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수술 가능한 췌장암 환자에서의 PET/CT 의 유용성: 림프절 전이 진단 및 생존율 예측

The utility of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography in patients with resectable pancreatic cancer: Diagnosing lymph node metastasis and predicting survival

울 산 대 학 교 대 학 원

의 학 과

김 형 래

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지 도 교 수　　조 재 철

이 논문을 의학석사 학위 논문으로 제출함

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울 산 대 학 교 대 학 원
의 학 과
김 형 래

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심사위원 박설훈 인

심사위원 조재철 인

심사위원 박형우 인

울 산 대 학 교 대 학 원

2017년 12월

ABSTRACT

Hyung Rae Kim

Department of Internal Medicine,

Graduate School, University of Ulsan

Directed by Professor Jae-Cheol Jo M.D.

Purpose: To evaluate the diagnostic accuracy of ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) for lymph node (LN) metastasis and the prognostic significance of FDG PET/CT LN parameters in patients with resectable pancreatic cancer.

Patients and Methods: Patients with resectable pancreatic cancer who underwent staging FDG PET/CT between May 2007 and September 2016 were retrospectively enrolled and analyzed through medical record and image reevaluation. The diagnostic accuracy of FDG

PET/CT in predicting LN metastasis was evaluated and compared with that of enhanced CT. Prognostic variables, including LN parameters assessed by FDG PET/CT (standardized uptake value $[SUV]_{LN}$ and LN/tumor SUV ratio), that affect disease-free survival (DFS) and overall survival (OS) were evaluated by regression analysis.

Results: When predicting LN metastasis, FDG PET/CT showed greater sensitivity, positive predictive value, negative predictive value, and accuracy than enhanced CT. Among prognostic factors affecting DFS, PET-positive LN (p = 0.008) and LN/tumor SUV ratio (p = 0.003) were found to be significant by regression analysis. Among variables affecting OS, lympho-vascular invasion (p = 0.018) and LN/tumor SUV ratio (p = 0.046) were found to be significant.

Conclusion: FDG PET/CT showed higher diagnostic accuracy in predicting LN metastasis than enhanced CT in patients with resectable pancreatic cancer. Only LN/tumor SUV ratio of

FDG PET/CT was an independent prognostic variable in both DFS and OS.

Keywords: pancreatic cancer, FDG PET/CT, LN metastasis, lymph node to tumor SUV ratio, disease free survival, overall survival

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Abbreviations

CA 19-9, carbohydrate antigen 19-9

CI, confidence interval

CT, computed tomography

DFS, disease free survival

FDG, ^{18}F-fluorodeoxyglucose

HR, hazard ratio

LN, lymph node

LN ratio, metastatic LNs/retrieved LNs

LN/tumor SUV ratio, LN SUV_{max}/ tumor SUV_{max}

LVI, lympho-vascular invasion

MD, moderate differentiation

NPV, negative predictive value

OS, overall survival

PD, poor differentiation

PET/CT, positron emission tomography/computed tomography

pLN stage, pathologic LN stage

pN1 stage, pathologic N1 stage

PNI, perineural invasion

PPV, positive predictive value

pT stage, pathologic T stage

SUV, standardized uptake value

SUV_{LN}, LN SUV_{max}

SUV_{max}, maximum standardized uptake value

SUV_{tumor}, tumor SUV_{max}

WD, well differentiation

INTRODUCTION

Despite advances in medical technology, pancreatic cancer remains one of the world's deadliest malignancies. Although complete resection is curative in early-stage pancreatic cancer, only 15%-20% of cancers are found to be resectable at the time of diagnosis [1]. Even when complete resection is performed, recurrence develops in as high as 42% to 68% of patients, especially within the first 6 to 12 months [2]. Inoperative pancreatic cancer is known to have a poor prognosis. The 5-year overall survival rate is usually poor, reports being as low as <5% for locally advanced unresectable pancreatic cancer [3].

Known prognostic factors for pancreatic cancer include carbohydrate antigen 19-9 (CA 19-9) [4], pathologic T stage (pT stage), tumor size, lympho-vascular invasion (LVI), perineural invasion (PNI), involvement of resection margin, and lymph node (LN) metastasis [5-7]. Due to the aggressive biology of pancreatic cancer, LN metastasis is often present from the time of cancer detection [8] and is associated with poor prognosis [9]. Thus,

accurate evaluation of LN metastasis is important for determining operative field and predicting prognosis in pancreatic cancer [9].

Among modalities for detecting LN metastasis, conventional anatomical imaging such as enhanced computed tomography (CT) is initially recommended [10]. However, the diagnostic accuracy of CT in evaluating LN metastasis in pancreatic cancer is relatively low because of the presence of many sub-centimeter LN metastases [11]. The fact that ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) shows higher accuracy in the detection of pancreatic cancer and distant metastasis than enhanced CT has been demonstrated by many previous studies [12-15]. However, although many reports have shown that FDG PET/CT is more accurate for LN staging than enhanced CT [16-18] in various cancers, few studies have assessed LN detection by FDG PET/CT in pancreatic cancer, and these have presented conflicting results, with a wide range of diagnostic accuracy [1, 19-21]. Moreover, to our knowledge, there is no study on the prognostic significance of LN parameters in pancreatic cancer.

The aim of our study was to determine the diagnostic performance of FDG PET/CT in predicting LN metastasis and to evaluate whether the obtained LN parameters have prognostic significance for survival in patients with resectable pancreatic cancer.

PATIENTS AND METHODS

1. *Patients*

From May 2007 to September 2016, 85 patients underwent radical surgery and were found to have pancreatic ducal adenocarcinoma. Exclusion criteria were as follows; preoperative FDG PET/CT not performed (n=9), incomplete FDG PET/CT information (ex.: outside PET/CT, could not measure FDG uptake, n=3), and patients treated with neoadjuvant therapy (n=3). Finally, 70 patients were enrolled in this study.

All clinical and pathological data such as sex, age, dates of clinical importance (operation, disease recurrence, death, and last follow-up), initial serum CA 19-9 level, history of postoperative chemotherapy and/or radiotherapy, pT stage, pathologic LN stage (pLN stage), tumor differentiation, T size, status of LVI or PNI, number of metastatic LNs and LN ratio (total number of metastatic LNs divided by total number of retrieved LNs) were collected and reviewed. TNM staging of pancreatic cancer was determined according to the 7th edition of the American Joint Committee on Cancer manual [22]. This

retrospective study was approved by the institutional review board of our hospital.

2. *PET/CT acquisition*

FDG PET/CT scans were obtained from the skull base to the upper thigh using dedicated PET/CT scanners (DSTe 8, Milwaukee, WI & Gemini 64, Philips Medical Systems, Andover, MA, USA) after at least 6 hours of fasting and checking the blood glucose level. The injection dose of FDG was 0.1 (Gemini) to 0.2 (DSTe) mCi/body weight (kg) and the time interval between FDG injection and image acquisition was approximately 60 to 70 min. Low-dose non-contrast CT was performed for attenuation correction, followed by PET acquisition of 1.5 (Gemini) to 2.5 (DSTe) min per bed (a total of 6-9 bed positions) in 3D mode. All PET/CT images were reconstructed using an ordered-subsets expectation maximization algorithm. Maximum intensity projection and cross-sectional (trans-axial, coronal, sagittal) images with PET/CT fusion were generated and uploaded into the GE AW 4.5 workstation.

3. *Image analysis*

All FDG PET/CT images were analyzed on a GE AW 4.5 workstation. To determine whether a specific LN was positive on PET (PET-positive LN), two experienced nuclear medicine physicians visually analyzed the scans without knowledge of the patient's pathologic findings. PET-positive LNs were defined as LNs whose FDG uptake was higher than that of adjacent blood pool activity. To compare diagnostic accuracy, positive LN on CT was defined as when the short-axis size is greater than 1 cm. Quantitative analysis of primary tumor and LN parameters on FDG PET/CT was performed using maximum standardized uptake value (SUV_{max}). SUV_{tumor} and SUV_{LN} were defined as the SUV_{max} of the most avid tumor and LN. When there was no visible LN on FDG PET/CT, adjacent blood pool activity was considered as the SUV_{LN}. The margin of volume of interest was manually readjusted by visual inspection to avoid overlapping of adjacent LN or non-LN FDG uptakes. LN/tumor SUV ratio was defined as the SUV_{max} ratio of LN to primary tumor.

4. *Survival analysis*

This study assessed both disease-free survival (DFS) and overall survival (OS) as primary outcomes. DFS was defined as the time interval (months) between the surgery and tumor recurrence or death from any cause. Tumor recurrence based on clinical follow-up data of the medical record was used in this study. OS was defined as the time interval (months) between surgery and death or last follow-up.

5. *Statistical Analysis*

The sensitivity, specificity, positive predictive value, and negative predictive value and accuracy of FDG PET/CT and enhanced CT in predicting LN metastasis were statistically compared using McNemar's test. The chi-square test and Fisher's exact test were used to evaluate the association between categorical variables. The independent t-test was used to evaluate the association between categorical variables and continuous variables. Median value was used to determine the cut-off value of continuous variables. Survival

analysis was conducted using the Kaplan-Meier method. The Cox proportional-hazards model was used to assess prognostic variables. All statistical analyses were performed using SPSS (version 24 for windows; SPSS Inc.). *P*-value of less than 0.05 was considered statistically significant.

RESULTS

1. *Patients characteristics*

The median age of the 70 patients was 69 (41-89) years and 30 patients were men (42.9%). The median value (range) of baseline CA 19-9 level was 67.3 (0.01-6694.6) U/mL. The median value (range) of primary tumor size was 30 (15–120) mm, and resection margin was positive in 12 patients (17.1%). LVI and PNI were positive in 42 (60.0%) and 60 (85.7%) patients, respectively. N1 stage was present in 41 patients (58.6%), The median value of LN ratio was 0.049 (0.000-1.000). The majority of pancreatic cancers showed moderate differentiation (62.9%). In FDG PET/CT analyses, PET-positive LN was present in 31 patients (44.3%). The median values of SUV_{tumor}, SUV_{LN}, and LN/tumor SUV ratio were 3.95 (1.2–20.9), 1.5 (0.7–3.8), and 0.384 (0.060–1.455) respectively. Adjuvant therapy (chemotherapy and/or radiotherapy) was performed in 47 (67.1%) patients. The detailed characteristics of the 70 study patients are shown in Table 1.

Table 1.Clinico-pathologic Characteristics

Characteristics	All patients (n = 70)	Recurrence (n = 46)	Nonrecurrence (n = 24)	*P-value*
Age*	69 (41-89)	65.5 (41-81)	71 (50-89)	0.003
Male, n (%)	30 (42.9)	19 (41.3)	11 (45.8)	0.716
Surgery, n (%)				
Pancreaticoduodenectomy	51 (72.9)	34 (73.9)	17 (70.8)	
Distal pancreatectomy	19 (27.1)	12 (26.1)	7 (29.2)	
Adjuvant therapy (+), n (%)	47 (67.1)	31 (67.4)	16 (66.7)	0.951
CA 19-9*, U/mL	67.3 (0.01-6694.6)	81.0 (0.01-6694.6)	63.3 (1.75-2817.1)	0.085
Primary tumor				
Tumor size*, mm	30 (15-120)	30 (16-120)	30 (15-60)	0.366
LVI (+), n (%)	42 (60.0)	31 (67.4)	11 (45.8)	0.081
PNI (+), n (%)	60 (85.7)	40 (87.0)	20 (83.3)	0.727
Resection margin (+), n (%)	12 (17.1)	9 (19.6)	3 (12.5)	0.526
Tumor differentiation, n (%) (WD/MD/PD)	10/44/16 (14.3/62.9/22.8)	4/31/11 (8.7/67.4/23.9)	6/13/5 (25.0/54.2/20.8)	0.179
T stage, n (%)				0.266
T2	2 (2.9)	2 (4.3)	0 (0.0)	
T3	67 (95.7)	44 (95.7)	23 (95.8)	
T4	1 (1.4)	0 (0.0)	1 (4.2)	
SUV_{tumor}*	3.95 (1.2-20.9)	4.35 (1.7-20.9)	3.10 (1.2-9.1)	0.028

Metastatic LN				
pN1 stage, n (%)	41 (58.6)	26 (56.5)	15 (62.5)	0.630
LN ratio*	0.049 (0.000-1.000)	0.052 (0.000-0.667)	0.048 (0.000-1.000)	0.861
CT positive LN, n (%)	14 (21.2)	11 (25.6)	3 (13.0)	0.346
PET positive LN, n (%)	31 (44.3)	23 (50.0)	8 (33.3)	0.183
SUV_{LN}*	1.5 (0.7-3.8)	1.6 (0.7-3.6)	1.4 (1.0-3.8)	0.999
TNM stage, n (%)				0.530
ⅠB	2 (2.9)	2 (4.3)	0 (0.0)	
ⅡA	27 (38.6)	18 (39.1)	9 (37.5)	
ⅡB	40 (57.1)	26 (56.6)	14 (58.3)	
Ⅲ	1 (1.4)	0 (0.0)	1 (4.2)	
LN/tumor SUV ratio*	0.384 (0.060-1.455)	0.362 (0.060-0.958)	0.542 (0.190-1.455)	0.010

* Median (range)

CA 19-9, carbohydrate antigen 19-9; LVI, lympho-vascular invasion; PNI, peri-neural invasion; RM, resection margin; WD, well differentiation; MD, moderate differentiation; PD, poor differentiation; SUV_{tumor}, tumor SUV_{max}; LN, lymph node; pN1 stage, pathologic N1 stage; LN ratio, metastatic LNs/retrieved LNs; SUV_{LN}, LN SUV_{max}; LN/tumor SUV ratio, LN SUV_{max}/ tumor SUV_{max}

2. ***Diagnostic performance for prediction of LN metastasis; FDG PET/CT vs enhanced CT***

Among the 70 patients, 4 were excluded because enhanced CT was not performed, and the remaining 66 were analyzed. Although enhanced CT showed slightly higher specificity than FDG PET/CT, FDG-PET/CT showed higher diagnostic performance in sensitivity (61.0%), positive predictive value (PPV, 80.7%), negative predictive value (NPV, 59.0%), and accuracy (68.6%) than enhanced CT ($p < 0.001$) (Table 2).

Table 2. Diagnostic peformance of FDG PET/CT and enhanced CT for LN metastasis

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
FDG PET/CT	61.0	79.3	80.7	59.0	68.6
Enhanced CT	25.0	84.6	71.4	42.3	48.5

PPV, positive predictive value; NPV, negative predictive value,

3. *Evaluation of prognostic factors for DFS and OS*

The cut-off values for tumor size, SUV_{tumor}, LN ratio, SUV_{LN}, LN/tumor SUV ratio, and CA 19-9 level were 30 mm, 3.95, 0.049, 1.5, 0.384, 67.30 U/mL, respectively. In univariate analysis for DFS, the resection margin (p = 0.045), LVI (p = 0.018), SUV_{tumor} (p = 0.021), PET positive LN (p = 0.049) and LN/tumor SUV ratio (p = 0.018) were statistically significant (Table 3). Multivariate analysis was performed using these significant parameters and only PET-positive LN (p = 0.008, hazard ratio [HR] 2.294, 95% confidence interval [CI] 1.247 to 4.211) and LN/tumor SUV ratio (p = 0.003, HR 2.396, 95% CI 0.213 to 0.735) were determined to be independent prognostic factors associated with DFS (Table 4). Figure 1 shows Kaplan-Meier survival graphs according to PET-positive LN and LN/tumor SUV ratio in DFS.

Table 3. Univariate analysis of prognostic factors for DFS and OS

Prognostic factors	DFS				OS			
	No. Patients	No. Recurrence	Median [month]	*P-value*	No. Patients	No. Death	Median [month]	*P-value*
Tumor size, mm								
≤ 30	39	24	15.87	0.201	39	12	78.57	0.430
> 30	31	22	12.93		31	10	26.43	
Resection margin								
-	58	37	15.17	0.045	58	20	78.57	0.940
+	12	9	7.57		12	2	20.79	
Tumor differentiation								
WD & MD	54	35	14.20	0.580	54	16	78.57	0.285
PD	16	11	12.77		16	6	45.6	
LVI								
-	28	15	58.37	0.018	28	4	93.62	0.003

	+	42	31	12.77		42	18	26.43	
PNI									
	-	10	6	20.47	0.457	10	2	68.38	0.273
	+	60	40	13.40		60	20	78.57	
SUV_{tumor}									
	≤ 3.95	35	20	25.67	0.021	35	9	78.57	0.073
	> 3.95	35	26	8.40		35	13	41.64	
pLN stage									
	N0	29	20	13.40	0.993	29	11	68.15	0.686
	N1	41	26	14.20		41	11	78.57	
LN ratio									
	≤ 0.049	35	23	15.17	0.500	35	11	74.86	0.645
	> 0.049	35	23	12.93		35	11	41.23	
PET positive LN									
	-	39	23	16.87	0.049	39	12	78.57	0.435

+	31	23	9.97		31	10	41.23	
SUV_{LN}								
≤ 1.5	38	23	16.87	0.058	38	13	78.57	0.724
> 1.5	32	23	8.40		32	9	31.87	
LN/tumor SUV ratio								
≤ 0.384	34	26	10.70	0.018	34	15	26.43	0.007
> 0.384	36	20	20.47		36	7	90.86	
Adjuvant therapy								
-	23	15	12.77	0.554	23	5	72.34	0.678
+	47	31	13.87		47	17	41.23	
CA19-9, U/mL								
≤ 67.30	35	23	14.20	0.707	35	14	41.23	0.420
> 67.30	35	23	12.93		35	8	72.22	

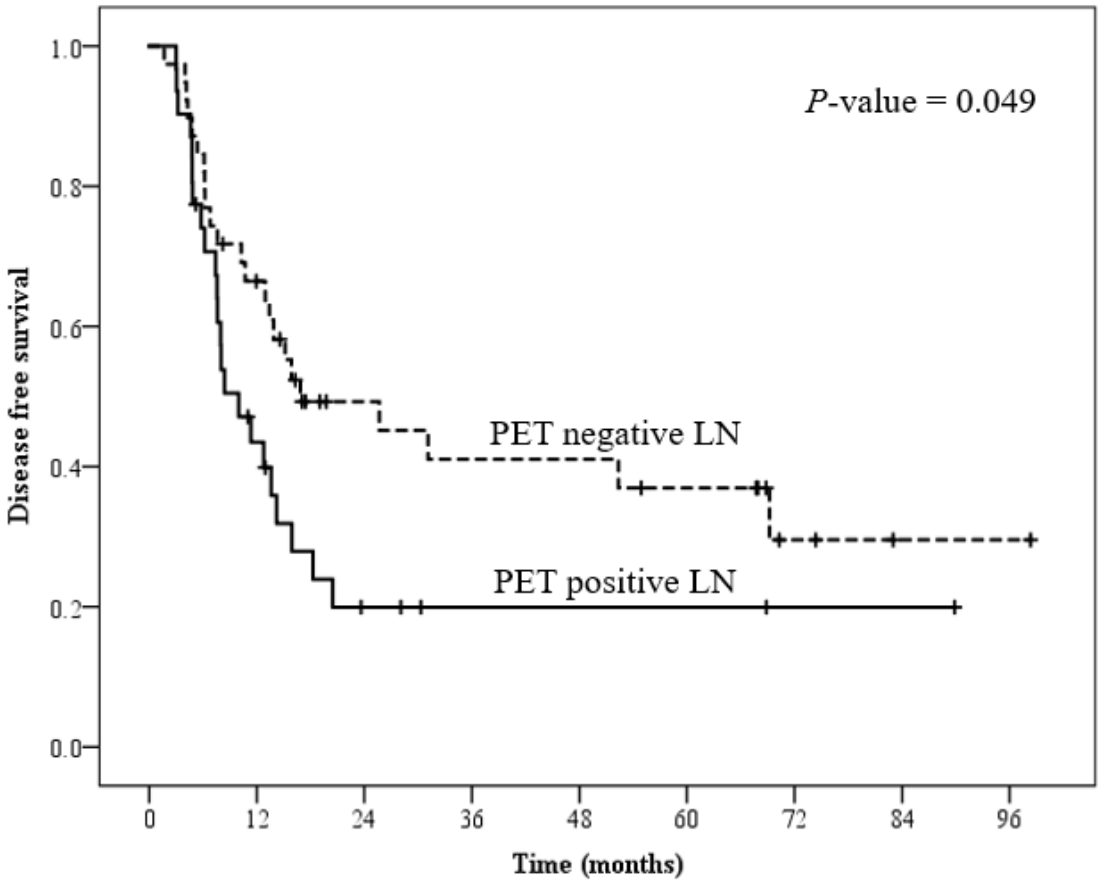
DFS, disease free survival; OS, overall survival; WD, well differentiation; MD, moderate differentiation; PD, poor differentiation; LVI, lympho-vascular invasion; PNI, peri-neural invasion; SUV_{tumor}, tumor SUV_{max}; LN, lymph node; pLN stage, pathologic LN stage; LN ratio, metastatic LNs/retrieved LNs; SUV_{LN}, LN SUV_{max}; LN/tumor SUV ratio, LN SUV_{max}/ tumor SUV_{max}; CA 19-9, carbohydrate antigen 19-9

Table 4. Multivariate analysis for DFS

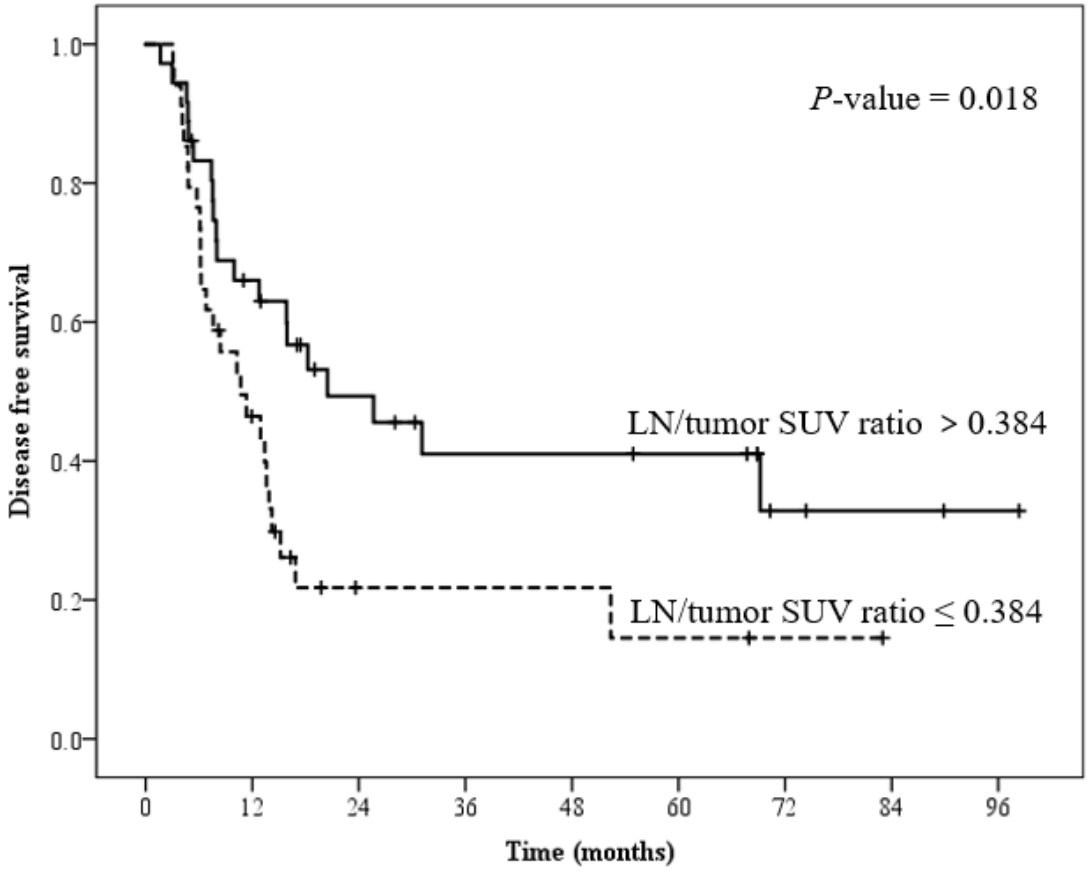
Prognostic factors	*P-value*	Hazard Ratio (Confidence interval)
PET positive LN	0.008	2.294 (1.247-4.211)
LN/tumor SUV ratio	0.003	0.396 (0.213-0.735)

DFS, disease free survival; LN/tumor SUV ratio, LN SUV_{max}/ tumor SUV_{max}

Figure 1. Kaplan-Meier survival curve for DFS according to PET positive LN(A), LN/tumor SUV ratio (B).



(A)



(B)

DFS, disease free survival; LN/tumor SUV ratio, LN SUV_{max}/ tumor SUV_{max};

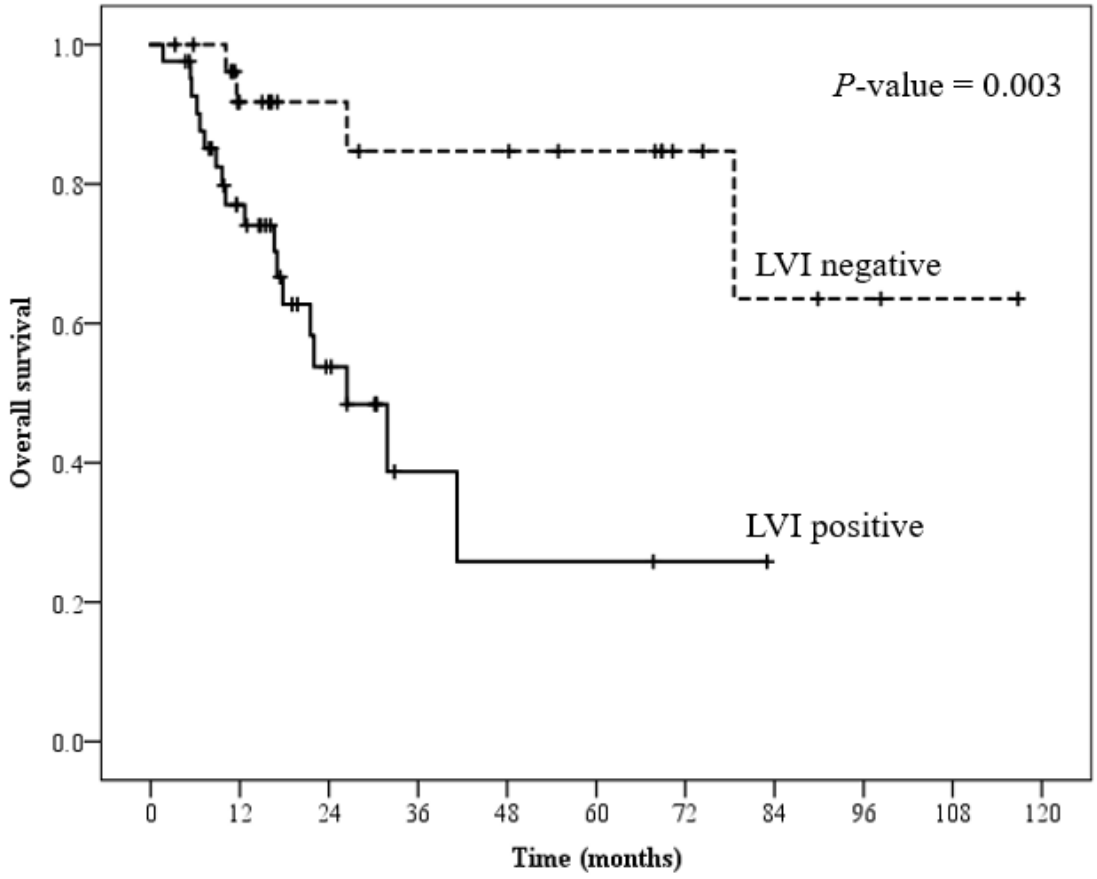
In univariate analysis for OS, LVI (p = 0.003) and LN/tumor SUV ratio (p = 0.007) were significant factors. The LVI (p = 0.018, HR 3.894, 95% CI 1.263 to 12.005) and LN/tumor SUV ratio (p = 0.046, HR 0.390, 95% CI 0.155 to 0.983) were also found to be statistically independent prognostic factors in multivariate analysis (Table 5). Figure 2 shows Kaplan-Meier survival graphs according to LVI and LN/tumor SUV ratio in OS.

Table 5. Multivariate analysis for OS

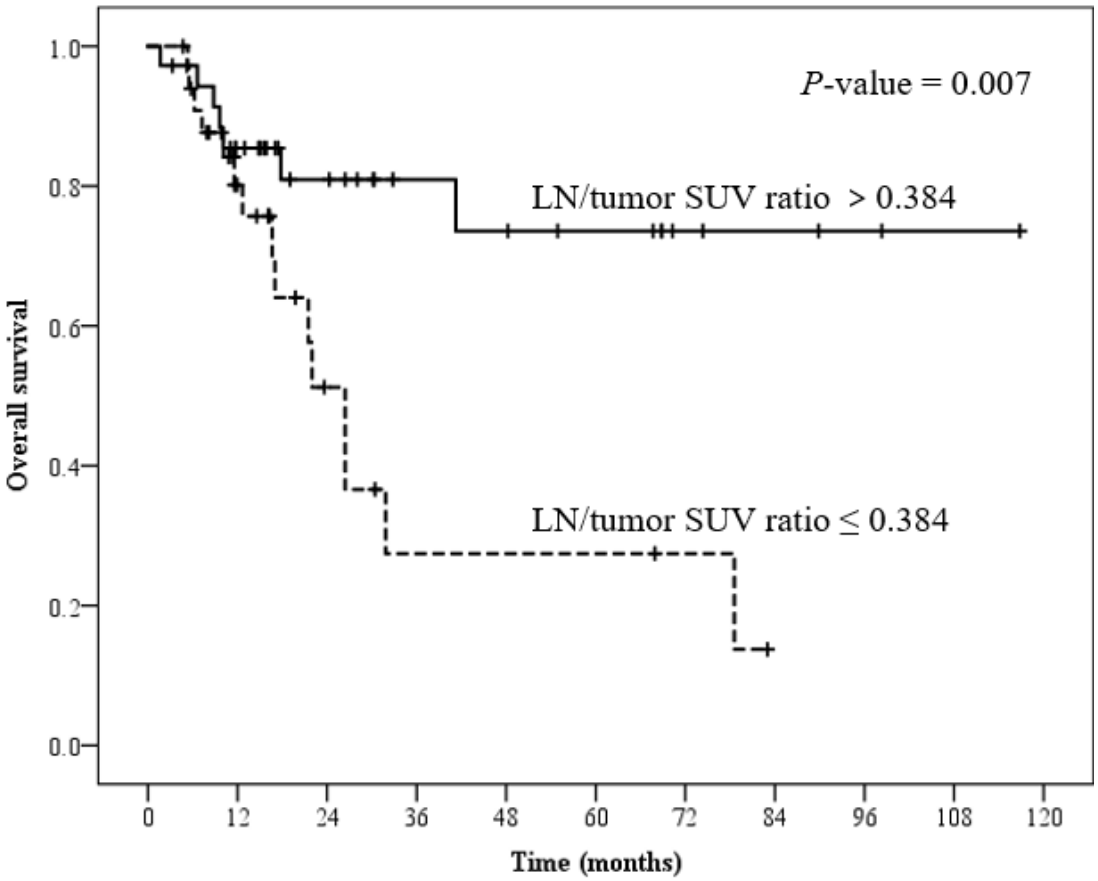
Prognostic factors	*P-value*	Hazard Ratio (Confidence interval)
LVI	0.018	3.894 (1.263 - 12.005)
LN/tumor SUV ratio	0.046	0.390 (0.155 - 0.983)

OS, overall survival; LVI, lympho-vascular invasion; LN/tumor SUV ratio, LN SUV_{max}/ tumor SUV_{max}

Figure 2. Kaplan-Meier survival curve for OS according to LVI (A), LN/tumor SUV ratio (B).



(A)



(B)

OS, overall survival; LVI, lympho-vascular invasion; LN/tumor SUV ratio, LN SUV_{max}/ tumor SUV_{max}

DISCUSSION

The aims of this study were to evaluate whether LN evaluation by FDG PET/CT is feasible for predicting LN metastasis and whether FDG PET/CT-derived LN parameters may serve as prognostic factors in patients with resectable pancreatic cancer. The present study found that FDG PET/CT has a higher diagnostic accuracy than enhanced CT and that PET-positive LN and LN/tumor SUV ratio are independent prognostic factors for survival. To our knowledge, this study is the first to assess the value of PET/CT-derived LN parameter as a prognostic parameter in patients with pancreatic cancer.

Unlike other types of cancer, only a small number of studies have assessed LN metastasis by using FDG PET/CT in pancreatic cancer. When first reported in 1994, the sensitivity of PET for predicting LN metastasis was 76%, whereas that of CT was as low as 18% in 17 patients with pancreatic cancer [21]. Another study reported that the sensitivity, specificity, and accuracy of FDG PET for predicting metastasis were 70%, 97%, and 87% [20], and suggested that FDG PET might help in evaluating LN metastasis in pancreatic

cancer. However, the sensitivity of FDG PET/CT was as low as 30% in a prospective study [1]. The reason for this variability in diagnostic performance is thought to be due to the differences in study population and cut-off values used for determining LN metastasis. In the present study in which we evaluated a relatively larger population and used blood-pool activity for cut-off SUV values, the diagnostic performance of FDG PET/CT was statistically greater than that of enhanced CT and results were similar to those of a previous meta-analysis [14].

Several studies have assessed the value of FDG PET/CT for predicting prognosis in pancreatic cancer. SUV_{tumor} reflects glucose metabolic activity of the primary tumor and its prognostic significance has been reported in several studies [23-27]. Although SUV_{tumor} is associated with survival in pancreatic cancer, the optimal cut-off SUV_{max} of primary tumor has been variably reported, with a wide range from 3.0 to 6.8 [23-27]. The reason for various cut-off values may be due to differences in patient number and characteristics (cancer stage). A recent study with similar patient characteristics and cut-off value as in our study reported

that SUV_{tumor} > 4.2 (p = 0.047) is an independent prognostic factor for recurrence-free survival in pancreatic cancer [28]. In our study, SUV_{tumor} was significantly associated with DFS (p = 0.021) by univariate analysis, even though it was not significant by multivariate analysis. SUV_{tumor} was not significantly associated with OS. For these reasons, SUV_{tumor} alone may not be enough to predict preoperative prognosis in resectable pancreatic cancer despite its importance.

The association between the PET/CT-derived LN parameter and prognosis has not been reported in pancreatic cancer. In other types of cancer, as with high metabolic activity of the primary tumor, high metabolic activity of LNs is also associated with poor prognosis [29-32]. In the present study, metabolic activity of LNs higher than that of the adjacent blood pool was positively associated with DFS (p = 0.049). We suggest that pancreatic cancer with PET-positive LN may require close follow-up to quickly detect tumor recurrence. However, this was a retrospective study performed at a single center and there may be limitations in immediately applying the findings of our study in clinical practice. Further prospective

multicenter trials are needed to evaluate the prognostic value of PET-positive LN in pancreatic cancer.

Because a LN is usually much smaller than the primary tumor, its metabolic activity often shows a partial volume effect [33]. For this reason, a PET-derived LN parameter, such as SUV_{LN}, is often underestimated and may not be a reliable prognostic factor. To overcome this problem, LN/tumor SUV ratio was proposed as a factor that is less affected by the partial volume effect because it assesses the relationship between SUV_{max} values of the primary tumor and the LN. Several recent studies have evaluated the clinical significance of this new parameter [34-37]. Mattes et al. reported that LN/tumor SUV ratio was more accurate than SUV_{tumor} when assessing nodes of low-to-intermediate SUV in non-small cell lung cancer [34]. Cerfolio et al. reported that LN/tumor SUV ratio of the mediastinal lymph nodes predicts mediastinal nodal pathology in patients with non-small cell lung cancer [37]. Park et al. reported that LN/tumor SUV ratio predicts the presence of axillary LN metastasis in breast cancer [36]. Kim et al. reported that LN/tumor SUV ratio

was an independent factor for predicting relapse in invasive ductal breast cancer [35].

To date, the prognostic significance of LN/tumor SUV ratio in pancreatic cancer has not been reported. In the present study, LN/tumor SUV ratio was a statistically significant parameter for predicting both DFS and OS. Unlike previous studies that showed a positive correlation, we detected a negative correlation between LN/tumor SUV ratio and survival, using a cut-off ratio value of 0.384. This may be because unlike in other types of cancer, SUV_{LN} was much lower than SUV_{tumor} and was within a narrow range. Primary tumor SUV seems to be a more significant factor for LN/tumor SUV ratio than in other types of cancer. Further studies are needed to clarify the relationship between LN/tumor SUV ratio and survival in pancreatic cancer.

This study also analyzed other well-known prognostic factors obtained from clinicopathologic data along with PET-derived LN parameters. Among these, resection margin and LVI were statistically significant factors for DFS by univariate analysis. However, these were not independent prognostic factors after adjustment for other

parameters in multivariate analysis. For OS, LVI alone was an independent factor. There is a limitation in applying these results in the general population because this study assessed only a limited group with resectable pancreatic cancer. There have been conflicting results on the prognostic significance of LVI [38-40]. Further large studies are needed to clarify the extent to which LVI affects prognosis.

This study had several limitations. First, it was a retrospective study performed at a single institution. Selection bias may be present, although our study had relatively more patients than those of prior studies. Second, these results were derived from patients who underwent surgical resection and may not be applicable to patients with inoperable pancreatic cancer. Third, partial volume effects in small sized tumors and LNs may have affected the results of this study. However, LN/tumor SUV ratio, which is relatively unaffected by the partial volume effect, was found to be an independent prognostic factor in this study.

The clinical implication of the present study is that FDG PET/CT is applicable for risk

stratification in pancreatic cancer before surgery. In particular, PET/CT-derived LN parameters, such as PET-positive LN and LN/tumor SUV ratio, were significant for survival in resectable pancreatic cancer. Unlike pathologic parameters that are assessable only after surgery, PET/CT-derived LN parameters can predict prognosis before surgery and may be useful for establishing a fast and proper treatment plan. In addition, the parameters can help in selecting a high-risk group that requires active surveillance for the early detection of recurrence after treatment.

CONCLUSION

FDG PET/CT has a higher diagnostic accuracy in predicting LN metastasis than that of enhanced CT in patients with resectable pancreatic cancer. This is the first study to evaluate the prognostic significance of PET/CT-derived LN parameters in pancreatic cancer. PET-positive LN and LN/tumor SUV ratio were independent prognostic factors for DFS. LVI and LN/tumor SUV ratio were significant factors for OS. LN/tumor SUV ratio was the only prognostic parameter for DFS and OS and may be used for risk stratification in patients with resectable pancreatic cancer.

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국문 요약

연구목적: 수술 가능한 췌장암 환자의 림프절 전이를 평가하는 데 있어 양전자 단층 촬영 검사의 진단 정확도를 평가하고, 양전자 단층 촬영 검사에서 얻어진 림프절 관련 변수 중 이 환자 군의 예후를 예측하는데 의미 있는 인자들에 대해 알아본다.

방법: 2007년 5월부터 2016년 9월까지 본원에서 췌장암 진단 하에 수술 전 양전자 단층 촬영 검사를 시행하고 이어서 수술을 시행 받은 환자들의 의무기록 및 영상 검사를 후향적으로 분석 하였다. 병리 소견을 기준으로 양전자 단층 촬영 검사와 조영 증강 전산화 단층촬영 사이 림프절 전이 진단 정확도를 McNemar test를 통해 통계학적으로 비교하였다. 양전자 단층 촬영 검사를 통해 얻어진 림프절 관련 변수들이 무병생존기간 및 전체생존기간에 미치는 영향은 Kaplan-Meier survival analysis와 Cox proportional-hazards regression을 통하여 평가하였다.

결과: 림프절 전이를 예측하는데 있어서 양전자 단층 촬영 검사는 조영 증강 전산화 단층 촬영보다 높은 민감도, 양성예측도, 음성 예측도, 정확도를 보여주었다. 무병생존기간은 양전자 단층 촬영 검사에서 림프절이 주변 혈액풀보다 높은 섭취를 보일 때 (p = 0.008), 림프절과 원발 종양 사이의 FDG 섭취 비가 낮을수록 (p = 0.003) 통계학적으로 의미 있는 감소를 보였다. 전체 생존 기간은 수술 후 얻은 종양조직에서 림프관 침윤이 있을 때 (p = 0.018) 그리고 림프절과 종양 사이의 FDG 섭취 비가 낮을수록 (p = 0.046) 의미 있게 감소하는 것으로 나타났다.

결론: 양전자 단층 촬영 검사는 췌장암 환자에서 수술 전 림프절 전이를 평가하는데 있어서 전통적인 영상 검사인 조영 증강 전산화 단층 촬영 보다 높은 진단 정확도를 나타내었다. 그리고 림프절과 원발 종양 사이의 FDG 섭취 비는 수술 가능한 췌장암의 무병 생존 기간과 전체 생존 기간을 예측하는 데 좋은 예후인자로 생각된다.

중심단어: 췌장암, 양전자 단층 촬영 검사, 림프절 전이, 림프절과 원발 종양 사이의 FDG 섭취 비, 무병 생존 기간, 전체 생존 기간