Preoperative CA19-9 level and dual time point FDG-PET/CT as strong biological indicators of borderline resectability in pancreatic cancer: A retrospective study

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Abstract. Tumor resectability, which is increasingly determined based on preoperative chemotherapy, is critical in determining the best treatment for pancreatic cancers. The present study evaluated the usefulness of serum carbohydrate antigen 19-9 (CA19-9) and the preoperative 8F-fluorodeoxyglucose positron emission tomography/computed tomography standardized uptake value (SUV) percentage change (SUVmax%=[(SUVmax2-SUVmax1)/SUVmax1] x100, where SUVmax1 and SUVmax2 represent the initial and delayed phases, respectively) as biological factors indicative of tumor resectability. The present study included patients with resectable pancreatic cancer who underwent complete surgical resection, for whom both CA19-9 and SUVmax% were documented using cut-off values of 500 U/ml and 24.25%, respectively. Patients were classified as follows: i) High CA19-9 and SUVmax%: both CA19-9 and SUVmax% were elevated; ii) high CA19-9 or SUVmax%: either CA19-9 or SUVmax% were elevated; or iii) low CA19-9 and SUVmax%: neither value met the cut-off. Relapse-free survival (RFS) and overall survival (OS) were calculated, for which univariate and multivariate analyses were performed. Of the 86 patients included, 39 were classified as high CA19-9 or SUVmax% and 12 as high CA19-9 and SUVmax%, with the former group having a significantly worse RFS (vs. low CA19-9 and SUVmax%; P<0.001; vs. high CA19-9 or SUVmax%; P=0.011) and OS (vs. low CA19-9 and SUVmax%, P=0.002; vs. high CA19-9 or SUVmax%, P<0.001). Therefore, high CA19-9 and SUVmax% was an independent predictor of worse RFS (P<0.001) and OS (P=0.003). In conclusion, CA19-9 and SUVmax% can be utilized as biological indicators of resectability.

Introduction

At present, surgical resection is the only curative treatment for patients with pancreatic cancer, whom often have poor prognoses (1,2). Treatment plans are generally selected based on tumor resectability status, classified according to the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines (v2.2021) as either resectable (R), borderline resectable (BR), or unresectable (3).

Occasionally, patients may experience an early disease recurrence after surgery, even in cases diagnosed with a resectable tumor. In fact, the feasibility of determining resectability status by looking only at the anatomical relationship between the tumors and surrounding major vessels, such as the portal vein, superior mesenteric artery/vein, common hepatic artery, and celiac artery, remains a topic of controversy (4). Recently the use of biological factors as indicators of resectability status, such as the preoperative serum CA19-9 levels, has become a subject of clinical research (2,4).

CA19-9 is a sialylated antigen of the Lewis A sugar chain of the Lewis blood group and is a major tumor marker that is known to be elevated in pancreatic cancer. Several recent reports have shown that preoperative serum CA19-9 levels can predict early recurrence (5-8), and have advocated for CA19-9 to be included as a factor indicating biological resectability. CA19-9 levels, however, can be influenced by obstructive jaundice and the Lewis blood group [Le(a-b-)] (9). For obstructive jaundice, appropriate bile reduction procedures,

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Abbreviations: BR, borderline resectable; FDG-PET/CT, 8F-fluorodeoxyglucose positron emission tomography/computed tomography; GS, gemcitabine plus S-1; NAC, neoadjuvant chemotherapy; NCCN, National Comprehensive Cancer Network; NPV, negative predictive value; OS, overall survival; PDAC, pancreatic ductal adenocarcinoma; PPV, positive predictive value; R, resectable; RFS, relapse-free survival; SUV, standardized uptake value

Key words: pancreatic cancer, resectability, biological borderline resectable, FDG-PET/CT, SUVmax, CA19-9

such as endoscopic retrograde biliary drainage (ERBD), could minimize its effects. Since the influence of Lewis blood type cannot be completely ruled out, we believe that the use of CA19-9 alone is not sufficient for the diagnosis of tumors that are biologically BR.

We recently reported on the usefulness of dual time point ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) in predicting early postoperative recurrence in cases of pancreatic cancer (10). Diederichs *et al* (11) previously indicated that hyperglycemia (fasting blood glucose >130 mg/dl) significantly reduced the standardized uptake value (SUV) of pancreatic cancer lesions. In a prior study, we reported that dual time point FDG-PET/CT reduced the influence of hyperglycemia, making it useful for the prognostication of patients with pancreatic cancer (10). Based on these results, in the present study, a combined evaluation of the biological factors of CA19-9 levels and dual time point FDG-PET/CT results was performed to enable a more accurate identification of tumors that are biologically BR.

Materials and methods

The present study was approved by the institutional review board of the National Defense Medical College (approval no. 4610).

Patients. We retrospectively reviewed the medical records of patients who underwent radical (R0) resection for pancreatic ductal adenocarcinoma (PDAC) at the National Defense Medical College Hospital in Japan between January 2013 and August 2022. All of the patients included in the present study provided written informed consent for the publication of their clinical details and images.

All PDAC diagnoses were histopathologically confirmed prior to initiating chemotherapy via pancreatic juice cytology, endoscopic retrograde cholangiopancreatography biopsy, or endoscopic ultrasound-guided fine-needle aspiration biopsy. Only patients diagnosed as having biologically R tumors based on the NCCN Guidelines v2.2021 (3) were included for analysis. The treatment plan for each patient was discussed at a multidisciplinary treatment team meeting, which included gastroenterologists, radiologists, and hepatobiliary and pancreatic surgeons. For biologically R diseases, patients underwent upfront surgery until 2018; however, from 2019 on, patients received gemcitabine plus S-1 (GS) as neoadjuvant chemotherapy (NAC) prior to surgical resection (12), the method for which was based on the tumor location. Each patient underwent a regional lymph node dissection, for which the pathological stage was determined based on the tumor, node, metastasis (TNM) classification system provided by the Union for International Cancer Control (8th edition).

Postoperatively, each patient was administered adjuvant chemotherapy with S-1 for six months as the standard treatment, with the follow-up consisting of blood tests performed every three months and computed tomography (CT) every six months. In cases in which recurrence was suspected, PET-CT was performed at the discretion of the patient's attending physician.

Cut-off values. The standardized uptake value (SUV) percentage change (SUVmax%) was calculated using the following formula:

SUVmax%=[(SUVmax2-SUVmax1)/SUVmax1] x100, where SUVmax1 and SUVmax2 represent the initial (60 min after FDG injection) and delayed (120 min after FDG injection) scan phases, respectively.

The cut-off values of SUVmax% and CA19-9 were 24.25% and 500 U/ml, respectively, based on the values used in previous studies (4,10). All FDG-PET/CT imaging was performed prior to patients starting NAC. In patients with obstructive jaundice, the CA19-9 values were collected after biliary drainage was performed, and the serum total bilirubin levels decreased to 3.0 mg/dl or lower.

Grouping. Using the aforementioned cut-off values for CA19-9 (500 U/ml) and SUVmax% (24.25%), the patients were classified as follows: i) high CA19-9 and SUVmax%, in which both CA19-9 and SUVmax% were elevated; ii) high CA19-9 or SUVmax%, either CA19-9 or SUVmax% was elevated; iii) low CA19-9 and SUVmax%, neither value exceeded the cut-off. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of the CA19-9 level, SUVmax%, and the combination thereof for predicting relapse within one year of surgery were calculated, as well as relapse-free survival (RFS) and two-year overall survival (OS). Univariate and multivariate analyses were performed for RFS and OS.

Sites of recurrence. Tumor recurrence was diagnosed based on imaging studies, primarily CT, although PET-CT was occasionally performed, and was classified as local, distant, or both. Local recurrence was defined as enlarged soft tissue shadows or lymph nodes around the celiac, hepatic, splenic, or superior mesenteric artery in the peripancreatic region.

Statistical analysis. The Mann-Whitney U test was used to compare continuous variables, which were presented as the median and range, while Fisher's exact test was used to compare categorical variables. We utilized the Kaplan-Meier method to determine RFS and OS. Differences in the survival curves were analyzed using log-rank tests, and a Cox proportional hazards model was used to perform univariate and multivariate RFS and OS analyses. EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface designed to add statistical functions frequently used in biostatistics to R (The R Foundation for Statistical Computing, Vienna, Austria), was used to perform all statistical analyses. Statistical significance was set at $P<0.05$.

Results

Patient profiles. A total of 86 patients were included in the study, 49 (57%) of which were men, with a median age at the time of surgery of 72 years (range, 48-86 years). Of these patients, 61 (71%) had tumors located in the pancreatic head, 25 (29%) had tumors located in the pancreatic body or tail, and 19 (22%) received NAC with GS. Postoperatively, 67 patients (78%) received adjuvant chemotherapy, with S-1 administered in 61 patients (91%) and gemcitabine in the other six (9%).

Table I. Patient characteristics according to their SUVmax% and CA19-9 values.

Parameter	Total (n=86)	High CA19-9 and SUVmax% (n=12)	High CA19-9 or SUVmax% (n=39)	Low CA19-9 and SUVmax% (n=35)	P-value	P-value of high CA19-9 and SUVmax% vs. high CA19-9 or SUVmax%
Sex (men/women)	49/37	5/7	22/17	22/13	0.439	0.511
Age, years	72 (48-86)	71 (58-84)	73 (54-86)	70 (48-83)	0.443	0.417
Neoadjuvant chemotherapy	19 (22%)	1 (8%)	9 (23%)	9 (26%)	0.447	0.417
Preoperative diabetes mellitus	24 (28%)	3 (25%)	11 (28%)	10 (29%)	0.971	1.00
Preoperative CA19-9 value	171 (0.4-4510)	1173 (598-4510)	206.4 (0.4-2812)	64.6 (2.8-474)	<0.001	<0.001
ΔSUVmax%	23.7 (-13.86-84.40)	38.6 (24.87-59.62)	27.36 (-13.86-84.4)	12.99 (-10.49-23.27)	<0.001	0.059
Tumor location (head/body or tail)	61/25	12/0	28/11	21/14	0.031	0.048
Operative method						
PD	61	12	28	21	0.111	0.048
DP or TP	25	0	11	14		
Pathological T-factor, (1/2/3/4)	3/1/80/2	0/0/12/0	1/1/36/1	2/0/32/1	0.897	1.00
Pathological N-factor, positive/negative	64/22	10/2	28/11	26/9	0.725	0.706
Residual tumor, R0/R1	77/9	11/1	37/2	29/6	0.233	0.561
Adjuvant chemotherapy	67 (78%)	8 (73%)	29 (74%)	30 (88%)	0.279	1.00

Categorical variables are shown as n (%), whereas continuous variables are presented as medians (range). CA19-9, carbohydrate antigen 19-9; SUV, standardized uptake value; PD, pancreaticoduodenectomy; DP, distal pancreatectomy; TP, total pancreatectomy.

Comparison of clinical and histopathological factors based on CA19-9 and SUVmax%. Table I shows the characteristics of each group, classified as described above, based on each patient's CA19-9 and SUVmax% values. Of the 86 patients, 12 (14%) were classified as high CA19-9 and SUVmax%, 39 (45%) as high CA19-9 or SUVmax%, and the rest as low CA19-9 and SUVmax%. A scatter plot of the patients' SUVmax% and CA19-9 levels is presented in Fig. 1, differentiating those patients who experienced a recurrence from those who did not. The sensitivity and specificity of predicting tumor recurrence within one year of surgery were 29 and 94.5%, respectively, in the high CA19-9 and SUVmax% group (Table II).

Survival outcomes. The median postoperative follow-up period was 28 months, during which a total of 30 patients (35%) were censored, including 16 who did not experience a tumor relapse. From the high CA19-9 and SUVmax%, high CA19-9 or SUVmax%, and low CA19-9 and SUVmax% groups, 1 (8%), 19 (49%), and 10 (29%) patients were censored, respectively. The median RFS was 8, 16, and 26 months in the high CA19-9 and SUVmax%, high CA19-9 or SUVmax%, and low CA19-9 and SUVmax% groups, respectively, with a significant difference (P<0.001) (Fig. 2). The two-year OS was 19, 75, and 67% in the high CA19-9 and SUVmax%, high CA19-9 or SUVmax%, and low CA19-9 and SUVmax% groups, respectively, which also showed significant differences (P<0.001) (Fig. 3).

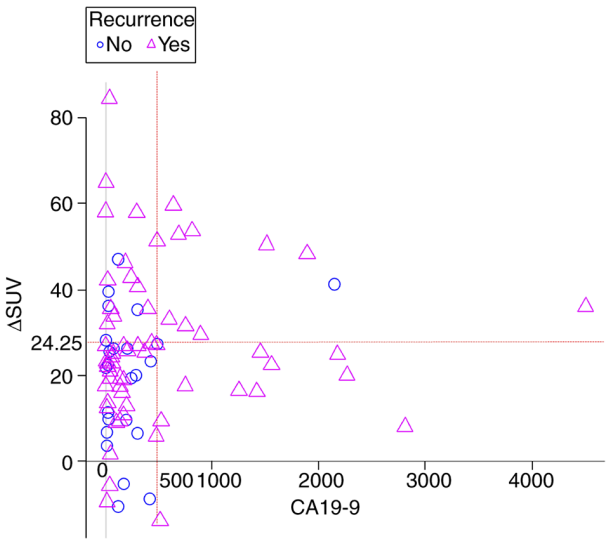

Figure 1. Scatterplot of SUVmax% and CA19-9 values. Triangles indicate tumor recurrence after surgery, and circles indicate other cases. Red lines are drawn at 24.25% and 500 U/ml, which represent the cut-off values for SUVmax% and CA19-9, respectively. SUV, standardized uptake value; SUVmax%, SUV percentage change; CA19-9, carbohydrate antigen 19-9.

Univariate and multivariate analyses for the predictors of poor RFS. The univariate analysis of potential predictors showed that lymph node metastasis [hazard ratio (HR), 2.626;

Table II. Accuracy of CA19-9, SUVmax% and the combination thereof for predicting tumor relapse within 1 year after surgery.

Parameter	Number of cases		P-value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
	Total	Relapse						
CA19-9, U/ml			0.016					
>500	20	12 (60%)		38.7	85.5	60	71.2	68.6
≤500	66	19 (29%)						
SUVmax%, %			0.072					
≥24.25	43	20 (47%)		64.5	58.2	46.5	74.4	60.5
<24.25	43	11 (26%)						
Combination of CA19-9 >500 U/ml and SUVmax% ≥24.25%	12	9 (75%)	0.007	29.0	94.5	75.0	70.3	70.9

PPV, positive predictive value; NPV, negative predictive value; CA19-9, carbohydrate antigen 19-9; SUV, standardized uptake value.

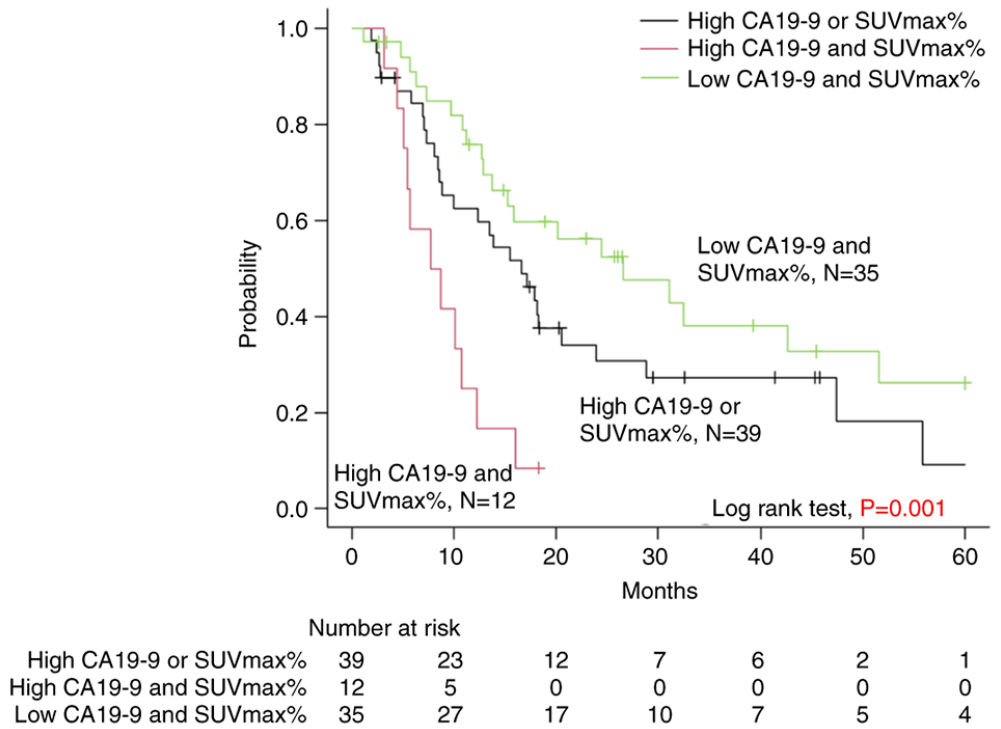

Figure 2. Kaplan-Meier curve of RFS based on the CA19-9 and SUVmax% values. Patients were classified as: i) High CA19-9 and SUVmax%: both CA19-9 and SUVmax% were elevated; ii) high CA19-9 or SUVmax%: either CA19-9 or SUVmax% was elevated; or iii) low CA19-9 and SUVmax%: neither value met the cut-off. The median RFS was 8, 16 and 26 months for the high CA19-9 and SUVmax%, high CA19-9 or SUVmax% and low CA19-9 and SUVmax% groups, respectively (P<0.001). The high CA19-9 and SUVmax% group showed significantly improved survival compared with the high CA19-9 or SUVmax% (P=0.011) and low CA19-9 and SUVmax% (P<0.001) groups. RFS, relapse free survival; SUV, standardized uptake value; SUVmax%, SUV percentage change; CA19-9, carbohydrate antigen 19-9.

95% confidence interval (CI), 1.289-5.350; P=0.008] and classification as high CA19-9 and SUVmax% (HR, 4.449; 95% CI, 2.041-9.70; P<0.001) were significant predictors of poor RFS, while high CA19-9 or SUVmax% was not found to be a predictor of poor RFS (HR, 1.697; 95% CI, 0.949-2.997; P=0.074). The multivariate analysis of potential predictors revealed that the pathological N-factor and high CA19-9 and SUVmax% remained independent predictors of poor RFS (Table III).

Univariate and multivariate analyses for the predictors of poor OS. The univariate analysis of potential predictors showed that pancreatic head cancer (HR, 2.638; 95% CI, 1.105-6.299; P=0.029), no adjuvant chemotherapy (HR, 2.166; 95% CI, 1.114-4.212; P=0.023), and high CA19-9 and SUVmax% (HR=3.193; 95% CI, 1.450-7.032; P=0.003) were predictors of poor OS, while high CA19-9 or SUVmax% was not found to be a predictor of poor OS (HR, 1.222; 95% CI, 0.615-2.427; P=0.565). The multivariate analysis of potential

Table III. Univariate and multivariate analysis for the predictors of poor RFS.

A, Preoperative parameters

		Univariate		Multivariate	
Parameters	Group	Hazard ratio (95% CI)	P-value	Hazard ratio (95% CI)	P-value
Sex	Men vs. Women	1.037 (0.618-1.741)	0.890		
Age, years	<70 vs. ≥70 years	1.016 (0.604-1.708)	0.953		
Tumor location	Head vs. Body or Tail	1.703 (0.939-3.089)	0.079	1.514 (0.660-3.471)	0.326
Preoperative diabetes	Yes vs. No	1.026 (0.570-1.844)	0.933		
NAC	Performed vs. Not performed	1.225 (0.646-2.326)	0.534		

B, Biological factors

		Univariate		Multivariate	
Parameters	Group	Hazard ratio (95% CI)	P-value	Hazard ratio (95% CI)	P-value
High CA19-9 or SUVmax% vs. Others		1.222 (0.615-2.427)	0.565		
High CA19-9 and SUVmax% vs. Others		3.193 (1.450-7.032)	0.003	3.041 (1.471-6.289)	0.005

C, Pathological factors

		Univariate		Multivariate	
Parameters	Group	Hazard ratio (95% CI)	P-value	Hazard ratio (95% CI)	P-value
Pathological T-factor	≥3 vs. <3	1.334 (0.326-5.485)	0.689		
Pathological N-factor	≥1 vs. <1	2.626 (1.289-5.350)	0.008	2.071 (0.845-5.074)	0.111

D, Postoperative parameters

		Univariate		Multivariate	
Parameters	Group	Hazard ratio (95% CI)	P-value	Hazard ratio (95% CI)	P-value
Adjuvant chemotherapy	Not performed vs. Performed	1.521 (0.847-2.733)	0.160		

RFS, recurrence-free survival; CI, confidence interval; NAC, neoadjuvant chemotherapy; CA19-9, carbohydrate antigen 19-9; SUV, standardized uptake value.

predictors revealed that high CA19-9 and SUVmax% remained independent predictors of poor OS (Table IV).

Sites of tumor recurrence within one year. Table V shows the sites at which tumors recurred within one year of surgery for the three groups. Tumor recurrence was observed in nine patients (75%) categorized as high CA19-9 and SUVmax% and 14 (36%) categorized as high CA19-9 or SUVmax% cases, with a significant difference (P=0.023). Concurrent local and distant recurrences in the high CA19-9 and SUVmax% and high CA19-9 or SUVmax% groups occurred in four (33%) and three (8%) of the patients, respectively, showing significant differences (P=0.044).

Discussion

In the present study, high CA19-9 and SUVmax% were found to predictors of early (within a year) tumor relapse, with a sensitivity of 29% and specificity of 94.5%. This finding suggests that patients categorized as high CA19-9 and SUVmax% have a higher risk of early postoperative recurrence; however, among these, a percentage of patients categorized as high

Table IV. Univariate and multivariate analysis for the predictors of poor OS.

A, Preoperative parameter

		Univariate		Multivariate	
Parameters	Group	Hazard ratio (95% CI)	P-value	Hazard ratio (95% CI)	P-value
Sex	Men vs. Women	1.134 (0.670-2.114)	0.693		
Age, years	<70 vs. ≥70 years	1.079 (0.579-2.013)	0.810		
Tumor location	Head vs. Body or Tail	2.683 (1.105-6.299)	0.029	1.061 (0.557-2.019)	0.857
Preoperative diabetes	Yes vs. No	1.051 (0.512-2.156)	0.893		
NAC	Performed vs. Not performed	1.157 (0.485-2.762)	0.742		

B, Biological factors

		Univariate		Multivariate	
Parameters	Group	Hazard ratio (95% CI)	P-value	Hazard ratio (95% CI)	P-value
High CA19-9 or SUVmax% vs. Others		0.594 (0.313-1.087)	0.092	1.704 (0.954-3.044)	0.071
High CA19-9 and SUVmax% vs. Others		3.655 (1.726-7.220)	<0.001	3.910 (1.753-8.724)	<0.001

C, Pathological factors

		Univariate		Multivariate	
Parameters	Group	Hazard ratio (95% CI)	P-value	Hazard ratio (95% CI)	P-value
Pathological T-factor	≥3 vs. <3	1.106 (0.150-8.121)	0.921		
Pathological N-factor	≥1 vs. <1	2.555 (0.995-6.526)	0.051	2.424 (1.158-5.072)	0.018

D, Postoperative parameters

		Univariate		Multivariate	
Parameters	Group	Hazard ratio (95% CI)	P-value	Hazard ratio (95% CI)	P-value
Adjuvant chemotherapy	Not performed vs. Performed	2.166 (1.114-4.212)	0.023		

OS, overall survival; CI, confidence interval; NAC, neoadjuvant chemotherapy; CA19-9, carbohydrate antigen 19-9; SUV, standardized uptake value.

CA19-9 or SUVmax% or high CA19-9 and SUVmax% are also at risk of early recurrence. Moreover, the high CA19-9 and SUVmax% classification was found to be an independent predictor of poor RFS. CA19-9 has modifiers such as Lewis blood type, and this study suggests that ΔSUVmax% might compensate for its limitations.

The usefulness of FDG-PET/CT as a prognostic indicator has thus far been controversial (13-16). Various FDG-PET/CT-based volumetric imaging parameters, such as metabolic tumor volume and total lesion glycolysis, have been suggested as prognostic indicators for pancreatic cancer (17-19). Despite this, these indicators are not widely utilized because of their complexity. Therefore, in the present study we focused on using SUVmax as a convenient indicator to assess tumor biokinetics. Higashi *et al* (20) and Sun *et al* (21) reported that FDG uptake (SUVmax) was largely dependent on the number of activated tumor cells rather than on their proliferative activity. Tumors with high proliferative activity express that the tumor was prone to local invasion. It was not clear what high tumor activity expresses clinically. Dual time point imaging used in PET/CT imaging of 18F-FDG takes advantage of the accumulation of FDG by tumor cells over

Table V. Recurrence status within 1 year after surgery.

Parameter	High CA19-9 and SUVmax% (n=12)	High CA19-9 or SUVmax% (n=39)	Low CA19-9 and SUVmax% (n=35)	P-value	P-value of high CA19-9 and SUVmax% vs. high CA19-9 or SUVmax%
1 year recurrence after surgery	9 (75%)	14 (36%)	8 (23%)	0.005	0.023
Local and distant recurrence	4 (33%)	3 (8%)	1 (3%)	0.016	0.044
Local recurrence	2 (17%)	3 (8%)	1 (3%)	0.236	0.580
Distant recurrence	3 (25%)	8 (21%)	6 (17%)	0.757	0.706
Sites of distant recurrence					
Lung	0	2	1		
Liver	2	4	4		
Para-aortic lymph node	0	1	1		
Peritoneal dissemination	1	1	0		

CA19-9, carbohydrate antigen 19-9; SUV, standardized uptake value.

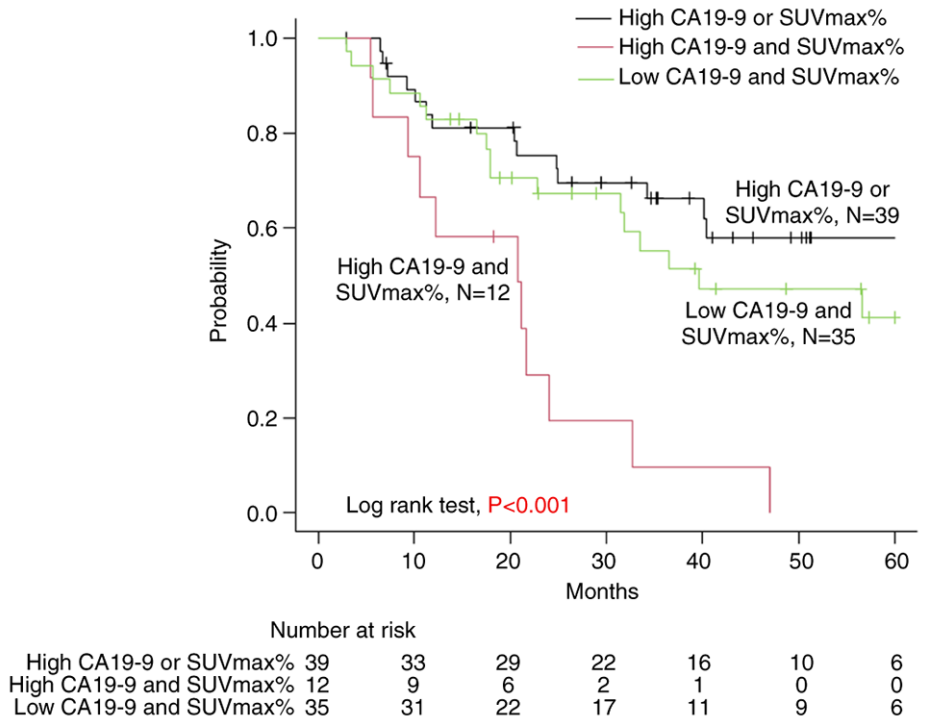

Figure 3. Kaplan-Meier curve of OS based on the CA19-9 and SUVmax% values. The two-year OS was 19, 75 and 67% for the high CA19-9 and SUVmax%, high CA19-9 or SUVmax%, and low CA19-9 and SUVmax% groups, respectively. The high CA19-9 and SUVmax% group showed significantly improved survival compared with the high CA19-9 or SUVmax% (P<0.001) and low CA19-9 and SUVmax% (P=0.002) groups. OS, overall survival; SUV, standardized uptake value; SUVmax%, SUV percentage change; CA19-9, carbohydrate antigen 19-9.

time (22,23), suggesting that a higher SUVmax% indicates a greater number of active tumor cells. In the present study, SUVmax% was found to be a predictor of the one-year tumor recurrence rate with a higher sensitivity (64.5%) than the other indicators, suggesting that tumor activity may be a valuable predictor of future metastatic susceptibility.

Preoperative CA19-9 levels have been previously reported to be a useful predictor of recurrence (6,24). The results of the present study showed it to have a specificity of 85.5% for the prediction of recurrence within one year after surgery. On the other hand, SUVmax% ≥24.25% had the lowest specificity, at 58.2%. The relatively good prognoses of patients categorized as high CA19-9 or SUVmax% were affected by the inclusion of patients with high SUVmax% and low CA19-9 values. In contrast to its low specificity, SUVmax% ≥24.25% could predict the one-year recurrence rate with the highest sensitivity, at 64.5%, while being categorized as high CA19-9 and SUVmax% has the highest accuracy, at 70.9%. We propose, therefore, that the combination of CA19-9 and SUVmax% values, rather than each index alone, is a reliable indicator of biological resectability. Because being categorized as high CA19-9 and SUVmax% is an indicator of concurrent distant

and local recurrence, it is within reason to consider surgical therapy for patients who fall into this category, followed by strong chemotherapy, such as a combination of oxaliplatin (L-OHP), irinotecan (CPT-11), and 5-fluorouracil/leucovorin (5-FU/l-LV), known as FOLFILINOX.

In Japan, the standard treatment for resectable pancreatic cancer at present is NAC with GS, followed by resection. Tajima *et al* (25) reported that pancreatic cancer tissues following NAC are rich in chemoresistance steam like-cells and epithelial-mesenchymal transition (EMT) markers. EMT markers induced by NAC play an important role in the aggressive behavior of tumors. This suggests that NAC may change the biological nature of the tumor. In the present study, FDG-PET/CT was routinely performed prior to the start of NAC because of the impact of NAC on the tumor tissues. Because insurance restrictions allowed only one FDG-PET/CT every three months, most patients were only administered one round of FDG-PET/CT. Further studies are warranted to determine whether the change in SUVmax% before and after NAC is an indicator of early recurrence.

In some cases, FDG-PET/CT may not be feasible, for which it is important to use other modalities, such as MRI, for the biological evaluation of tumors. Multiparametric MRI radiomic nomograms have been used to differentiate early recurrent cases of pancreatic cancer (26). If both FDG-PET/CT and MRI are available, a combined evaluation of the tumor biology could improve the accuracy of diagnosis in cases of early recurrence.

This study has some limitations. First, this was a retrospective single-center study; therefore, a multicenter study with a larger cohort is warranted. Second, this study included a small study population. Thus, the usefulness of these results will need to be verified using a larger sample size. Additionally, the follow-up period was short, with 35% of cases being excluded. Although there was no significant difference between high CA19-9 or SUVmax% and low CA19-9 and SUVmax% excluded cases (P=0.097), patients should receive sufficient follow-up to monitor their prognoses. Finally, only a few patients in the present study received NAC, which is currently the standard treatment for resectable pancreatic cancers. The ideal timing for FDG-PET/CT evaluations, however, has not yet been standardized, and further studies are needed to determine whether or not SUV fluctuations before and after NAC play a role in tumor resectability.

To summarize, high levels of CA19-9 and SUVmax% were found to be independent risk factors for prognosis, with a specificity of 94.5% for the prediction of early recurrence within one year of surgery. Additionally, the combination of CA19-9 and SUVmax% values appear to be a feasible biological indicator of borderline resectability in pancreatic cancers.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

KK, YK, HT, and HU drafted and critically reviewed the manuscript for important intellectual content. KK and YK made substantial contribution to conception and design. TT, MT and TE contributed substantially to the clinical data acquisition. NY and YT analyzed and interpreted the patient data and contributed to the preparation of the manuscript. HT and HU made substantial contribution of analysis of patient data. KT and JI contributed substantially to the interpretation of the PET/CT results, as well as data accumulation. KK and TE confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was approved by our institute's committee on human research, and all patients provided their written informed consent to retrospectively registered (approval no. 4610; 24 June 2022).

Patient consent for publication

All patients provided their written informed consent for the publication of their clinical details and images.

Competing interests

The authors declare that they have no competing interests.

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