The pancreas-to-muscle signal intensity ratio on T 1 -weighted MRI as predictive biomarker for postoperative pancreatic fistula after distal pancreatectomy: A single-center retrospective study

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Abstract

Background: Postoperative pancreatic fistula (POPF) is the most serious complication in pancreatic surgery. When POPF occurs and becomes severe, it causes secondary complications and leads to a longer treatment period. We previously reported a correlation between pancreatic fibrosis and magnetic resonance imaging (MRI) findings, and MRI may have potential to predict for POPF. This study aimed to assess the diagnostic ability of the pancreas-to-muscle signal intensity ratio on T_1-weighted MRI (SIR on T_1-w MRI) for POPF after distal pancreatectomy (DP).

Methods: This retrospective, single-institution study comprised 117 patients who underwent DP for pancreatic disease between 2010 and 2021 at the Gifu University Hospital. We statistically analyzed pre-, intra-, and post-operative factors to assess the correlation with POPF.

Results: According to the definition and grading of the International Study Group of Pancreatic Fistula (ISGPF), 29 (24.8%) of 117 patients had POPF grades B and C. In the univariate analysis, POPF was significantly associated with the pancreas-to-muscle SIR on T_1-w MRI, the drainage fluid amylase concentration (D-Amy) levels on postoperative day (POD)1 and 3, white blood cell count on POD1 and 3, C-reactive protein level on POD3, and heart rate on POD3. In multivariate analysis, only the pancreas-to-muscle SIR on T_1-w MRI (>1.37; odds ratio [OR] 23.25; 95% confidence interval [CI] 3.93 – 454.03; $p < 0.01$) and D-Amy level on POD3 (>737 U/L; OR 3.91; 95% CI 1.02 – 16.36; $p = 0.046$) were identified as independent predictive factors. In addition, the pancreas-to-muscle SIR on T_1-w MRI showed significant positive correlations with D-Amy levels both on POD1 and 3($p < 0.01$), and was significantly higher in non-pancreatic ductal adenocarcinoma cases ($p < 0.01$) and soft pancreas cases ($p=0.04$).

Conclusions: The pancreas-to-muscle SIR on T_1-w MRI was able to diagnose the development of POPF after DP as well as postoperative D-Amy levels. Furthermore, the pancreas-to-muscle SIR on T_1-w MRI also showed significantly correlated with pancreatic disease and pancreatic texture. The pancreas-to-muscle SIR on T_1-w MRI may be a potential objective biomarker reflecting pancreatic status.

Background

Postoperative pancreatic fistula (POPF) is the most serious complication of pancreatic surgery for pancreatic disease. POPF causes secondary complications, such as abdominal abscess, delayed gastric emptying, and postoperative bleeding, and may lead to not only prolonged hospital stay but also surgery-related death [1–3]. Although standardization of surgical procedures and development of surgical devices have been achieved in pancreatic surgery, the incidence of POPF has been reported to range from 3 to 50% even at high-volume centers [4–7]. Furthermore, POPF still occurs at as high a rate as 24–39% even after distal pancreatectomy (DP) without pancreaticoenteral anastomosis [8–13]. Therefore, POPF is considered to be caused by not only surgery-related factors, but also pancreas-related factors.

Pancreatic parenchyma becomes hardened because of fibrosis, and the hardness of the pancreatic parenchyma, the so-called soft pancreas, is known to be associated with POPF [14, 15]. We previously reported a significant correlation between the pathological classification of the pancreatic fibrosis grade and the development of POPF [16, 17]. We also reported the use of the pancreas-to-muscle signal intensity ratio on T_1-weighted MRI (SIR on T_1-w MRI) in evaluating pancreatic fibrosis and predicting POPF [16, 17].

The aim of this study was to assess i) the potential of the pancreas-to-muscle SIR on T_1-w MRI as a predictive factor for POPF after DP, and ii) the correlation between the pancreas-to-muscle SIR on T_1-w MRI and other pancreas-related factors.

Methods

Patients

In this single-center retrospective study, we enrolled 134 consecutive patients who underwent DP for pancreatic disease at Gifu University Hospital between January 2010 and December 2021. All procedures were conducted by expert surgeons who had qualified through the board certification system of the Japanese Society of Hepato-Biliary-Pancreatic Surgery (JSHBPS). We excluded 17 patients in total (simultaneous resection of other organs), so 117 patients were included in this study (Fig. 1). We conducted our study in accordance with the World Medical Association Declaration of Helsinki and the study was approved by the Ethics Committee of Gifu University (approval number: 2021-026).

Patient characteristics were classified into three categories: pre-, intra-, and post-operative factors (Fig. 2). The 9 preoperative factors were age, sex, body mass index (BMI), diabetes mellitus, serum albumin level, pancreatic disease (pancreatic ductal adenocarcinoma (PDAC) or non-PDAC), tumor size, tumor location, and the pancreas-to-muscle SIR on T_1-w MRI. The 6 intraoperative factors included operative time, blood loss, surgical procedure (i: open or laparoscopic surgery, ii: spleen preserving or non-preserving), pancreatic resection procedure (hand-sewn or stapler), pancreas texture (soft or hard), and pancreas thickness measured intraoperatively on resection site. Finally, the 6 postoperative factors included the amylase concentration levels of drainage fluid and serum (D-Amy and S-Amy), the white blood cell (WBC) count, C-reactive protein (CRP) level, body temperature, and heart rate on postoperative day (POD) 1 and 3. Body temperature was defined as the maximum value and heart rate was defined as the average value on the measurement day.

Perioperative management

In cases of DP for PDAC, regional lymph node dissection with splenectomy in accordance with the classification of pancreatic carcinoma of the Japan Pancreas Society [18], and pancreatic resection on the portal vein were performed. In the case of DP for non-PDAC, systematic lymph node dissection was

omitted, and pancreatic resection was performed with sufficient margin from the tumor. Pancreatic resection was performed with hand-sewn closure or using a linear stapler.

In the hand-sewn closure group, the pancreas was resected after the identification of the main pancreatic duct, and the main pancreatic duct ligated with a 3 – 0 silk suture. The stump of the remnant pancreas was closed with vertical mattress suture using 5 – 0 polypropylene. Among the group that underwent pancreatic resection using a linear stapler, and the pancreas resected using Endo GIA™ Tri-Staple or Signia™ stapling system (Medtronic plc., Dublin, Ireland) with a purple or black cartridge. The closure jaw was clamped carefully and slowly, taking 5 minutes at a fixed speed. The firing was performed at a speed of 1 cm per minute by firmly fixing the stapler. After firing, the jaws of the stapler were held shut for 1 minute. One 19Fr. Blake silicon drain (Johnson and Johnson Inc. New Brunswick, NJ, USA) was placed near the stump of the remnant pancreas. The drain was to be removed on POD 4–5 when the drainage fluid was clear and the postoperative course could pose no problem. The D-Amy and S-Amy levels were measured on POD 1, 3, and 5. All patients received prophylactic antibiotics (cefmetazole) only intraoperatively or for 2 days postoperatively.

The pancreas-to-muscle signal intensity ratio on T_1-weighted MRI

Previously, we studied the potential value of preoperative MRI in evaluating pancreatic properties [16, 17] and reported that the pancreas-to-muscle SIR on T_1-w MRI significantly correlated with pancreatic fibrosis, and that it may be a potential biomarker for predicting POPF for pancreatic surgery. The signal intensity (SI) of the pancreatic parenchyma on the portal vein and the paraspinal muscle was measured using fat-suppressed axial T_1-weighted imaging (Fig. 3). The pancreas-to-muscle SIR on T_1-w MRI was calculated using the following equation: [SI of the pancreatic parenchyma] / [SI of the paraspinal muscle].

Definition of POPF

In this study, we included only clinically symptomatic POPF. Therefore, only grades B and C pancreatic fistulas were defined as POPF (Grade B, symptomatic fistula requiring therapeutic intervention such as antibiotics and percutaneous drainage; Grade C, symptomatic fistula associated with a severe general condition of patients, sepsis, and multiorgan failure requiring aggressive treatment in the intensive care unit and surgical intervention), based on International Study Group of Pancreatic Fistula (ISGPF) definitions [19]. Diagnosis day of POPF was defined as the date when intra-abdominal fluid collection with positive cultures was identified by ultrasonography (US) or computed tomography (CT).

Statistical analysis

Continuous variables are expressed as median (range) values, and categorical variables are expressed as frequencies (percentages). For comparisons of variables between the POPF and non-POPF groups, a Fisher’s exact test was used for categorical variables, and a Mann-Whitney U test was used for

continuous variables. The predictive ability for POPF after DP was assessed by calculating the area under the receiver operating characteristic (ROC) curve. Youden's index was used to determine the optimal cut-off value to calculate both specificities and sensitivities in the ROC curve analysis. The variables identified as potentially significant by univariate analysis were selected for multivariate analysis with a logistic regression model to identify the independent predictors of POPF after DP. The correlation analysis was performed using Spearman's rank correlation coefficient to examine the correlation between the pancreas-to-muscle SIR on T_1-w on MRI and D-Amy levels. The limit of statistical significance for all analyses was defined as a 2-sided p-value of 0.05. All statistical analyses were performed using JMP software (SAS Institute Inc., Cary, NC, USA).

Results

Comparison of clinical outcomes between patients with and without POPF

In total, 117 patients underwent DP for pancreatic disease. Symptomatic POPF occurred in 29 (24.8 %) patients. Patients' clinical outcomes after DP are summarized in Table 1. The median time at which POPF was confirmed was POD 7 (range, 3-25 days). In the patients with POPF, the median time until hospital discharge was 35 days postoperatively (range, 12-121 days), and 2 patients had died within 30 postoperative days. A comparison between patients with and without POPF indicated that there were significant differences in hospital days ($p < 0.01$).

Comparison of pre-, intra-, and post-operative status between patients with and without POPF

Table 2 shows a summary of the 21 factors (classified into three categories) compared between patients with and without POPF.

Among pre-operative factors, the pancreas-to-muscle SIR on T_1-w MRI was significantly higher in the POPF group than in the non-POPF group ($p < 0.01$). Among intra-operative factors, there was no significant difference between two groups. Among post-operative factors, D-Amy level on POD 1 and 3 ($p = 0.02$ and $p < 0.01$, respectively), WBC on POD1 and 3 ($p < 0.01$ and $p = 0.048$, respectively), CRP level on POD3 ($p < 0.01$), and heart rate on POD3 ($p < 0.01$) were significantly higher in the POPF group than in the non-POPF group.

Cut-off values of the pancreas-to-muscle SIR on T_1-w MRI, D-Amy levels for predicting POPF

The ROC curves for generating cut-off values of the pancreas-to-muscle SIR on T_1-w MRI, D-Amy level on POD 1 and 3 are shown in Figure 4. The cut-off value of the pancreas-to-muscle SIR on T_1-w MRI was +1.37, with an area under the curve (AUC) of 0.741, a sensitivity of 96.3%, and specificity of 52.0% (Figure 4a). The cut-off value of D-Amy level on POD1 was 7238 U/L, with an AUC of 0.729, a sensitivity of 55.2%, and specificity of 80.5% (Figure 4b). The cut-off value of D-Amy level on POD3 was 737 U/L, with an AUC of 0.721, a sensitivity of 72.4%, and specificity of 65.5% (Figure 4c).

Uni- and multivariate analysis of prediction for POPF after DP

In univariate logistic regression analysis, POPF after DP was significantly associated with the pancreatic-to-muscle SIR on T_1-w MRI ($p < 0.01$), D-Amy level on POD1 and 3 (both $p < 0.01$), WBC on POD1 and 3 ($p < 0.01$ and $p = 0.04$, respectively), CRP level on POD3 ($p < 0.01$), and heart rate on POD3 ($p=0.02$).

A multivariate logistic regression analysis revealed that the pancreas-to-muscle SIR on T_1-w MRI (>1.37; odds ratio [OR] 23.25; 95% confidence interval [CI] 3.93 – 454.03; $p < 0.01$) and D-Amy level on POD3(>737 U/L; OR 3.91; 95% CI 1.02 – 16.36; $p = 0.046$), were independent predictive factors of POPF after DP (Table 3).

Correlation analysis between the pancreas-to-muscle SIR on T_1-w MRI and other pancreas-related factors

Next, we evaluated the correlation between the pancreas-to-muscle SIR on T_1-w MRI and other pancreas-related factors, such as pancreatic disease, pancreatic texture, and D-Amy levels. There was a significant positive correlation between the pancreas-to-muscle SIR on T_1-w MRI and D-Amy levels on both POD1 and POD3 (both $p < 0.01$) (Figure 5a and 5b). In addition, the pancreas-to-muscle SIR on T_1-w MRI was significantly higher in non-PDAC cases ($p< 0.01$, non-PDAC: median 1.57 [range 0.74 – 2.68] vs PDAC: 1.31[0.82 – 1.86]) and soft pancreatic cases ($p=0.04$, soft: 1.56 [0.74 – 2.01] vs hard: 1.32[0.86 – 2.68]) (Figure 5c and 5d).

Discussion

A high incidence of POPF is still reported in pancreatic surgery despite ongoing attempts to reduce the frequency of POPF with the development of surgical techniques and devices [4–13]. The clinical nuisance of POPF is that delayed therapeutic intervention for POPF can lead to secondary complications [1–3]. This can lead to severe disease and prolonged treatment. In this study, patients with POPF showed increase in both hospital days and mortality. Furthermore, we have previously reported that in PDAC cases, the onset of POPF leads to a delay in the initiation of postoperative adjuvant chemotherapy. Thus, POPF may affect not only short-term but also long-term prognosis. Therefore, early and accurate

prediction and diagnosis of POPF and the promptest possible intervention are required. However, the median time for POPF diagnosis was 7 days (range, 3–25) in this study, making early diagnosis difficult with only routine postoperative examination. We identified two predictive factors for POPF: i) the pancreas-to-muscle SIR on T_1-w MRI > 1.37, and ii) D-Amy level on POD3 > 737U/L.

D-Amy levels are one of the most established predictive and diagnostic factors for POPF. Therefore, the definition of POPF according to the ISGPF offers the standard diagnosis according to the D-Amy level on POD3. In this study, D-Amy levels were also significantly correlated with POPF. There is no doubt that amylase in the drainage fluid is useful in the diagnosis of POPF, as has been reported many times [20–41]. However, the following remain somewhat unclear: (1) the optimal timing of measurement, (2) the optimal cutoff value, (3) the optimal drain placement site, and (4) whether drainage fluid concentration or total amount of amylase is more reliable. In addition, postoperative drain obstruction due to fibrin or clots and drain misalignment often occur, which can interfere with accurate D-Amy level measurements.

The nature of the pancreas itself is thought to play a profound role in the development of POPF. In particular, the texture of pancreatic parenchyma, (soft pancreas) has been reported to be an important risk factor for POPF. However, the problem is that the pancreatic texture is very subjective and cannot be quantified. To solve this problem, we previously investigated the correlation between preoperative pancreatic MRI features and the histopathological pancreatic fibrosis grade of surgical specimens (fibrosis was graded as follows: F0 = normal pancreatic parenchyma, no fibrotic changes; F1 = mild fibrosis with thickening of periductal fibrosis tissue; F2 = moderate fibrosis with marked sclerosis of interlobular septa and no evidence of architectural changes; and F3 = severe fibrosis with detection of architectural destruction) [16, 17]. We found that the pancreas-to-muscle SIR on T_1-w MRI had a significantly negative correlation with the pancreatic fibrosis grade. This is because normal pancreatic parenchyma exhibits hyperintensity on T_1-w MRI, as pancreatic juice is rich in glycoproteins, and the endoplasmic reticulum within the pancreatic cells contributes to the T_1 shortening effect. However, the signal intensity gradually decreases with progression of pancreatic atrophy, fibrosis, interstitial edema, or fat deposition [42, 43]. In our previous study, the mean pancreas-to-muscle SIR on T_1-w MRI values for F0 and F1, which correspond to soft pancreas, were 1.51 and 1.48, respectively. Furthermore, the pancreas-to-muscle SIR on T_1-w MRI in the patients with POPF was significantly higher than that in patient without POPF. Based on these findings, we hypothesized that the pancreas-to-muscle SIR on T_1-w MRI might be a potential biomarker for predicting POPF and calculated the cutoff value of 1.41 [16]. Yoon et al conducted a similar study and also reported the mean pancreas-to-muscle SIR on T_1-w MRI values for F0 and F1 and the cut-off value for predicting POPF were 1.51, 1.48, and 1.40, respectively [44]. Interestingly, the calculated cut-off value for predicting POPF (1.37) in this study is very close to that in the previous studies. Furthermore, the pancreas-to-muscle SIR on T_1-w MRI also showed a significant correlation with not only POPF, but also pancreatic disease, texture of pancreatic parenchyma, and D-Amy levels.

This study had some limitations. First, it was retrospective in design and undertaken at a single institution, and involved a small number of study patients. The relatively small sample size may have

caused a selection bias. This limitation should be considered when evaluating our study results. A prospective, multi-centered study is needed involving a larger number of patients in the future. Second, this study was limited to DP, for which the surgical technique is relatively simple compared to pancreaticoduodenectomy (PD). In this study, no significant correlation was found between surgical-related factors, especially surgical technique (open or lap, spleen preserving or non-preserving, hand sewn or stapler) and POPF. Therefore, the pancreas-to-muscle SIR on T_1-w MRI may be effective in predicting POPF after PD and gastrectomy.

Conclusions

We found that the pancreas-to-muscle SIR on T_1-weighted MRI has excellent predictive and diagnostic ability for POPF as well as D-Amy level. The pancreas-to-muscle SIR is an objective and quantitative biomarker reflecting pancreatic characteristics.

Postoperative management based on the pancreas-to-muscle SIR on T_1-weighted MRI may contribute to shortened hospital stay.

Abbreviations

BMI, body mass index; CI, confidence interval; CT, computed tomography; D-Amy, drainage fluid amylase; DP, distal pancreatectomy; MRI, magnetic resonance imaging; OR, odds ratio; ISGPF, International Study Group of Pancreatic Fistula; PD, pancreaticoduodenectomy; PDAC, Pancreatic ductal adenocarcinoma; POD, postoperative day; POPF, Postoperative pancreatic fistula; ROC, receiver operating characteristic; S-Amy, serum amylase; SIR on T_1-w MRI, signal intensity ratio on T_1-weighted MRI; US, ultrasonography

Declarations

Ethics approval and consent to participate:

The present study was conducted in accordance with the World Medical Association Declaration of Helsinki and was approved by the Ethics Committee of Gifu University (approval number ‘2021-26’). As this study was a retrospective study and did not include any potentially identifiable patient data, informed consent was not obtained from the enrolled patients. This retrospective study was approved by our Institutional Review Board.

Consent for publication:

Not applicable

Availability of data and materials:

The datasets used during this study are available from the corresponding author upon reasonable request.

Competing interests:

T. Takahashi received honoraria for lectures from Takeda Pharmaceutical Co., Ltd. The remaining authors declare that they have no conflicts of interest.

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Authors' contributions:

MF conceived the study concept and planned the design as the principal investigator. MF interpreted the results and wrote the manuscript draft.

KM and TH revised the manuscript draft through adding intellectual content and providing critical advice. MF, KM, TH, SF, MK, IY, YS, SK, YT, NO, NM, and TT obtained the data and provided critical comments to improve the manuscript and gave final approval for submission.

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Tables

Table 1

Comparison of clinical outcomes between patients with and without POPF after distal pancreatectomy.

	Patients with POPF (n=29)		Patients without POPF (n=88)	*p*-value
Diagnosis days of POPF (day)	7 (3-25)		-	-
Grade of POPF¶				-
Grade B	27(93.1)		-	
Grade C	2 (6.9)		-	
Treatment for POPF	Drain replacement and irrigation	19 (65.5)	-	-
	Endoscopic transgastric drainage	7 (24.1)		
	Antibiotics and octreotide	3(10.4)		
Postoperative death within 30 days	2 (6.9)		0 (0.0)	0.06
Hospital days (days)	35 (12-121)		13 (7-23)	<0.01

Data are expressed as median (range) or number of patients (percentage)

POPF: postoperative pancreatic fistula

¶: International Study Group (ISGPS) definition and grading of POPF as follow: Grade B, symptomatic fistula requiring therapeutic intervention such as antibiotics and percutaneous drainage; Grade C, symptomatic fistula associated with a severe general condition of patients, sepsis, and multiorgan failure requiring aggressive treatment in the intensive care unit and surgical intervention.

§: Period until the start of postoperative adjuvant chemotherapy was calculated from the date of the surgery.

: $p<0.05$

Table 2

Comparison of pre-, intra-, and post-operative status between patients with and without POPF after distal pancreatectomy.

Data are expressed as median (range) or number of patients.

POPF: postoperative pancreatic fistula

		Patients with POPF (n=29)	Patients without POPF (n=88)	*p*-value
Pre-operative	Age (years)	67 (40-82)	67 (11-84)	0.87
	Sex			0.67
	Male	18 (62.1)	50 (56.8)	
	Female	11 (37.9)	38 (43.2)	
	BMI (kg/m^2)	23.6 (17.6-32.2)	22.4 (16.2-32.2)	0.37
	Diabetes mellitus	7 (24.1)	29 (33.0)	0.37
	Serum albumin level (g/dl)	4.1 (3.3-5.0)	4.3 (2.7-4.9)	0.38
	Pancreatic ductal adeno carcinoma	12 (41.4)	43 (48.9)	0.53
	Tumor size (mm)	22.5 (10-88)	27 (4-120)	0.61
	Location			0.28
	Pb	14 (48.3)	54 (61.4)	
	Pt	15 (51.7)	34 (38.6)	
	Pancreas-to-muscle SIR on T_1-w MRI	1.64 (1.25-2.68)	1.35 (0.74-2.16)	<0.01
Intra-operative	Operative time (min)	284 (174-537)	264 (143-564)	0.13
	Blood loss (ml)	190 (10-1910)	260 (0-1840)	0.84
	Surgical procedure			
	Open	23 (79.3)	60 (68.2)	0.35
	Laparoscopic	6 (20.7)	28 (31.8)	
	Spleen preserving	3 (10.3)	15 (17.1)	0.56
	Non spleen preserving	26 (89.7)	73 (82.9)	
	Resection procedure			0.83
	Hand-sewn	11 (37.9)	36 (40.9)	
	Stapler	18 (62.1)	52 (59.1)	
	Pancreas texture			0.37
	Soft	21 (72.4)	54 (61.4)	

	Hard	8 (27.6)	34 (38.6)	
	Pancreas thickness (mm)	11 (8-17)	12 (3-24)	0.46
Post-operative	D-Amy levels (U/l)			
	POD1	7652 (108-34076)	1899 (42-61075)	0.02
	POD3	1290 (42-16515)	403 (35-43873)	<0.01
	S-Amy levels (U/l)			
	POD1	113 (47-1108)	163 (35-1921)	0.24
	POD3	40 (11-223)	50 (15-663)	0.10
	WBC ($\times 10^3$/μl)			
	POD1	12.6 (7.5-26.5)	11.1 (5.3-18.2)	<0.01
	POD3	13.3 (5.9-26.9)	11.3 (3.9-23.9)	0.048
	CRP (mg/dl)			
	POD1	9.3 (1.8-15.4)	8.3 (0.2-17.5)	0.16
	POD3	20.1 (8.0-33.5)	14.5 (0.3-26.5)	<0.01
	Body temperature (°C)			
	POD1	38.0 (37.1-39.4)	38.0 (36.9-39.3)	0.55
	POD3	37.4 (36.1-38.9)	37.4 (36.2-39.4)	0.30
	Heart rate (bpm)			
	POD1	98 (81-142)	92 (61-122)	0.07
	POD3	88 (72-111)	82 (56-119)	<0.01

BMI: body mass index

Pancreas-to-muscle SIR on T_1-w MRI: The pancreas-to-muscle signal intensity ratio on unenhanced T_1-weigthed magnetic resonance imaging

S-Amy: Serum amylase concentration

D-Amy: Drainage fluid amylase concentration

POD: postoperative day

WBC: white blood cell

CRP: c-reactive protein

▯: $p < 0.05$

Table 3

Uni- and multivariate predictive factors of POPF after DP.

POPF: postoperative pancreatic fistula

OR: odds ratio

95%CI: 95% confidence interval

BMI: body mass index

Pancreas-to-muscle SIR on T_1-w MRI: The pancreas-to-muscle signal intensity ratio on unenhanced T_1-weigthed magnetic resonance imaging

D-Amy: Drainage fluid amylase concentration

S-Amy: Serum amylase concentration

POD: postoperative day

WBC: white blood cell

CRP: c-reactive protein

▯: $p < 0.05$

Figures

		n	Univariate			Multivariate		
			OR	95%CI	p-value	OR	95%CI	*p*-value
Pre-operative	Age (years)			0.32-1.89	0.61			
	>70	45	0.79					
	<70	72	1					
	Sex			0.53-3.01	0.62			
	Male	68	1.24					
	Female	49	1					
	BMI (kg/m^2)			0.85-5.00	0.10			
	>24	39	2.07					
	<24	77	1					
	Diabetes mellitus	36	0.65	0.23-1.63	0.36			
	yes	81	1					
	no							
	Serum albumin level (mg/dl)			0.12-1.90	0.27			
	>3.6	10	0.46					
	<3.6	107	1					
	Pancreatic ductal adeno carcinoma			0.31-1.72	0.48			
	yes	55	0.74					
	no	62	1					
	Tumor size (mm)			0.39-2.29	0.88			
	>20	70	0.93					
	<20	43	1					
	Location		0.59	0.25-1.37	0.22			
	Pb	68	1					
	Pt	49						
	Pancreas-to-muscle			5.83-543.73	<0.01		3.93-454.03	<0.01

	SIR on T_1-w MRI					23.25		
	>1.37	61	29.7			1		
	<1.37	41	1					
Intra-operative	Operative time (min)							
	>300	38	1.36	0.55-3.24	0.50			
	<300	78	1					
	Blood loss (ml)			0.33-2.07	0.73			
	>400	39	0.86					
	<400	77	1					
	Surgical procedure							
	Open	83	1.79	0.69-5.28	0.24			
	Laparoscopic	34	1					
	Spleen preserving	18	0.56	0.12-1.87	0.37			
	Non spleen preserving	99	1					
	Resection procedure	47		0.36-2.07	0.78			
	Hand-sewn	70	0.88					
	Stapler		1					
	Pancreas texture			0.68-4.35	0.28			
	Soft	75	1.65					
	Hard	42	1					
	Pancreas thickness (mm)			0.30-1.64	0.42			
	>12	56	0.71					
	<12	61	1					
Post-operative	D-Amy levels (U/l) – POD1	33	5.07	2.07-12.78	<0.01*	1.21	0.31-4.75	0.78
	>7238	83	1			1		
	<7238							
	D-Amy levels (U/l) – POD3	51	4.99	2.04-13.25	<0.01*		1.02-16.36	0.046*
	>737	65	1					
						3.91		

<737					1		
S-Amy levels (U/l) – POD1	85	0.51	0.21-1.28	0.15			
>100	32	1					
<100							
S-Amy levels (U/l) - POD3	16	1	0.26-3.17	1.00			
>100	100	1					
<100							
WBC (×10^3/μl) – POD1	48	3.16	1.34-7.75	<0.01*		0.69-9.12	0.17
>1.20	69	1			2.44		
<1.20					1		
WBC (×10^3/μl) - POD3	34	2.59	1.07-6.29	0.04*	1.03	0.27-3.73	0.96
>1.40	83	1			1		
<1.40							
CRP (mg/dl) – POD1	40	1.51	0.63-3.58	0.35			
>10	77	1					
<10							
CRP (mg/dl) - POD3	34	3.89	1.61-9.60	<0.01*	2.75	0.75-10.70	0.13
>20	83	1			1		
<20							
Body temperature (℃) – POD1			0.32-1.75	0.49			
>38.0	71	0.74					
<38.0	46	1					
Body temperature (℃) - POD3			0.07-1.87	0.31			
>38.0	14	0.47					
<38.0	103	1					
Heart rate (bpm) – POD1			0.85-4.88	0.11			
	38	2.05					

>100	79	1					
<100							
Heart rate (bpm) - POD3			1.32-14.81	0.02	3.84	0.77-21.40	0.10
>100	13	4.35			1		
<100	104	1					

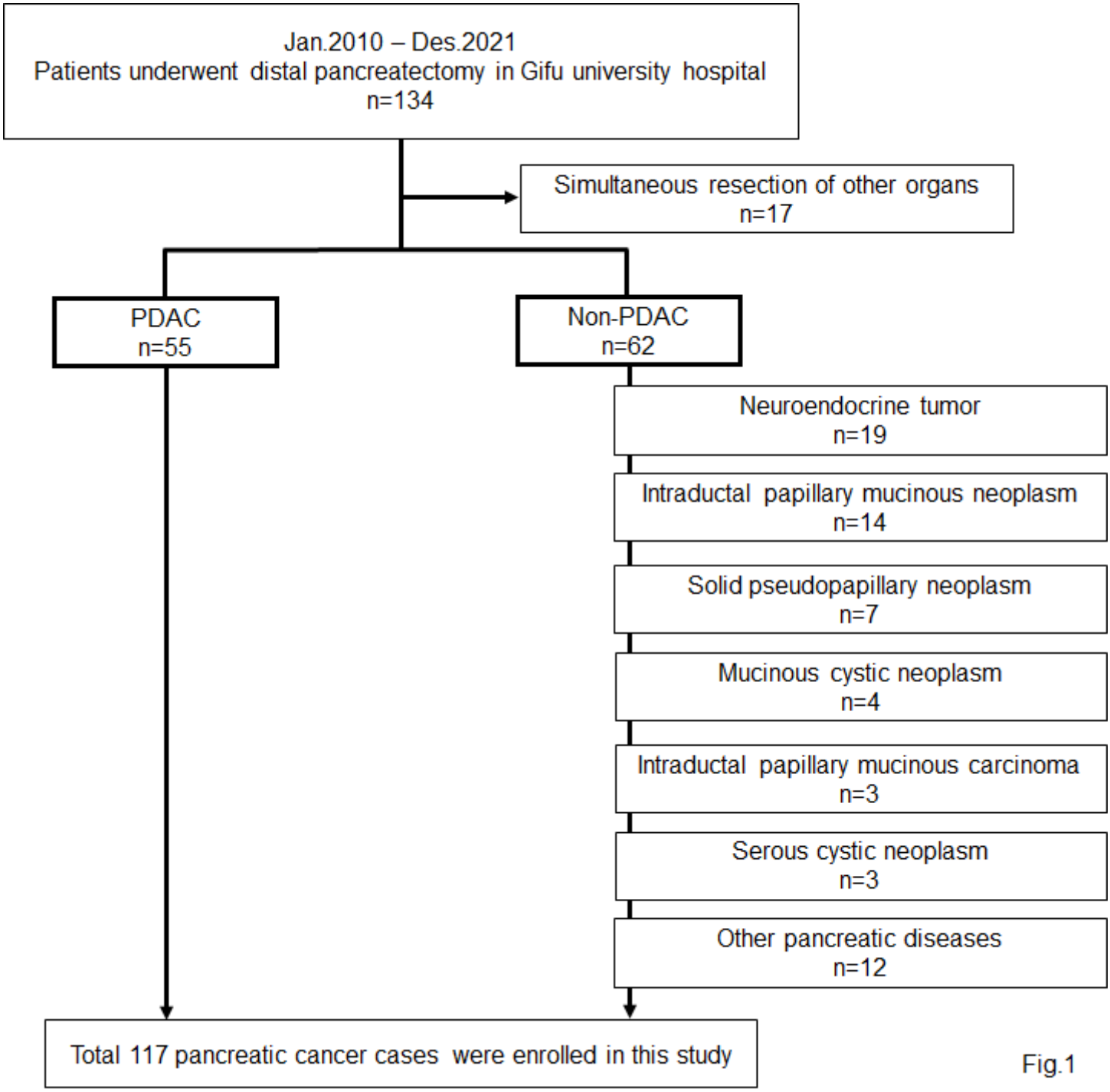

Figure 1

Exclusion criteria

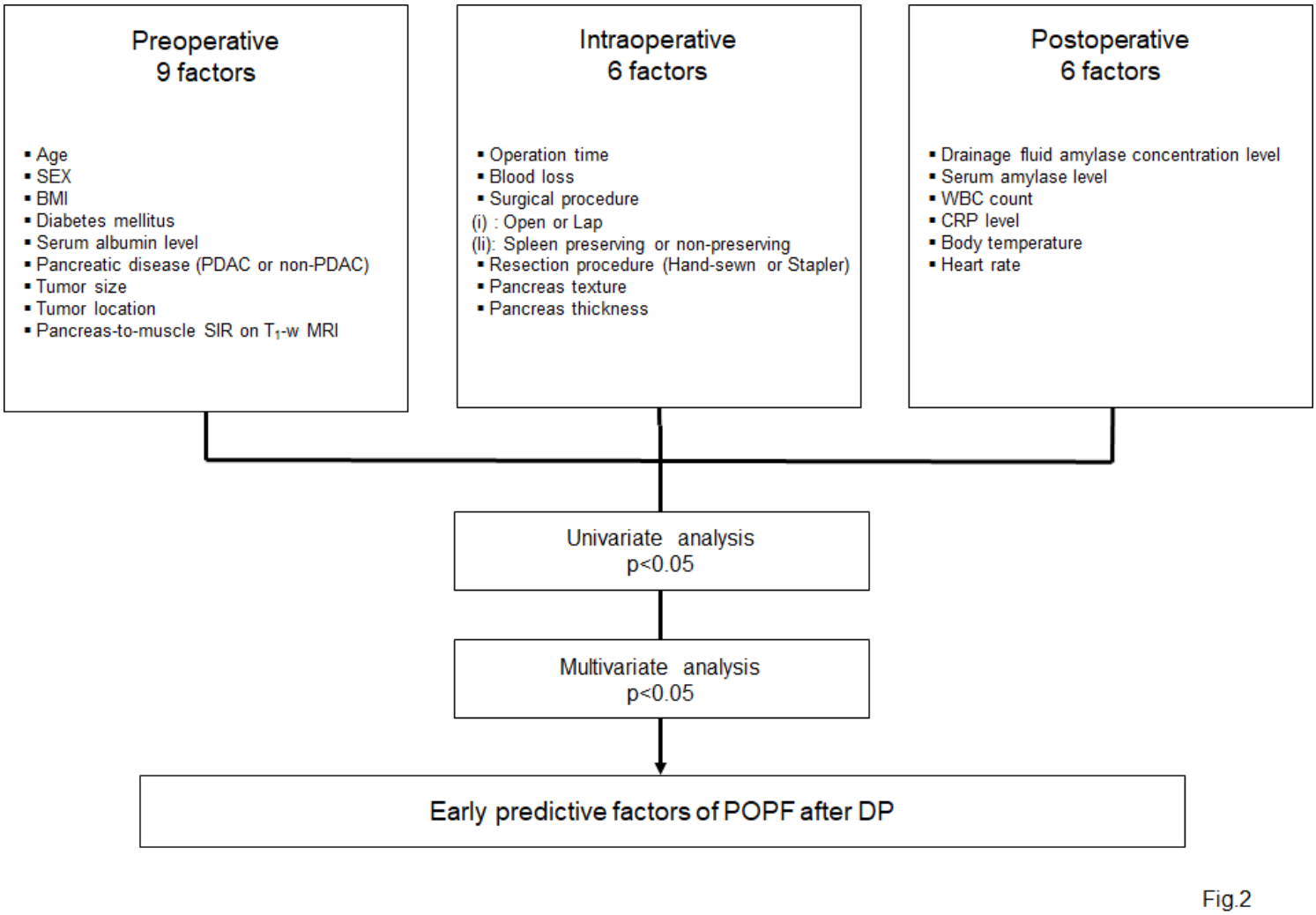

Figure 2

Analysis flow chart for identifying predictive factors for postoperative pancreatic fistula (POPF) after distal pancreatectomy (DP)

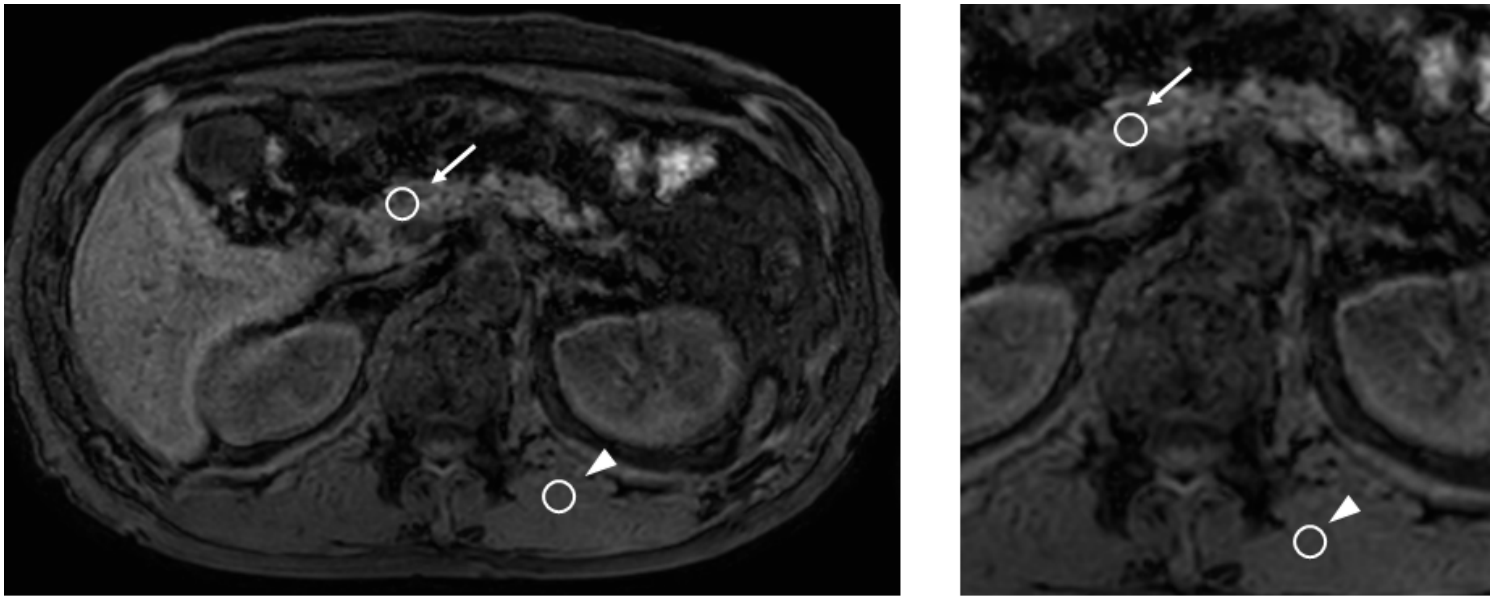

Fig.3

Figure 3

The pancreas-to-muscle signal intensity ratio on fat-suppressed axial T_1-weighted MRI was calculated by [Signal intensity of the pancreatic parenchyma] (arrow) / [Signal intensity of the paraspinal muscle] (arrowhead).

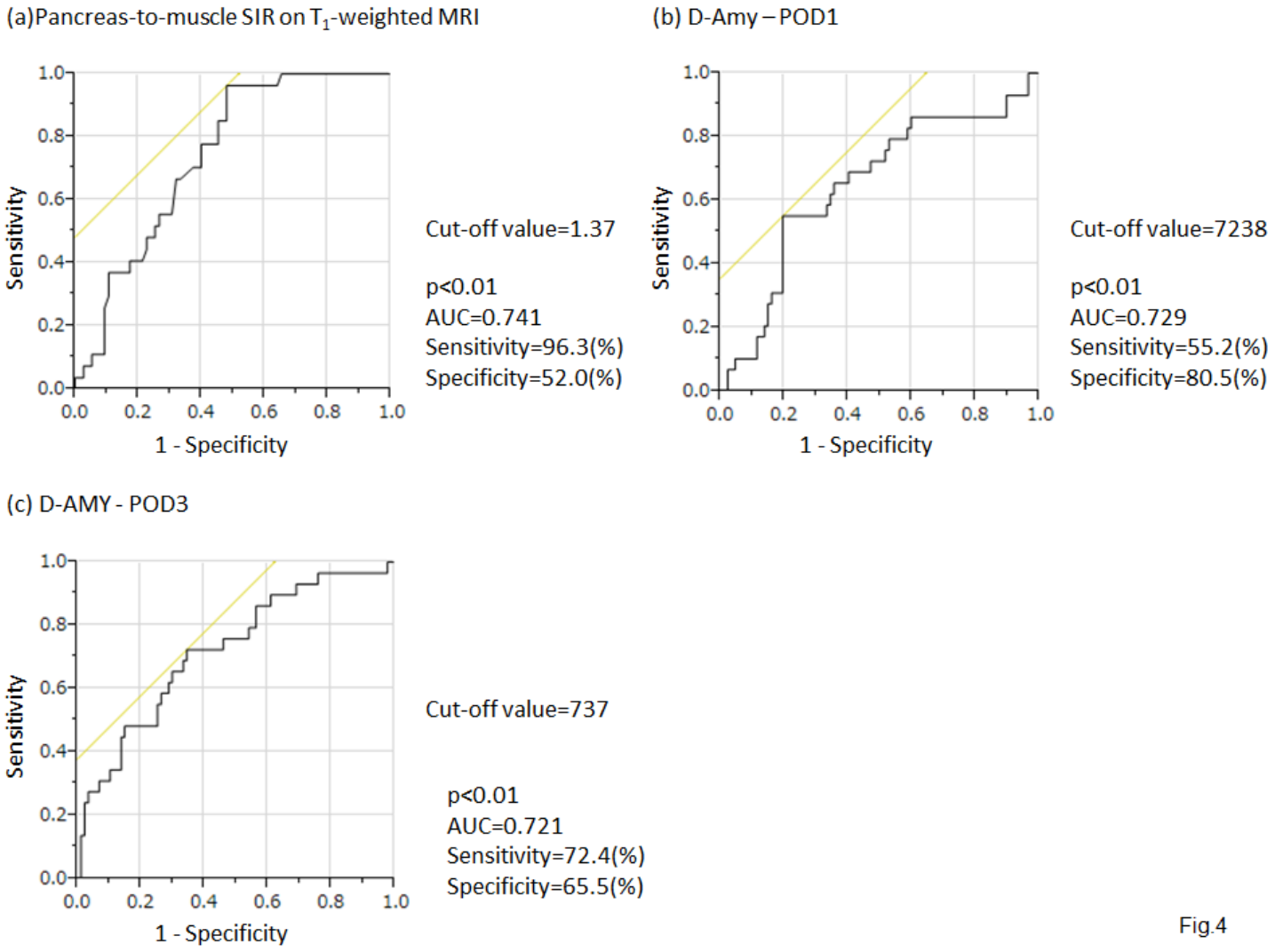

Figure 4

Receiver operating characteristics (ROC) curve analysis of pancreas-to-muscle SIR on T_1-weighted MRI and D-Amy level on POD 1 and 3 for discriminating to POPF.

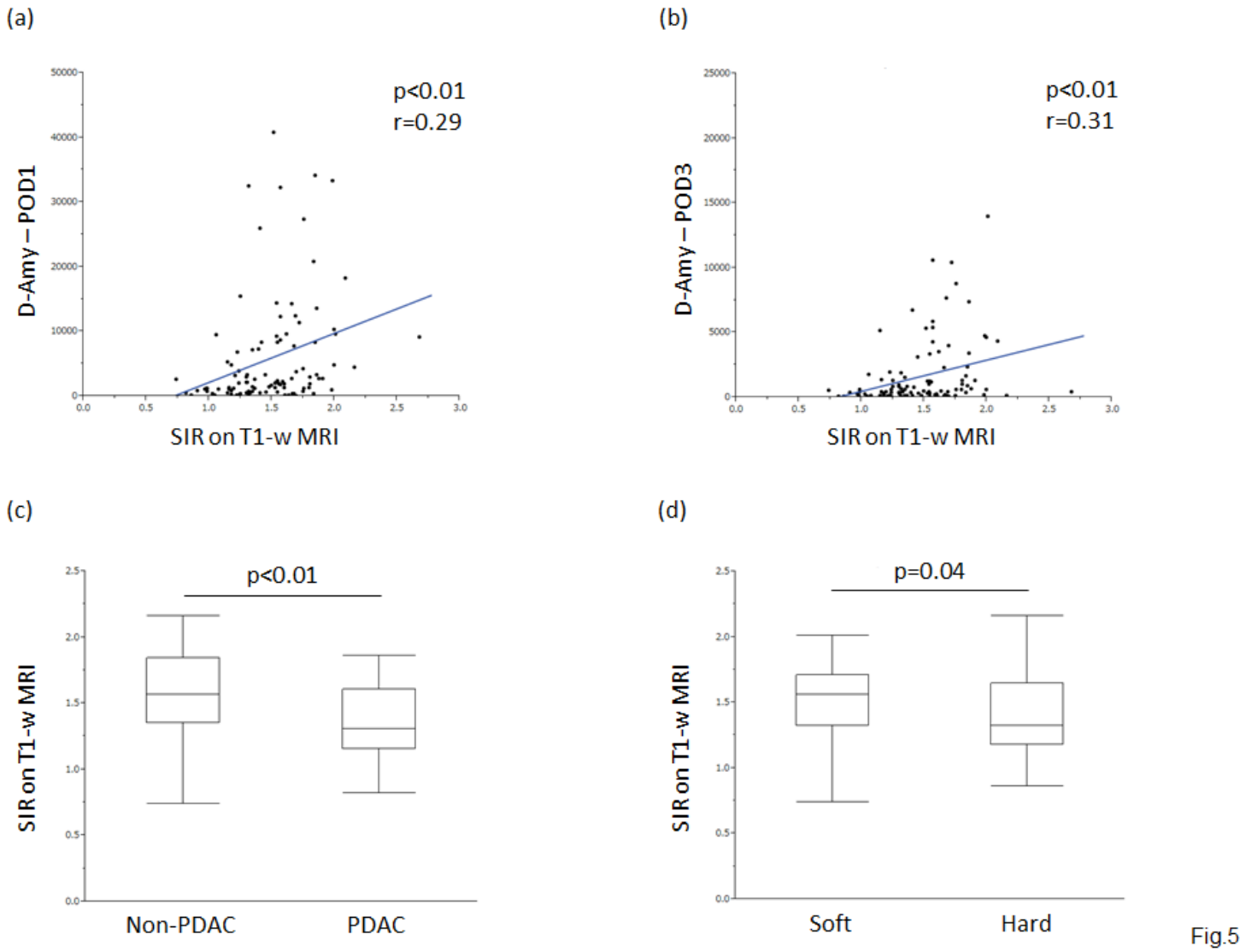

Figure 5

(a) (b) Correlation between the pancreas-to-muscle SIR on T_1-weighted MRI and D-Amy levels on POD1 and 3. Pearson's rank correlation coefficient (r) is shown.

(c) The pancreas-to-muscle SIR on T_1-weighted MRI between non-PDAC cases (n = 62) and PDAC cases (n = 55). The Wilcoxon signed-rank test was performed for comparisons between groups.

(d) The pancreas-to-muscle SIR on T_1-weighted MRI between soft pancreas (n = 75) and hard pancreas (n = 42). The Wilcoxon signed-rank test was performed for comparisons between groups.