Preoperative Volume-Based PET Parameter, MTV2.5, as a Potential Surrogate Marker for Tumor Biology and Recurrence in Resected Pancreatic Cancer

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Abstract: This study aims to evaluate the role of volume-based positron emission tomography parameters as potential surrogate markers for tumor recurrence in resected pancreatic cancer. Between January 2008 and October 2012, medical records of patients who underwent surgical resection for pancreatic ductal adenocarcinoma and completed 18F-fluorodeoxyglucose positron emission tomography/CT as a part of preoperative staging work-up were retrospectively reviewed. Not only clinicopathologic variables but also positron emission tomography parameters such as SUVmax, MTV2.5 (metabolic tumor volume), and TLG (total lesion glycolysis) were obtained.

Twenty-six patients were women and 31 were men with a mean age of 62.9 ± 9.1 years. All patients were preoperatively determined to resectable pancreatic cancer except 1 case with borderline resectability. R0 resection was achieved in all patients and 45 patients (78.9%) received postoperative adjuvant chemotherapy with or without radiation therapy. Median overall disease-free survival was 12.8 months with a median overall disease-specific survival of 25.1 months. SUVmax did not correlate with radiologic tumor size (P = 0.501); however, MTV2.5 (P = 0.001) and TLG (P = 0.009) were significantly associated with radiologic tumor size. In addition, MTV2.5 (P < 0.001) and TLG (P < 0.001) were significantly correlated with a tumor differentiation. There were no significant differences in TLG and SUVmax according to lymph node ratio; only MTV2.5 was related to lymph node ratio with marginal significance (P = 0.055). In multivariate analysis, lymph node ratio (Exp[β] = 2.425, P = 0.025) and MTV2.5 (Exp[β] = 2.273, P = 0.034) were identified as independent predictors of tumor recurrence following margin-negative resection. Even after tumor size-match analysis, MTV2.5 was still identified as a significant prognostic factor in resected pancreatic cancer (P < 0.05). However, preoperative neoadjuvant treatment attenuated adverse oncologic impact of high preoperative MTV2.5 (P = 0.210).

INTRODUCTION

Pancreatic cancer is one of the most lethal malignant tumors arising from the gastrointestinal tract. Margin-negative pancreatectomy is an essential step for cure of disease; however, most patients are diagnosed at advanced stages of pancreatic cancer that preclude curative resection. Even after R0 resection, most patients experience systemic tumor recurrence and finally die due to cancer progression. Therefore, further investigations are needed to determine optimal strategies for early diagnosis, safe margin-negative pancreatectomy, the stratification of patients in terms of recurrence risk, and effective adjuvant treatment.

For the purpose of accurate and reliable clinical and prognostic assessment, positron emission tomography (PET), which has the benefit for revealing the information about biological properties of tumors, has been frequently used in clinical practice. In fact, PET has been shown to provide several important clinical information about pancreatic cancer in terms of differential diagnosis between benign and malignant neoplasms, preoperative staging, the evaluation of therapeutic response, and the prediction of prognosis.

Fluorine-18 fluorodeoxyglucose (18F-FDG) is metabolized similarly to glucose in tumor cells, which is transported into a cytoplasm through specific glucose transporters in cell membrane and phosphorylated by hexokinase. However, phosphorylated FDG cannot be metabolized further; therefore, it accumulates in tumor cells, forming the basis of tumor detection via increased FDG uptake. 18F-FDG PET/CT has become an important imaging modality in staging, restaging, and monitoring of treatment responses in many malignant tumors, as it can provide a quantification of tumor metabolic activity to clinicians. The standard uptake value (SUV) is a commonly used semiquantitative parameter for the interpretation of PET images. The maximum SUV (SUVmax), which can be calculated from a 1-pixel region of interest corresponding to the maximum pixel value in the tumor, is a very commonly used parameter for estimating the prognosis and assessing treatment responses. However, SUVmax is known to be an observer-dependent measurement that can be influenced by the region of interest, and in whole, with credit to the author.

DOI: 10.1097/MD.0000000000002595
which is usually determined by an observer. Furthermore, a single pixel is unlikely to reflect the activity of metabolically heterogeneous tumors accurately. In order to resolve these clinical problems related to the use of SUV\textsubscript{max}, several volume-based PET parameters have been introduced to estimate accurate and objective measurement of tumor biology. Recently, metabolic tumor volume (MTV) and total lesion glycolysis (TLG) were developed to measure the metabolic activity of an entire tumor.\textsuperscript{11}

In this study, we correlated these 2 volume-based PET parameters with clinicopathologic characteristics of resected pancreatic cancer and sought to establish whether these recently developed PET parameters can estimate the risk of tumor recurrence in pancreatic cancer after curative resection.

MATERIALS AND METHODS

Clinicopathologic Parameters

We retrospectively reviewed medical records of patients who underwent potentially curative resection of pancreatic ductal adenocarcinoma and completed preoperative 18\textsuperscript{F}-FDG PET/CT as part of a staging work-up between January 2008 and October 2012. Those who received preoperative neoadjuvant treatment due to unresectable pancreatic cancer on preoperative imaging modalities or who had undergone palliative surgery were excluded from the study. However, the data set of patients with neoadjuvant treatment followed by pancreactectomy was used for evaluating the potential impact of neoadjuvant treatment on biologic impact of PET-based parameters. All patients underwent 18\textsuperscript{F}-FDG PET/CT and conventional radiologic examinations including contrast-enhanced CT and/or magnetic resonance imaging (MRI). Additionally, serum CA19–9 levels were measured before treatment. This study was approved by the Institutional Review Board at our institution, and written informed consent was obtained from all patients. During the follow-up period, patients were clinically assessed every 3 to 6 months by blood tests including serum CA19–9 and contrast-enhanced abdominopelvic CT. If the clinical assessment or follow-up studies revealed abnormal findings, additional diagnostic studies and biopsy with histopathologic confirmation were performed to evaluate cancer recurrence. Clinicopathologic variables that were retrospectively collected regarding gender, age, tumor location, operation type, tumor size, grade (differentiation), pathologic tumor (pT) stage, presence of lymph node metastasis, lymph node ratio (total number of metastatic lymph nodes divided by total number of retrieved lymph node), microscopic perineural invasion, lymphovascular invasion, recurrence pattern, and time to recurrence, which was defined as the time from surgical resection to recurrence or last clinical follow-up visit at our medical center.

Volume-based PET parameter (MTV\textsubscript{2.5} and TLG): 18\textsuperscript{F}-FDG PET/CT scans were performed with a dedicated PET/CT scanner (Discovery STe, GE Healthcare; or Biograph TruePoint 40, Siemens Healthcare). All patients fasted for at least 6 hours before the PET/CT scan. A dose of approximately 5.5 MBq/kg of 18\textsuperscript{F}-FDG was intravenously injected 60 minutes before imaging. First, a CT scan was performed at 30 mA and 130 kVp for the Discovery STe instrument, and 36 mA and 120 kVp for Biograph TruePoint instrument without contrast-enhancement. After the CT scan was complete, a PET scan was performed for extending from the neck to the proximal thighs with an acquisition time of 3 min per bed position in 3D mode. PET images were reconstructed using ordered subset expectation maximization (OSEM) with an attenuation correction. 18\textsuperscript{F}-FDG PET/CT images were reviewed by 2 nuclear medicine physicians using an Advantage Workstation 4.4 (GE Medical Systems). Maximum standardized uptake value (SUV\text{max}) and MTV\textsubscript{2.5} on PET images were measured using the volume viewer software. Each tumor was examined with a spherical-shaped volume of interest (VOI) that included the entire lesion in the axial, sagittal, and coronal planes. By using CT images, 18\textsuperscript{F}-FDG uptake of normal organs such as the bowel, stomach, and liver was not included in the VOI. The SUV\text{max} of the VOI was calculated as (decay-corrected activity/tissue volume)/(injected dose/body weight). MTV\textsubscript{2.5} was defined as the total tumor volume with an SUV \geq 2.5, and the MTV and mean SUV of the VOI were automatically calculated. TLG was calculated as (mean SUV) \times (MTV). In patients with SUV\text{max} < 2.5, MTV\textsubscript{2.5} and TLG were not measured.

Statistics

Continuous variables were described as mean \pm standard deviation, and categorical variables were described as a frequency (%). Student’s t-test, chi-squared tests with Fisher’s exact tests, and linear regression analyses were performed. Survival curves were estimated using the Kaplan–Meier method to calculate cumulative recurrence-free survival rates. Statistical analyses were performed using SPSS 20.0 for Windows (SPSS Inc, Chicago, IL). P values < 0.05 were considered to be statistically significant. Propensity score matching was performed for reducing confounding bias between MTV\textsubscript{2.5} and tumor size. Total populations were divided into 2 subgroups regarding small and large tumor groups according to mean value of pathologic tumor size which 2.4 cm (median and mean value of tumor size) was selected as cut-off value. And then, logistic regression was conducted to estimate propensity score of each patient. In each of the small and large tumor groups, the matching between high and low MTV\textsubscript{2.5} patients were undergone by greedy algorithm based on calculated propensity score (1:2 ratio matching in small tumor group and 1:1 matching ratio in large tumor group). The comparisons of clinicopathologic factors between selected high and low MTV\textsubscript{2.5} patients in each tumor size group were performed in terms of sex, age, tumor size, T stage, N stage, perineural invasion, lymphovascular invasion, tumor differentiation, lymph node ratio, and CA 19–9. Difference of disease-free survival between high and low MTV\textsubscript{2.5} was calculated by the Kaplan–Meier method and log-rank test to estimate the prognostic effect of MTV\textsubscript{2.5} value in small and large tumor groups.

RESULTS

Patient Demographics

Twenty-six patients were women and 31 were men with an average age of 62.9 \pm 9.1 years. Only 1 patient was determined to have a borderline resectable pancreatic cancer, and the others were all resectable lesions. All patients underwent margin-negative pancreatectomy. Most patients required pancreaticoduodenectomy (41 patients, 71.9%). The clinicopathologic characteristics are described in Table 1. Forty-five patients (78.9%) received postoperative adjuvant chemotherapy with or without radiation therapy. Median overall disease-free survival was 12.8 months (95% confidence interval: 9.2–16.3) and median overall disease-specific survival was 25.1 months (95% confidence interval: 15.3–34.9).

Correlation Between Radiologic Tumor Size and PET Parameters

When correlating PET parameters and radiologic tumor size, SUV\text{max} had no association with radiologic tumor size.
(SUV\textsubscript{max} = 0.419 × radiologic tumor size (cm) + 4.557, \( R^2 = 0.010, P = 0.501 \)). However, volume-based PET parameters MTV\textsubscript{2.5} (MTV\textsubscript{2.5} = 3.177 × radiologic tumor size (cm) – 2.343, \( R^2 = 0.213, P = 0.001 \)) and TLG (TLG = 12.737 × radiologic tumor size (cm) – 9.596, \( R^2 = 0.149, P = 0.009 \)), were both significantly associated with radiologic tumor size (Figure 1).

Correlation Between Lymph Node Ratio and PET Parameters

There were no significance differences in SUV\textsubscript{max} (5.3 ± 2.8 vs 5.1 ± 2.6, \( P = 0.749 \)), TMV\textsubscript{2.5} (3.6 ± 3.4 vs 5.2 ± 5.1, \( P = 0.93 \)), or TLG (13.1 ± 14.5 vs 21.7 ± 24.6, \( P = 0.124 \)) according to lymph node metastasis. However, the lymph node ratio (LNR) was correlated with MTV\textsubscript{2.5} (TMV\textsubscript{2.5} = 0.11 × LNR + 1.260, \( R^2 = 0.035, P = 0.055 \), Figure 1 and Table 2), but not with TLG (\( R^2 = 0.037, P = 0.158 \)) and SUM\textsubscript{max} (\( R^2 = 0.006, P = 0.555 \)).

Correlation Between Tumor Grade and PET Parameters

Tumor grade was also significantly correlated with volume-based PET parameters. The values of MTV\textsubscript{2.5} and TLG in well-differentiated pancreatic cancer were much lower than those in moderately or poorly differentiated pancreatic cancer (\( P < 0.05 \)); however, there was no difference in SUV\textsubscript{max} between the 2 groups (\( P = 0.200 \), Table 2).

Predicting Tumor Recurrence in Resected Pancreatic Cancer Without Neoadjuvant Treatment

The results of univariate analysis indicate that gender (\( P = 0.636 \)), age (\( P = 0.301 \)), lymph node status (pN-stage, \( P = 0.558 \)), lymphovascular invasion (\( P = 0.705 \)), perineural invasion (\( P = 0.838 \)), tumor grade (\( P = 0.643 \)), and postoperative adjuvant treatment (\( P = 0.998 \)) were not predictive of tumor recurrence. In contrast, SUV\textsubscript{max} (<5 vs ≥5, median 13.6 months vs 8.9 months, \( P = 0.077 \)), TLG (<18 vs ≥18,

### TABLE 1. Clinicopathologic Characteristics of Patients

| Variables                          | Frequency (%) |
|------------------------------------|---------------|
| Age (y)                            | 62.9 ± 9.1    |
| Gender                             |               |
| Female/male                        | 26 (45.6)/31 (54.4) |
| Tumor location                     |               |
| Head/body/tail                     | 40 (70.2)/14 (24.6)/3 (5.3) |
| Radiologic tumor size (cm)         | 2.3 ± 0.7     |
| Preoperative CA 19–9 operation     | 483.4 ± 1618.3|
| Pathologic tumor size (cm)         | 2.4 ± 0.8     |
| pTstage                            |               |
| T1/T2/T3/T4                        | 2 (3.5)/2 (3.5)/3 (93)/0 (0) |
| pNstage                            | 26 (45.6)/31 (54.4) |
| Retrieved LN number                | 17.8 ± 7.8    |
| Metastatic LN number               | 1.3 ± 2.1     |
| PNI                                | 16 (28.1)/41 (71.9) |
| LVI                                | 36/63.2/21 (36.8) |
| Tumor grade                        |               |
| Well/moderate/poor                 | 9 (15.8)/42 (73.7)/6 (10.5) |
| Curative resection                 |               |
| R0/R1/R2                           | 57 (100)/0/0  |
| 30-day mortality                   | 0 (0)         |

DPS = distal pancreatectomy with splenectomy, LVI = lymphovascular invasion, PD = pancreaticoduodenectomy, PPPD = pylorus preserving pancreaticoduodenectomy, PNI = perineural invasion, TP = total pancreatectomy.

FIGURE 1. Correlation between volume-based PET parameters and radiologic tumor size (A), (B) and potential associations between MTV\textsubscript{2.5} and lymph node ratio (C). PET = positron emission tomography, MTV = metabolic tumor volume.
median 14.7 months vs 8.8 months, \( P = 0.017 \), MTV2.5 (<4.5 vs \( \geq 4.5 \), median 12.9 months vs 8.8 months, \( P = 0.011 \)), radiologic tumor size (<2.5 vs \( \geq 2.5 \), median 17.5 vs 7.3 months, \( P = 0.035 \)), operation mode (pancreatoduodenectomy vs pylorus preserving pancreaticoduodenectomy vs distal pancreatectomy with splenectomy vs total pancreatectomy, median 3.3 months vs 12.2 months, vs 14.7 months, vs 5.3 months, \( P = 0.01 \)), lymph node ratio (<0.08 vs \( \geq 0.08 \), median 15.0 months vs 8.8 months, \( P = 0.07 \)), and both volume-based PET parameters below a certain threshold (TLG \( < 18 \) AND MTV2.5 \( < 4.5 \) vs TLG \( \geq 18 \) OR MTV2.5 \( \geq 4.5 \), median 14.7 months vs 8.8 months, \( P = 0.017 \)) were found to predict tumor recurrence after curative pancreatectomy.

In multivariate analysis, only lymph node ratio (\( \geq 0.08 \)) and MTV2.5 (\( \geq 4.5 \)) were found to be independent prognostic factors predicting tumor recurrence in resected pancreatic cancer without neoadjuvant chemoradiation therapy (Table 3). In addition, disease-free survival varied significantly according to these 2 risk factors (Combination 0: LNR < 0.08 AND MTV2.5 < 4.5, median 14.7 months, Combination 1: LNR \( \geq 0.08 \) AND MTV2.5 < 4.5, OR LNR < 0.08 AND MTV2.5 \( \geq 4.5 \), median 12.2 months, Combination 2, LNR > 0.08 AND MTV2.5 \( \geq 4.5 \), median 6.1 months, \( P = 0.001 \), Figure 2).

**Tumor-Size Matched Analysis to Validate Oncologic Impact of MTV2.5**

Oncologic impact of MTV2.5 was evaluated again by tumor-size matched analysis using propensity scores. There was no significant clinicopathologic difference according to MTV2.5 (Table 4). However, regardless of tumor size, it was found that MTV2.5 still played a significant role in determining tumor recurrence in resected pancreatic cancer (\( P = 0.048 \) in small sized pancreatic cancer (<2.5 cm), Figure 3(A), and \( P = 0.001 \) in large sized pancreatic cancer (\( \geq 2.5 \) cm), Figure 3(B)).

### TABLE 3. Multivariate Analysis for Tumor Recurrence in Resected Pancreatic Cancer

| Variables | Exp (B) | 95% Confidence Interval | \( P \) Value |
|-----------|---------|-------------------------|--------------|
| LNR \( \geq 0.08 \) | 2.425 | 1.119–5.254 | 0.025 |
| MTV2.5 \( \geq 4.5 \) | 2.273 | 1.066–4.850 | 0.034 |

LNR = lymph node ratio, MTV = metabolic tumor volume

**FIGURE 2.** Disease-free survivals according to a combination of independent prognostic factors (MTV2.5 and LNR): Combination 0: MTV2.5 < 4.5 AND LNR < 0.08; Combination 1, MTV2.5 < 4.5 AND LNR \( \geq 0.08 \); Combination 2, MTV2.5 \( \geq 4.5 \) AND LNR \( \geq 0.08 \). LNR = lymph node ratio, MTV = metabolic tumor volume.

**DISCUSSION**

In clinical oncology, biologic behavior of the cancer is usually determined on the basis of pathologic examination of resected surgical specimens. Increased tumor size,12 positive
### Table 4. Propensity Score Matched Comparisons of Clinicopathologic Characteristics Between High and Low MTV Value in Small and Large Tumor Group

|                | Small Tumor Group (<2.4 cm) | Large Tumor Group (≥2.4 cm) |
|----------------|-----------------------------|-----------------------------|
|                | High MTV (n=11) (MTV2.5 ≥ 4.5) | Low MTV (n=12) (MTV2.5 < 4.5) | P Value |
| Age (years)    | 62.4 ± 10.2 | 64.2 ± 14.6 | 0.808 |
| Sex (male/female) | 3 (50%) / 6 (50%) | 8 (66.7%) / 4 (33.3%) | 0.428 |
| Diabetes history | 3 (50%) | 5 (41.7%) | 0.563 |
| Blood glucose before PET scan (mg/dL) | 93.3 ± 9.6 | 109 ± 24.4 | 0.104 |
| Body mass index | 23.9 ± 3.4 | 23.3 ± 3.1 | 0.865 |
| Tumor size (cm) | 2.4 ± 2.2 | 2.3 ± 3.0 | 0.934 |
| 
|                | High MTV (n=12) (MTV2.5 ≥ 4.5) | Low MTV (n=12) (MTV2.5 < 4.5) | P Value |
| Age (years)    | 62 ± 10.2 | 64.6 ± 14.6 | 0.037 |
| Sex (male/female) | 3 (50%) / 6 (50%) | 8 (66.7%) / 4 (33.3%) | 0.428 |
| Diabetes history | 3 (50%) | 5 (41.7%) | 0.563 |
| Blood glucose before PET scan (mg/dL) | 93.3 ± 9.6 | 109 ± 24.4 | 0.104 |
| Body mass index | 23.9 ± 3.4 | 23.3 ± 3.1 | 0.865 |
| Tumor size (cm) | 2.4 ± 2.2 | 2.3 ± 3.0 | 0.934 |

MTV2.5 as a Surrogate Marker of PDAC

It was hypothesized that PET parameters could reflect not only tumor burden, but also tumor biology, because 18F-FDG uptake correlates with cellular proliferation and tumor behavior in pancreatic cancer. According to our results, preoperative volume-based PET parameters MTV2.5 and TLG were found to represent some tumor biologic characteristics in resected pancreatic cancer. In the present study, the conventional PET parameter, SUVmax, did not correlate with radiologic tumor size, lymph node ratio, or tumor differentiation. In contrast, MTV2.5 and TLG were closely related to radiologic tumor size, lymph node ratio, and tumor grade, suggesting the clinical usefulness of these volume-based PET parameters for predicting tumor recurrence and tailoring the treatment of pancreatic cancer.

In this study, preoperative MTV2.5 and TLG were found to reflect tumor biologic behavior and were shown to be prognostic factors determining tumor recurrence in univariate analysis. However, only MTV2.5 was identified as an independent prognostic factor for predicting tumor recurrence among preoperatively detectable clinical parameters. Tumors with MTV2.5 ≥ 4.5 were revealed to have a higher risk of recurrence compared with tumors <4.5 (Exp (B) = 2.273, P = 0.034), a similar risk to that found for lymph node ratio in multivariate analysis (Exp (B) = 2.425, P = 0.025). Recently, the distribution of metastatic lymph nodes among all retrieved lymph nodes (lymph node ratio) has become a powerful prognostic factor for pancreatic cancer. However, the LNR can only be obtained from pathologic examination of resected surgical specimens. Therefore, the preoperative volume-based PET parameter, MTV2.5, can be a useful surrogate marker that can predict tumor recurrence before surgical intervention, and may even help oncologists counsel against surgery that would be unlikely to benefit the patient. For example, even in “resectable” pancreatic cancer, neoadjuvant chemotherapy with or without radiation therapy can be proposed as an alternative treatment for pancreatic cancer with a preoperative MTV2.5 ≥ 4.5, or an oncologist may recommend postoperative adjuvant treatment regardless of their pathological parameters. In fact, patients (N = 2) with 2 independent prognostic factors (MTV2.5 ≥ 4.5 and LNR ≥ 0.08), who had no postoperative adjuvant treatment typically showed early recurrence within 3 months from curative resection, whereas recurrence was found to be delayed in patients (N = 8) who had both 2 risk factors and received postoperative adjuvant chemotherapy (data not shown, P < 0.001).

It is one of the outstanding points of current study that MTV2.5 was again evaluated by propensity score matching analysis according to tumor size. It is well known that tumor size can be one of the prognostic factors to impact on oncologic outcome of resected pancreatic cancer. In the present study, MTV2.5 also showed strong relationship with radiologic lymph node metastasis, increased lymph node ratio, high tumor grade, positive lymphovascular or perineural invasion, and positive margin-status represent aggressive tumor behaviors in pancreatic cancer that lead to early treatment failure and resistance to conventional chemotherapy. Determining these prognostic factors is a key component of developing an effective and reasonable treatment strategy based on accurate cancer biologic behavior. Considering the high frequency of advanced and potentially systemic disease at the time of initial diagnosis of pancreatic cancer, preoperative prediction of early recurrence and aggressive biologic behavior of tumor can inform the prognosis and help patients avoid unnecessary surgery.
tumor size ($R^2 = 0.213, P = 0.001$, Figure 1(A)). Radiologic tumor size was found to be one of the prognostic factors to predict tumor recurrence in univariate analysis ($<2.5$ vs $\geq 2.5$, median 17.5 vs 7.3 months, $P = 0.035$). Although MTV$_{2.5}$ was identified as an independent prognostic factor in multivariate analysis, tumor size-matched analysis was performed again to remove all possible confounding bias from radiologic tumor size. MTV$_{2.5}$ was still analyzed as significant determinant in predicting disease-free survival in resected pancreatic cancer (Table 4, and Figure 3). There have been several studies evaluating the oncologic significance of MTV$_{2.5}$ and TLG in lung cancer, head and neck cancer, esophageal cancer, ovarian cancer, osteosarcoma, and colorectal cancer. Several previous studies have showed the efficacy of MTV$_{2.5}$ in predicting oncologic outcomes in various cancers. However, to the best of the authors’ knowledge, there have been only a few published clinical researches on the prognostic value of MTV$_{2.5}$ in patients with resected pancreatic cancer. Even recent studies successfully showing the potential oncologic role of MTV$_{2.5}$ in pancreatic cancer did not concern this possible confounding effect from tumor size. On top of that, our study showed that neoadjuvant chemoradiation therapy could attenuate potential adverse effect of high MTV on recurrence of resectable pancreatic cancer (Figure 4). Although this pilot study is based on a small number of selected patients, it is suggesting that preoperatively determined “resectable” pancreatic cancer can be treated in a different way according to preoperative PET-based parameter. In general, neoadjuvant chemoradiation therapy has performed usually based on anatomic relationship between tumor and major vessel. Beyond this anatomic relationship, clinical parameters representing tumor biology, such as PET-based parameter, and CA 19–9 could be possibly used even in preoperative “resectable” pancreatic cancer for selecting patients who would be benefit from neoadjuvant treatment followed by pancreatectomy. This effort will be a back bone of patient-oriented surgical approach to improve survival outcome and further study is mandatory to prove our observation.

There are several limitations to the present study, including retrospective study design, which can lead to significant selection bias even after case-matched comparisons. Therefore, these encouraging results should be validated based on large-scale prospective clinical data in the near future. Our study demonstrated that preoperative MTV$_{2.5}$ functions as a new, clinically detectable surrogate marker can predict the recurrence of pancreatic cancer following curative resection. In addition, differences in molecular expression according to volume-based PET parameters such as MTV$_{2.5}$ would be interesting topic to be further investigated to identify molecular mechanism in determining recurrence risk in resected pancreatic cancer.

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