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MDCT findings predicting post-operative residual tumor and survival in patients with pancreatic cancer

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Abstract

Objectives To predict residual tumor (R) classification and overall survival (OS) on preoperative MDCT in patients who underwent first-line surgery for pancreatic ductal adenocarcinoma (PDA).

Methods Three hundred sixteen patients with PDA who underwent MDCT and first-line surgery were included. Patients were divided into a test ($n = 216$) and a validation group ($n = 100$). The R classification was categorized into R0 (no residual tumor) and R1/R2 (microscopic/macroscopic residual tumor). We assessed the correlation between the MDCT findings and the R classification. For survival analysis, we used the Kaplan–Meier estimation and Cox proportional hazard model to determine the prognostic factors for OS. Validation of the prediction models for the R classification and OS was performed using C statistics and calibration plot.

Results Peritumoral fat stranding (odds ratio (OR) 3.826), suspicious distant metastasis (OR 2.916), portal vein involvement (OR 2.795), and tumor size (OR 1.045) were independent predictors for residual tumor ($p < .05$). On survival analysis, common hepatic artery involvement (hazard ratio (HR) 5.656), R1/R2 stage (HR 2.476), and N1 stage (HR 1.745) were predictors of poor OS ($p < .05$). C statistics for prediction models for R classification and OS were 0.816 and 0.662, respectively. Calibration plots showed good predictive performance in a high probability of the R1/R2 stage or poor OS.

Conclusion Preoperative MDCT is useful for predicting the R classification using the tumor size, peritumoral fat stranding, portal vein involvement, and suspicious distant metastasis, as well as for anticipating poor OS using the N1 stage, common hepatic artery involvement, and R1/R2 stage in patients with PDA.

Key Points

- *Thorough assessment of the involvement of common hepatic artery or portal vein and peritumoral fat stranding is warranted for predicting prognosis in patients with pancreatic ductal adenocarcinoma.*
- *Not only encasement but also abutment of common hepatic artery or portal vein by tumor predicts poor prognosis after upfront surgery.*
- *If residual tumor or poor overall survival is anticipated on preoperative MDCT, neoadjuvant treatment can be performed.*

Keywords Pancreas · Adenocarcinoma · Multidetector computed tomography · Residual tumor · Survival

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Abbreviations

CA	Celiac axis
CHA	Common hepatic artery
MDCT	Multiple detector computed tomography
OS	Overall survival
PDA	Pancreatic ductal adenocarcinoma
PV	Portal vein
R	Residual tumor
SMA	Superior mesenteric artery
SMV	Superior mesenteric vein

Introduction

The prognosis of pancreatic ductal adenocarcinoma (PDA) is dismal and the 5-year survival rate is only 8% for all stages combined [1]. Only complete surgical resection can offer the chance of a cure. When surgery is performed, no residual tumor at the resection margin, i.e., R0 resection, is a predictor of prolonged overall survival (OS) compared with that of residual tumor, i.e., R1/R2 resection [2–6]. Several studies have reported that the prognosis of R1 resection is equivalent to that of palliative chemoradiotherapy without resection [4, 5]. If R1/R2 resection is anticipated on preoperative examination before surgery, neoadjuvant treatment can be performed in order to improve the prognosis [7]. Therefore, prediction of the R classification before surgery would aid in predicting the prognosis and selecting the optimal treatment strategy in a patient with PDA.

Thorough assessment of the resectability of PDA is an important prerequisite before surgery, and MDCT is widely used for that purpose owing to its favorable spatial and temporal resolution [8]. Although there have been several studies for the predictive factors of the R classification on preoperative CT, however, those studies had small sample sizes or had been conducted with a spiral CT scanner [9–12]. Recently, there has been improvement of the CT techniques, including the multiple detector computed tomography (*MDCT*) *scanner* as well as image quality and more importantly, consensus guidelines regarding the evaluation of the resectability of PDA have been proposed [13, 14]. Therefore, the role of preoperative MDCT for prediction of the R classification should be re-evaluated.

Although there have been previous studies regarding the prognosis of resectable pancreatic cancer [5, 15], most of these studies were focused on the clinical and pathologic factors, such as the pathologic stage, serum level of the tumor marker or the resection margin status. Despite preoperative imaging being a vital tool in patients with PDA, there have been few published studies that investigated the prognostic value of preoperative MDCT and in which only image findings of a tumor or tumor–vessel relationship were evaluated [16, 17]. Comprehensive assessment of preoperative MDCT findings for prediction of the prognosis is still warranted. Therefore, we attempted to predict the R classification and OS on preoperative MDCT in patients who had undergone first-line surgery for PDA.

Materials and methods

This retrospective study was approved by the institutional review board of our hospital and written informed consent was waived.

Patients

Between 2006 and 2012, we searched the databases of our hospital for patients who underwent surgery for PDA. Initially, we found 381 patients and excluded 26 of them because the time interval between MDCT and surgery was more than 60 days. We also excluded 39 of them according to the following criteria: (i) PDA was not diagnosed in the surgical specimen; (ii) tumor was not located in the pancreas; (iii) preoperative treatment such as chemotherapy was performed; (iv) the quality of the MDCT was suboptimal; and (v) the intention of operation was palliative. Finally, 316 patients were randomly divided into two groups. The test group included 216 patients (M:F = 139:77; mean age, 62.8 ± 10.2 years) and the validation group included 100 patients (M:F = 64:36; mean age, 63.9 ± 10.3 years). The time interval between the CT and surgery was 12.2 ± 12.7 days. Details of the flow diagram of the study populations are described in Fig. 1.

CT technique

The MDCT protocol used in our hospital for patients with PDA had already been described elsewhere [8]. Briefly, most of the patients underwent quadruple-phase MDCT consisting of precontrast, early arterial, late arterial (pancreatic), and venous phases. In our hospital, early arterial phase images were obtained according to the request of surgeons for better evaluation of arteries. MDCT examinations were performed with various types of scanners and protocols and the detailed information is given in Supplementary material. The following MDCT parameters were used in most examinations: a detector collimation of 0.5–3 mm; a pitch of 0.75–1.35; a gantry rotation time of 0.35–0. 75 s; a tube current-time product of 150–240 mAs; and a peak voltage of 120 kVp; a thickness of 2.5–3.0 mm. For enhanced images, an automatic bolus tracking technique was used. In most examinations, a 1.5-mL dose of iodinated contrast material (Iopromide, Ultravist 370; Schering) per kilogram of body weight was administered using a power injector (Multilevel CT; Medrad) at a rate of 3–5 mL/s through an 18–20-gauge, plastic, intravenous catheter inserted in the antecubital vein and followed by a flush of 20–30-mL sterile saline. Contrast enhancement was measured

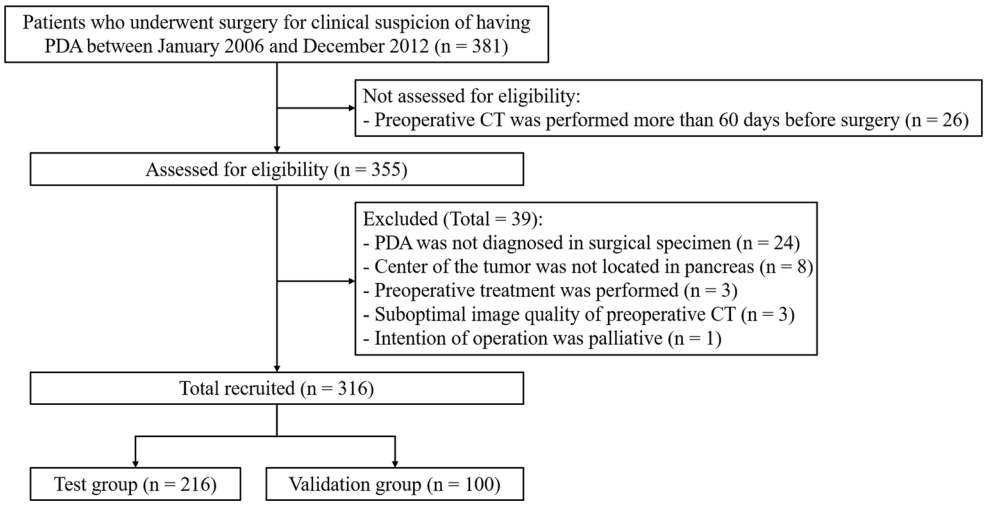

Fig. 1 Flow diagram of the study population. PDA, pancreatic ductal adenocarcinoma

by placing a region-of-interest at the abdominal aorta and the trigger threshold was 100 Hounsfield units. The early arterial phase images were automatically obtained 6 s after the trigger threshold was reached, and the pancreatic phase images were obtained using a minimum interscan delay of 5–9 s. The average scanning time delay was 23 s for the early arterial phase and 37 to 45 s for the pancreatic phase. For the venous phase, images were obtained 70 s after triggering.

CT image analysis

Two radiologists (I.J. and W.C. with 12 years and 8 years of clinical experience in abdominal imaging) independently assessed the MDCT findings, including the tumor size; location; grade of peritumoral fat stranding; resectability, i.e., resectable, borderline resectable ,or unresectable; abutment or encasement of the celiac axis (CA); superior mesenteric artery (SMA); common hepatic artery (CHA); portal vein (PV) or superior mesenteric vein (SMV); LN metastasis; and distant metastasis. The location of a tumor was classified as the pancreatic head or neck and body or tail. Peritumoral fat stranding was defined as increased CT attenuation of strands whose appearance was derived from the tumor into surrounding adipose tissue [18]. It was graded from no stranding (0), indeterminate (1), and to definite stranding (2). Portal venous phase images were used for the assessment of peritumoral fat stranding. Resectability was evaluated according to the criteria defined by the National Comprehensive Cancer Network [13] (Supplementary material). Evaluation of CA, CHA, and SMA was performed using late arterial phase images while PV or SMV was assessed using portal venous phase images. Major vascular involvement was categorized into three grades, i.e., absence, abutment, and encasement. Tumor contact with a major vessel $\leq 180°$ of the vessel circumference was referred to as abutment, and more than 180° of tumor contact with the vessel circumference was described as encasement [19]. LN metastasis was assessed for the following features: >1 cm in the shortest diameter, a rounded shape with enhancement, or necrosis. LN metastasis was graded from negative to indeterminate to definite metastasis. Finally, distant metastasis was classified as negative or suspicious. Examples of suspicious distant metastasis included a subtle omental or mesenteric haziness, a tiny and ill-defined low, attenuating hepatic lesion or pelvic ascites with minimal peritoneal thickening, all of which were too subtle to be confidently characterized as distant metastasis. Disagreements between the two reviewers were resolved by discussion with another radiologist (J.H.K. with 21 years of clinical experience in abdominal imaging).

Clinical and histopathological analysis

Clinical information, including the preoperative serum level of carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9), the type of surgery, and the patient's history of adjuvant or palliative chemotherapy, were gathered through the electronic medical records. The serum levels of CEA and CA 19-9 were dichotomized as normal (≤ 5 ng/mL and ≤ 37 U/mL, respectively) versus elevated (>5 ng/mL and >37 U/mL, respectively) [20, 21]. In addition, the patients' number of survival days after surgery and their status as to whether they remain alive or are deceased were also collected. OS was defined as the time interval between surgery and death or the date of the most recent follow-up visit date. Given the existence of extreme outliers, very different from other values, we assessed both median and mean survival to ensure a more realistic evaluation of OS. The type of surgery was classified as curative or palliative. Although curative resection was initially intended in all patients, surgery was converted to a palliative type in the 29 patients. Further information regarding the surgery is presented in Supplementary material.

From the pathologic database, histopathologic information, such as the T stage, N stage, differentiation of the tumor, and the R classification, was investigated based on the most recent TNM staging [22]. We used the R classification for residual tumors in the surgical specimen, according to the International Union Against Cancer, i.e., no residual tumor (R0), microscopic residual tumor (R1), and macroscopic residual tumor (R2) [22]. The microscopic evidence of tumor extension to within 1 mm from a resection margin or surface of the resected pancreas specimen was classified as R1 [23]. Both R1 and R2 resection stages were collectively classified as the R1/R2 resection group.

Statistical analysis

First, the diagnostic performance for R1/R2 resection was evaluated for each major vessel based on two criteria of vascular invasion, i.e., abutment and encasement versus encasement only. Sensitivity, specificity, and accuracy were calculated and were compared. Thereafter, we conducted univariate analysis using the independent *t* test and the Mann–Whitney *U* test for continuous variables as well as Fisher's exact test for categorical variables to assess the correlation between the MDCT findings and the R1/R2 resection. Those factors with $p < .05$ were included for multivariate logistic regression analysis to identify factors associated with R1/R2 resection. The coefficients of the statistically significant variables based on the results of multivariate logistic regression were reserved to make a predictive model for validation. Agreement between the reviewers was estimated using the intraclass correlation coefficient (ICC) [24]. Kaplan–Meier curves were constructed to demonstrate the differences in survival among the variables. Univariate and multivariate survival analysis were performed using the Cox proportional hazards model and the coefficients of the statistically significant variables were reserved to make a predictive model for validation.

Using the results of the test group, we made prediction models for R classification and OS and evaluated their performances by assessing the discrimination and calibration of the model. A concordance (C) statistic was used to estimate the discriminating power of the model between patients with R0 and R1/R2 resection. The predicted R1/R2 resection was assessed using the calibration plot [25]. For validation of the survival analysis, the probability of survival 5 years after surgery was determined using the coefficients of the variables yielded from the Cox proportional hazards model. A C statistic and a calibration plot for OS were calculated just as in the case of the R classification. All statistical analysis was

Table 1 Comparison of patient's demography and clinical characteristics between the R0 resection group and R1 or R2 resection group

	R0 resection ($n = 153$)	R1 or R2 resection ($n = 63$)	*p* value	Validation group ($n = 100$)
Sex ratio (M:F)	97:56	42:21	.755	64:36
Age (years), mean ± SD	62.6 ± 10.0	63.3 ± 10.3	.372	63.9 ± 10.3
Elevated preoperative CEA serum level (not elevated:elevated)	127:23	56:5	.187	83:13
Elevated preoperative CA 19-9 serum level (not elevated:elevated)	37:116	15:48	.953	58:38
Type of surgery			< .001	
Curative surgery	153	34		84
Palliative surgery	0	29		16
T stage			.336	
T1 or T2	6	1		0
T3	141	31		81
T4	5	3		3
N stage			.170	
N0	61	9		33
N1	89	25		51
Differentiation			> .999	
Well	4	0		3
Moderate	128	30		75
Poor	15	3		3
Adjuvant or palliative treatment	128 (92.8)	39 (78.0)	.010	73 (73.0)
Overall survival (months)*	29.2 (40.2)	12.2 (12.0)	< .001	14.0 (29.0)

SD, standard deviation; *CEA*, carcinoembryonic antigen; *CA*, carbohydrate antigen

*Median value was represented. Numbers in parentheses are interquartile ranges

Table 2 Comparison of the MDCT findings between the R0 resection group and R1 or R2 resection group

		R0 resection ($n = 153$)	R1 or R2 resection ($n = 63$)	Univariate analysis	Multivariate analysis			Interobserver agreement
				p value	Odds ratio	95% CI	*p* value	
Tumor size measured on MDCT (mm), mean ± SD		24.4 ± 8.4	28.6 ± 8.0	.001	1.045	1.005 to 1.086	.028	0.822
Location (head:body or tail)		105:48	40:23	.525				0.896
Peritumoral fat stranding	Negative	79	20	< .001			.001	0.485
	Indeterminate	51	13		0.870	0.375 to 2.015	.745	
	Definite	23	30		3.826	1.765 to 8.293	.001	
Abutment or encasement of major vessels*								
Celiac axis		4 (2.6)	7 (11.1)	.016				0.726
Common hepatic artery		5 (3.3)	11 (17.5)	.001				0.632
Superior mesenteric artery		12 (7.8)	15 (23.8)	.003				0.515
Portal vein		16 (10.5)	18 (28.6)	.002	2.795	1.216 to 6.423	.015	0.367
Superior mesenteric vein		58 (37.9)	35 (55.5)	.023				0.656
Lymph node involvement (negative: indeterminate: positive)		90:46:17	32:16:15	.068				0.585
Suspicious distant metastasis*		17 (11.1)	19 (30.2)	.001	2.916	1.296 to 6.561	.010	0.512

SD, standard deviation; *CI*, confidence interval

*Numbers in parentheses are percentages

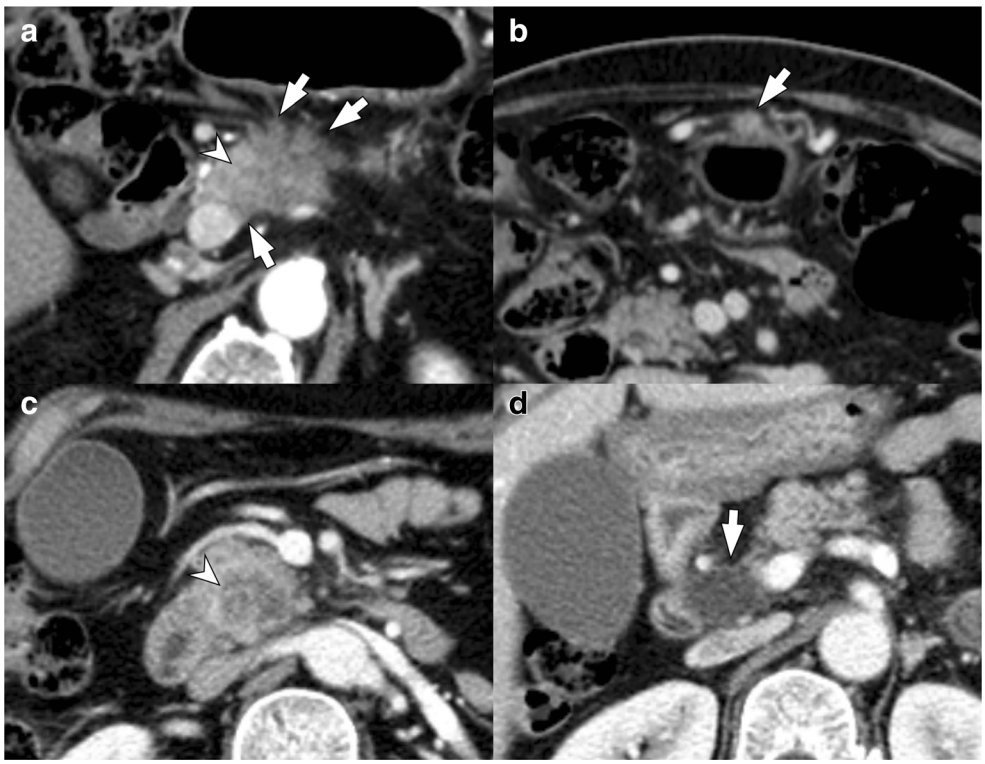

Fig. 2 Typical cases of patients with pancreatic cancer in the R0 resection group and R1/R2 resection group. (a, b) An 81-year-old male patient with pancreatic body cancer. **a** There is a subtle low attenuating 3.4-cm-sized mass at the pancreas body (arrowhead) which is abutting the portal vein (arrows). Definite peritumoral fat stranding (arrows) is also noted. **b** Along the greater omentum, there was a suspicious enhancing nodule (arrow). According to the operative record, there were multiple small peritoneal nodules when laparotomy was performed. Frozen biopsy confirmed peritoneal seeding and resection of the tumor was not performed. (c, d) A 68-year-old female patient with pancreatic uncinate process cancer. **c** A 2.7-cm-sized tumor (arrowhead) is confined in the pancreatic parenchyma and perivascular fat plane of the portal vein is preserved. **d** Although, common bile duct is dilated (arrowhead), there was no evidence of distant metastasis nor involvement of major vessels. Pancreaticoduodenectomy was performed and there was no residual tumor

performed using commercially available software (MedCalc, version 18.2.1; and IBM SPSS Statistics for Windows, version 23, IBM).

Results

The detailed demographics and clinical characteristics are described in Table 1. The type of surgery, adjuvant or palliative treatment, and OS showed statistically significant differences between the R0 resection and the R1/R2 resection group ($p < .001$). The radical surgery was performed in all of the patients in the R0 resection group, whereas palliative surgery was performed in 54% (34 of 63) of the patients in the R1/R2 resection group. Other characteristics did not demonstrate significant differences between the two groups. Information on the T stage, N stage, and tumor differentiation were not available in 29, 32, and 36 patients, respectively. Detailed information regarding adjuvant or palliative chemoradiation therapy and chemotherapy is described in the Supplementary material.

Important MDCT findings for predicting resectability

Comparison of the MDCT findings between the R0 resection and the R1/R2 resection group is summarized in Table 2. Among the MDCT findings, the size of a tumor was significantly larger in the R1/R2 resection group than in the R0 resection group. In addition, peritumoral fat stranding, involvement of major vessels, and suspicious distant metastasis were significantly different between the two groups. Multivariate logistic regression analysis revealed that definite peritumoral fat stranding (OR, 3.826;

Table 3 Important findings for predicting overall survival after surgery

		Univariate analysis			Multivariate analysis		
		Hazard ratio	95% CI	*p* value	Hazard ratio	95% CI	*p* value
Sex		0.981	0.719 to 1.340	.905			
Age		1.002	0.987 to 1.017	.805			
Elevated preoperative CEA serum level		1.077	0.693 to 1.672	.743			
Elevated preoperative CA 19-9 serum level		1.357	0.952 to 1.934	.092			
T stage	T1 or T2			.222			
	T3	1.873	0.596 to 5.885	.283			
	T4	3.035	0.805 to 11.448	.101			
N1 stage		1.578	1.112 to 2.241	.011	1.745	1.217 to 2.504	.002
Differentiation	Well			.051			
	Moderately	2.600	0.642 to 10.524	.180			
	Poorly	4.484	1.023 to 19.660	.047			
Adjuvant or palliative treatment		0.721	0.440 to 1.182	.195			
Tumor size measured on MDCT (mm)		1.029	1.013 to 1.046	.001			
Location		0.769	0.555 to 1.065	.114			
Peritumoral fat stranding	No			< .001			
	Indeterminate	1.492	1.043 to 2.135	.029			
	Definite	2.719	1.874 to 3.945	< .001			
Abutment or encasement of major vessels							
Celiac axis		1.907	1.004 to 3.625	.049			
Common hepatic artery		3.047	1.794 to 5.178	< .001	5.656	2.549 to 12.551	< .001
Superior mesenteric artery		1.658	1.068 to 2.575	.024			
Portal vein		1.250	0.833 to 1.874	.281			
Superior mesenteric vein		1.424	1.053 to 1.924	.022			
LN involvement	Negative			*.002*			
	Indeterminate	1.142	0.810 to 1.610	.448			
	Definite	2.145	1.402 to 3.282	< .001			
Suspicious distant metastasis		1.645	1.114 to 2.428	.012			
R1 or R2 resection		2.748	1.993 to 3.789	< .001	2.476	1.639 to 3.741	< .001

CEA, carcinoembryonic antigen; *CA*, carbohydrate antigen

95% CI, 1.765–8.293), suspicious distant metastasis (OR, 2.916; 95% CI, 1.296–6.561), abutment or encasement of the portal vein (OR, 2.795; 95% CI, 1.216–6.423), and larger tumor size (OR, 1.045; 95% CI, 1.005–1.086) were independent predictors for R1/R2 resection ($p < .05$) (Fig. 2). Agreement between the reviewers was almost perfect. For the criteria of major vascular invasion, not encasement only but abutment and encasement were used as the sensitivity was higher in the latter. Further details are given in Supplementary material.

Important findings for predicting the overall patient survival after surgery

The median patient survival period was 29.2 months in the R0 resection group (interquartile range, 40.2 months) and 12.2 months in the R1/R2 resection group (interquartile range, 12.0 months). The mean patient survival time was 38.6 ± 30.2 months in the R0 resection group (range, 1.9–137.5 months) and 16.8 ± 18.1 months in the R1/R2 resection group (range, 0.4–100.2 months). The number of censored patients was 34 (22.2%) in the R0 resection group and two (3.2%) in the R1/R2 resection group. Adjuvant or palliative chemotherapy or chemoradiation therapy was performed in 129 patients (84.3%) in the R0 resection group and in 39 patients (61.9%) in the R1/R2 resection group. The estimated overall 1-, 2-, and 3-year survival rates after surgery were 85.0%, 58.8%, and 38.6% in the R0 resection group and 47.6%, 17.5%, and 11.1% in the R1/R2 resection group, respectively.

The important findings for predicting OS after surgery are shown in Table 3. On univariate analysis, the N1 stage, poor histologic differentiation, larger tumor size, the presence of peritumoral fat stranding, abutment or encasement of major vessels except for the PV, involvement of LN on MDCT, suspicious distant metastasis, and the resection stage were statistically significant factors affecting OS. At multivariate analysis, abutment or encasement of the CHA (HR, 5.656; 95% CI, 2.549–12.551), the resection stage (HR, 2.476; 95% CI, 1.639–3.741), and the N1 stage (HR, 1.745; 95% CI, 1.217–2.504) were predictive factors for poor OS (Figs. 3 and 4). In subgroup analysis, according to the adjuvant or palliative treatment, these three variables all showed a statistically significant difference in patient OS.

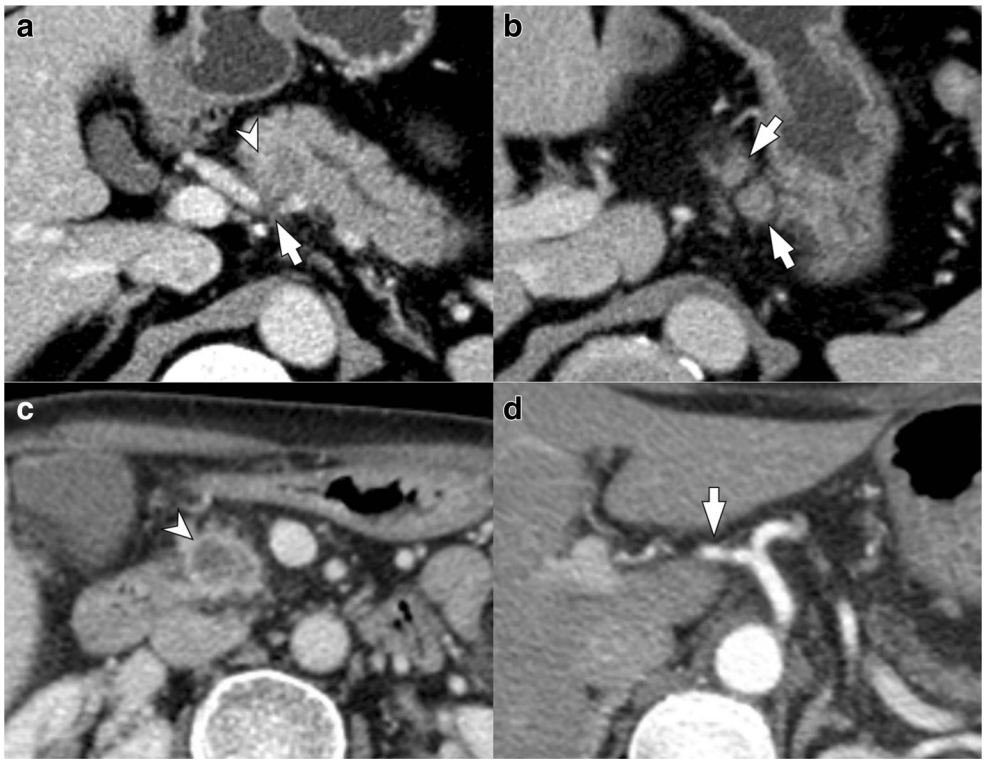

Fig. 3 Typical cases of patients with pancreatic cancer with poor overall survival (OS) and good OS. (a, b) A 69-year-old male patient with pancreatic body cancer. **a** There is a tumor located at the pancreas body (arrowhead) which is abutting the common hepatic artery (arrows). Dilatation of the upstream pancreatic duct is also noted. **b** There were indeterminate LNs in the peripancreatic area (arrows). Distal pancreatectomy was performed; however, microscopic residual tumor was reported (R1 resection). This patient died 10 months after the surgery. (c, d) A 64-year-old female patient with pancreatic head cancer. **c** The tumor is located in the pancreatic head (arrowhead). **d** There is no tumor infiltration around the common hepatic artery (arrow) and no enlarged lymph node. Pylorus-preserving pancreaticoduodenectomy was performed and R0 resection was achieved. This patient survived more than 98 months and was alive until the last day of follow-up period

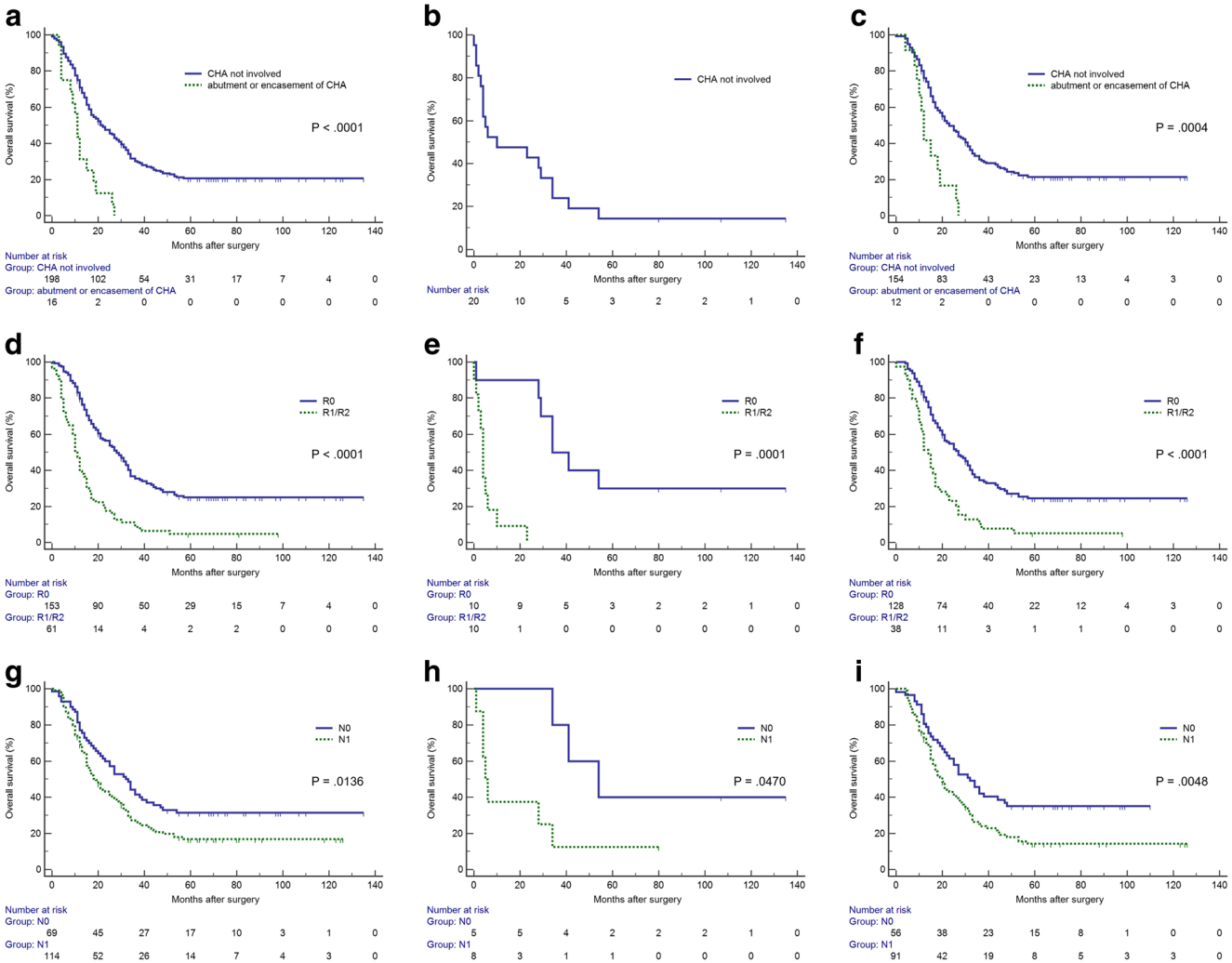

Fig. 4 Kaplan–Meier curves according to the predictors of poor overall survival. Survival curves were significantly different by the abutment or encasement of the common hepatic artery (a–c) in the total patients (**a**), patients without adjuvant or palliative treatment (**b**), and with adjuvant or palliative treatment (**c**). Difference in the survival curves according to the R1/R2 resection (d–f), and N1 stage (g–i) were also demonstrated in the total patients (**d**, **g**), patients without adjuvant or palliative treatment (**e**, **h**), and with adjuvant or palliative treatment (**f**, **i**)

Validation of predictive models for resectability and survival

The C statistic for the discriminative power of the prediction model for R classification was 0.816 (95% CI, 0.735–0.896). To obtain a calibration plot, variables that showed statistical significance in the multivariate logistic regression analysis were used. We calculated the probability of the R1/R2 resection in each patient and divided the patients into five groups regarding the increasing predicted probabilities. The calibration plot of the prediction model for R1/R2 resection is approximately a 45° line (Fig. 5a). Among the five patient groups, the three groups with higher predicted probabilities for R1/R2 resection that ranged from 35 to 80% closely matched the observed probabilities.

The discriminative power of the prediction model for OS was slightly lower than that for R1/R2 resection: the C statistic was 0.662 (95% CI, 0.602–0.723). The patients were divided into three groups based on the predictive variables of the N stage, abutment or encasement of CHA, and R1/R2 resection. The calibration plot of the prediction model for OS also is approximately a 45° line (Fig. 5b). In the group with lower predicted probabilities for 5-year OS after surgery, the actual 5-year OS probability was zero. In the other two patient groups with higher predicted probability for 5-year OS, the predicted and observed probability matched well.

Discussion

In patients with PDA who underwent first-line surgery, the preoperative MDCT findings, including definite peritumoral fat stranding, suspicious distant metastasis, abutment or

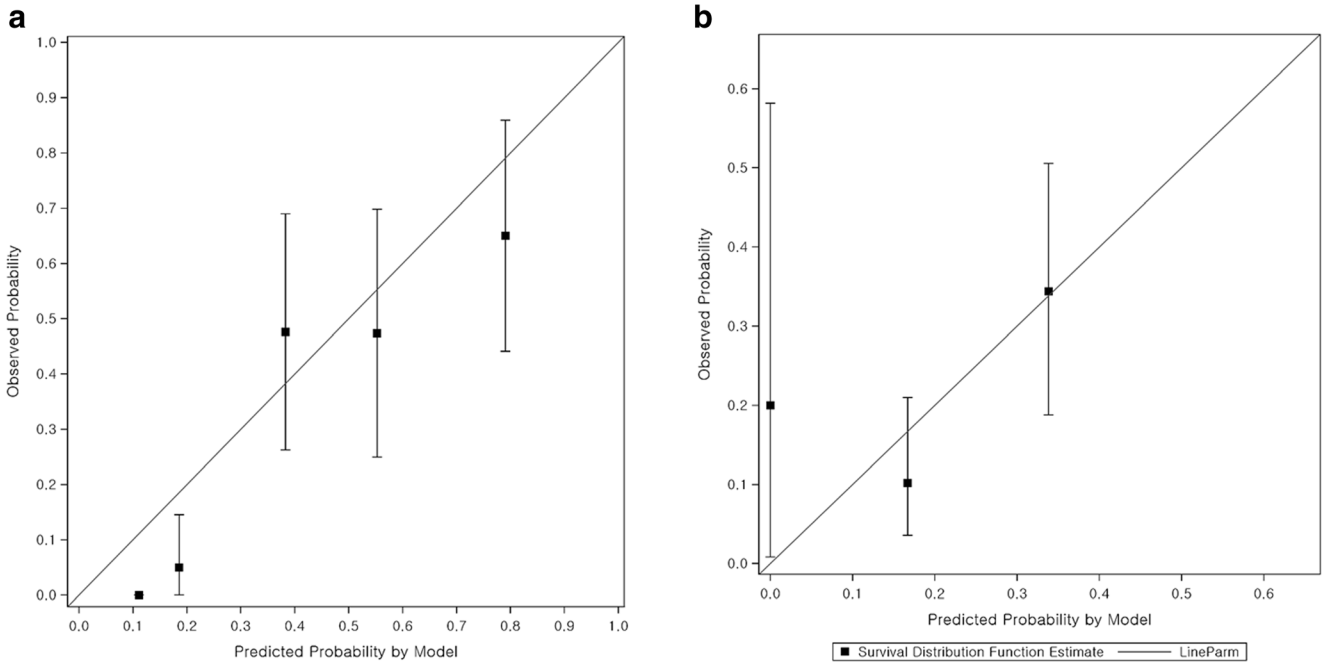

Fig. 5 Calibration plots of the predictive models obtained from the validation group. **a** The calibration plot of the prediction model for R1/R2 resection lies approximately a 45° line. Among the five groups, the three groups with higher predicted probabilities for R1/R2 resection that ranged from 35 to 80% closely matched the observed probabilities. **b** The calibration plot of the prediction model for 5-year overall survival also lies approximately a 45° line. In the group with lower predicted probabilities, the actual 5-year OS probability was zero. In the other two groups with higher predicted probabilities for 5-year OS, the predicted and observed probability matched well

encasement of PV, and the tumor size, were independent predictors for R1/R2 resection. Survival analysis revealed that abutment or encasement of CHA, R1/R2 resection, and the N1 stage were predictors of poor OS. The prediction models for the R classification and OS showed good performance (C statistic 0.816 and 0.662, respectively).

Achieving R0 resection is the goal of surgery for PDA owing to its prognostic impact. Invasion of major vessels, the presence of distant metastasis, and large tumor size have been reported to be predictors of resectability, which is in concordance with our results [9–12]. In our study, not only encasement but also PV abutment was a predictor of R1/R2 resection. A recent study which assessed the correlation between MDCT images and pathologic results also reported that even ≤ 90° contact between the tumor and a vessel is a significant risk factor for a positive resection margin [26]. Hence, even PV abutment by the tumor increases the risk of R1/R2 resection.

Peritumoral fat stranding was among the most important predictors of R1/R2 resection in our study. Peritumoral fat stranding has been reported to reflect fibrotic thickening of adipose tissue septa associated with tumor invasion or perineural and/or lymphatic invasion by a tumor [8, 18, 27]. A recent study also found a significant correlation between perineural invasion and a positive resection margin after surgery, which is in concordance with our results [28]. Therefore, the presence of peritumoral fat stranding may cause a positive resection margin. However, it is difficult to confirm the pathologic findings in each patient with peritumoral fat stranding. Therefore, further studies with a side-by-side correlation of peritumoral fat stranding on MDCT with pathologic findings are required.

We found and validated that R0 resection and the N0 stage are predictors of good OS. These results are in concordance with those of previous studies [4, 5, 13] and the importance of achieving R0 resection should be emphasized. In our study, CHA was the only major vessel that showed a predictive value for poor OS. A previous study also reported that abutment or encasement of CHA is an adverse prognostic factor for OS [29]. Our results also demonstrated that abutment or encasement of PV was correlated only with R1/R2 resection and not with OS, just as another recent study showed [30]. Several other studies have also reported poorer OS in patients with major arterial involvement [16, 31]. Although peritumoral fat stranding was a predictive factor for R1/R2 resection, it was not correlated with OS in our study. On the contrary, Chang et al suggested that perineural invasion, which can be regarded as a cause of peritumoral stranding, is associated with a positive resection margin and a poor prognosis [28]. Therefore, peritumoral fat stranding on preoperative MDCT might have an indirect impact on OS, possibly by causing R1/R2 resection.

If R1/R2 resection or poor OS is anticipated on preoperative MDCT, neoadjuvant treatment followed by surgery rather

than first-line surgery can be performed. Neoadjuvant treatment is beneficial for patients with borderline resectable PDA by increasing the odds of achieving R0 resection and improving OS [32, 33]. A recent meta-analysis compared neoadjuvant treatment with first-line surgery in patients with resectable or borderline resectable PDA also reported that neoadjuvant treatment improved OS [7], although randomized controlled trials of neoadjuvant treatment compared with upfront surgery are still lacking. In addition, patients who have progressive disease despite neoadjuvant treatment can avoid the morbidity associated with the surgery. In our study, the type of surgery was significantly different between the R0 resection group and R1/R2 resection groups. This finding is not surprising because if the tumor was locally advanced that impeded curative resection, palliative surgery rather than radical surgery was performed. Therefore, the type of surgery should have correlated well with the extent of the tumor and residual tumor after surgery.

There are several limitations in our study. First, MDCT was performed using various MDCT units due to the retrospective nature. However, our study could be considered to better reflect the real-world clinical practice in which various MDCT units are used. Second, only the patients who underwent first-line surgery were included in our study. Therefore, the results of our study would not be applicable for patients with borderline resectable PDA and who undergo neoadjuvant treatment. Third, the regimen of adjuvant or palliative therapy performed in our study was heterogeneous due to the retrospective nature of this study. In addition, the interpretation of peritumoral fat stranding had limitation because the differentiation between tumor infiltration into peripancreatic tissue or vessels and peripancreatic inflammation on imaging is difficult. Lastly, magnetic resonance imaging was not performed in all patients and the evaluation for the possibility of liver metastases was not fully performed in our study [34, 35].

In conclusion, peritumoral fat stranding and abutment or encasement of the CHA and/or PV on preoperative MDCT in patients with PAC are predictors for R1/R2 resection and poor OS. Neoadjuvant treatment can be performed for those patients in order to achieve R0 resection and to improve the OS.

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Methodology
- Retrospective
- Diagnostic or prognostic study
- Performed at one institution

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