	41 (64.1)	36 (50.0)	

[a]When the P-SUV value of a primary tumor lesion was $<$3.2, it was called ''undetectable,'' and when $\geq$3.2, it was called hypermetabolic.

Relations Between Clinicopathologic Parameters and Lymph Node Metastasis

The numbers of cases positive for lymph node metastasis were 63 (46%), and negative for lymph node metastasis were 73 (54%), respectively (Table III). The presence of ulcer and deeper depth of invasion have a higher rate of lymph node metastasis. Mean primary tumor size in cases with lymph node metastasis was 5.7 ± 3.4 cm, and mean primary tumor size was significantly larger than in the node negative group ($P < 0.001$).

In addition, in patients with lymph node metastasis, mean P-SUV was 65.5 ± 4.5, and in patients without mean P-SUV was 1.9 ± 3.5, which was highly significant. Gender, histology, and tumor location were no different in both groups.

P-SUV and Lymph Node Metastasis

The receiver operating characteristic (ROC) curve is shown in Figure 1. Using a P-SUV cutoff value of 3.2, the sensitivity of P-SUV for lymph node metastasis was 74.6% and its specificity was 74.0%.

Logistic Regression Analysis and the Relation between P-SUV and Lymph Node Metastasis

Multiple regression analysis showed that depth of invasion and P-SUV of primary tumors were associated with lymph node metastasis (Table IV). However, tumor size, the presence of an ulcer, and tumor histology were not associated with lymph node metastasis.

DISCUSSION

The main findings of the present study are as follows: (i) A hypermetabolic primary tumor based on PET-CT P-SUV is associated with a larger tumor size and deeper invasion. (ii) The P-SUV of a primary tumor is a potent indicator of the presence of lymph node metastasis.

TABLE III. Relations Between Clinicopathologic Parameters and the Presence of Lymph Node Metastasis

	Lymph node metastasis (−) (n = 73)	Lymph node metastasis (+) (n = 63)	*P*-value
Age (years)	64.1 ± 10.7	64.8 ± 10.4	0.706
Gender			0.592
Male	54 (74.0)	44 (69.8)	
Female	19 (26.0)	19 (30.2)	
BMI (kg/m^2)	23.2 ± 8.4	21.1 ± 7.4	0.120
Ulcer			<0.001
Absent	18 (24.7)	5(7.9)	
Present	55 (75.3)	58 (92.1)	
Size (cm)	2.56 ± 1.8	5.7 ± 3.4	<0.001
Operating time (minutes)	288.8 ± 82.5	292.1 ± 10.4	0.706
Depth of Invasion			<0.001
pT1	57 (78.1)	8(12.7)	
pT2	15 (20.5)	24 (38.0)	
pT3	1 (1.4)	21 (33.3)	
pT4	0 (0)	10 (15.9)	
Tumor location			0.356
Upper	10 (13.7)	4 (6.3)	
Middle	4 (5.5)	3 (4.8)	
Lower	39 (80.8)	56 (88.9)	
Histology			0.064
Differentiated	37 (50.7)	22 (34.9)	
Undifferentiated	36 (49.3)	41 (65.1)	
P-SUV of primary tumor	1.9 ± 3.5	65.5 ± 4.5	<0.001

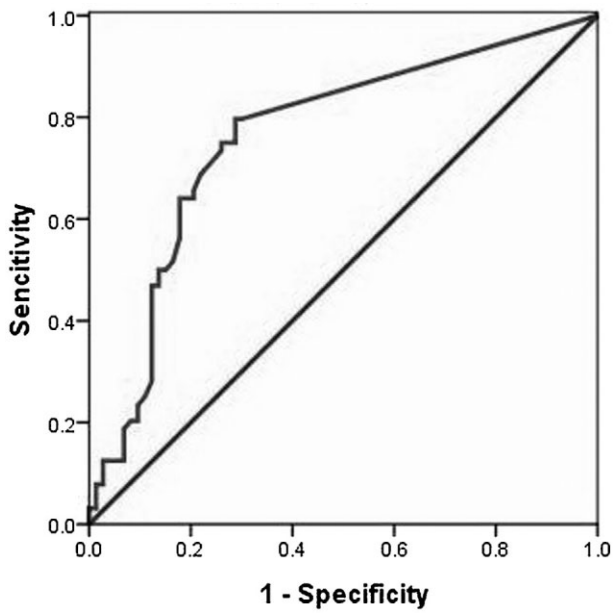

Fig. 1. Receiver operating characteristic curve for primary tumor P-SUV and the prediction of lymph node metastasis.

In another study, P-SUV values of tubular adenocarcinoma were higher than those of signet-ring cell carcinoma or mucinous carcinoma [11,17,18], but in the present study, histology had no significantly effect on P-SUV values.

Gastric cancer has a high prevalence and mortality, and thus, the accurate preoperative staging of local invasion, tumor size, lymph node involvement, and presence or absence of distant metastasis are important in terms of planning treatment and for achieving a good prognosis, and in particular, understanding the status of lymph node metastasis has much impact on both.

In terms of the tools used to diagnose lymph node metastasis, EUS provides an understanding of lymph node metastasis around lesions, but is little use for finding distant metastases. On the other hand, CT enables both regional and distant metastasis to be detected [19,20]. The usefulness of PET-CT in gastric cancer with lymph node metastasis is still controversial. Some studies on PET-CT in gastric cancer with lymph node metastasis concluded that its ability to detect and its sensitivity are low [21]. Dassen et al. reported that PET-CT has low sensitivity for the primary detection of gastric cancer, but that it provides a better understanding of lymph node metas-

TABLE IV. Multiple Logistic Regression Analysis of Relations Between Clinicopathologic Variables and Lymph Node Metastasis

	SE	OR	CI for OR	*P*-value
Size (<3.0 cm vs. ≥3.0 cm)	0.634	1.026	0.296–3.554	0.968
Ulcer (absent vs. present)	0.699	0.851	0.216–3.349	0.818
Depth of invasion pT1				0.001
pT2	0.656	7.755	2.145–28.037	0.002
pT3	1.252	101.386	8.179–1178.992	<0.001
pT4	130001.018	N.S.	N.S.	0.999
Histology (differentiated vs. undifferentiated)	0.551	2.678	0.910–7.882	0.740
P-SUV (<3.2 vs. ≥3.2)	0.552	4.452	1.508–13.146	0.007

N.S., non-significant.

tasis than CT. In fact, the consensus seems to be that PET-CT is a useful tool for assessing lymph node metastasis in gastric cancer [12,15,22].

Furthermore, hypermetabolic primary tumors are more likely to have metastasized to lymph nodes than non-hypermetabolic primary tumors. In the present study, primary tumor P-SUV values were significantly higher in cases with a positive lymph node, and multivariate analysis showed that primary lesions with a P-SUV of >3.2 were significantly more likely to have metastasized ($P < 0.001$).

In gastric cancer, no PET-CT P-SUV criterion has been devised that differentiates malignancy and benignity. Kim et al. [16] compared PET-CT with CT and found it less sensitive and exact than CT for diagnosing primary lesions and lymph node metastasis in gastric cancer, but when the CT diagnosis was equivocal, it was found that PET-CT was useful because of its high positive predictability. According to another study, PET-CT has also good specificity for LN staging in gastric cancer [10].

PET-CT has little value in detecting peritoneal carcinomatosis with a low sensitivity and a relatively high sensitivity due to extensive fibrosis around relatively few malignant cells [10,15].

CONCLUSIONS

To the best of our knowledge, the present study is the first to suggest an association between the P-SUV of a primary tumor and lymph node metastasis in gastric cancer.

Consequently, primary tumor lesions with a higher P-SUV require careful consideration with respect to the range of lymphadenectomy. However, the roles of PET-CT in the diagnosis of lymph node metastasis in patients with gastric cancer require considerably more study.

REFERENCES

1. Parkin DM, Bray F, Ferlay J, et al.: Global cancer statistics, 2002. CA Cancer J Clin 2005;55:74–108.
2. Shin H, Jung K, Won Y: National cancer incidence for the year 2002 in Korea. Cancer Res Treat 2007;39:139–149.
3. Soetikno R, Kaltenbach T, Yeh R, et al.: Endoscopic mucosal resection for early cancers of the upper gastrointestinal tract. J Clin Oncol 2005;23:4490–4498.
4. Lee SE, Lee JH, Ryu KW, et al.: Sentinel node mapping and skip metastases in patients with early gastric cancer. Ann Surg Oncol 2009;16:603–608.
5. Hyung WJ, Kim YS, Lim JS, et al.: Preoperative imaging of sentinel lymph nodes in gastric cancer using CT lymphography. Yonsei Med J 2010;51:407–413.
6. Lee JH, Ryu KW, Kim CG, et al.: Sentinel node biopsy using dye and isotope double tracers in early gastric cancer. Ann Surg Oncol 2006;13:1168–1174.
7. Park SR, Kim MJ, Ryu KW, et al.: Prognostic value of preoperative clinical staging assessed by CT in resectable gastric cancer patients: A viewpoint in the era of preoperative treatment. Ann Surg 2010;251:428–435.
8. Rosch T: Endosonographic staging of gastric cancer: A review of literature results. Gastrointest Endosc Clin N Am 1995;5: 549–557.
9. Squillaci E, Manenti G, Mancino S, et al.: Staging of colon cancer: Whole-body MRI vs. whole-body PET-CT-initial clinical experience. Abdom Imaging 2008;33:676–688.
10. Kim SK, Kang KW, Lee JS, et al.: Assessment of lymph node metastases using 18F-FDG PET in patients with advanced gastric cancer. Eur J Nucl Med Mol Imaging 2006;33:148–155.
11. Chen J, Cheong JH, Yun MJ, et al.: Improvement in preoperative staging of gastric adenocarcinoma with positron emission tomography. Cancer 2005;103:2383–2390.
12. Yun M, Lim JS, Noh SH, et al.: Lymph node staging of gastric cancer using (18)F-FDG PET: A comparison study with CT. J Nucl Med 2005;46:1582–1588.
13. Bombardieri E, Aktolun C, Baum RP, et al.: FDG-PET: Procedure guidelines for tumour imaging. Eur J Nucl Med Mol Imaging 2003;30:BP115–BP124.
14. Tschmelitsch J, Weiser MR, Karpeh MS: Modern staging in gastric cancer. Surg Oncol 2000;9:23–30.
15. Dassen AE, Lips DJ, Hoekstra CJ, et al.: FDG-PET has no definite role in preoperative imaging in gastric cancer. Eur J Surg Oncol 2009;35:449–455.
16. Kim EY, Lee WJ, Choi D, et al.: The value of PET/CT for preoperative staging of advanced gastric cancer: Comparison with contrast-enhanced CT. Eur J Radiol 2010. DOI: 10.1016/j.ejrad.2010.02.00
17. Berger KL, Nicholson SA, Dehdashti F, et al.: FDG PET evaluation of mucinous neoplasms: Correlation of FDG uptake with histopathologic features. AJR Am J Roentgenol 2000;174:1005–1008.
18. De Potter T, Flamen P, Van Cutsem E, et al.: Whole-body PET with FDG for the diagnosis of recurrent gastric cancer. Eur J Nucl Med Mol Imaging 2002;29:525–529.
19. Wakelin SJ, Deans C, Crofts TJ, et al.: A comparison of computerised tomography, laparoscopic ultrasound and EUS in the preoperative staging of oesophago-gastric carcinoma. Eur J Radiol 2002;41:161–167.
20. Cheong O, Oh ST, Kim BS, et al.: Large metastatic lymph node size, especially more than 2 cm: Independent predictor of poor prognosis in node-positive gastric carcinoma. World J Surg 2008;32:262–266.
21. Yang QM, Kawamura T, Itoh H, et al.: Is PET-CT suitable for predicting lymph node status for gastric cancer? Hepatogastroenterology 2008;55:782–785.
22. Mukai K, Ishida Y, Okajima K, et al.: Usefulness of preoperative FDG-PET for detection of gastric cancer. Gastric Cancer 2006;9:192–196.