Preoperative percent body fat in bioelectrical impedance analysis predicts pancreatic fistula after pencreaticoduodenectomy

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Research Article

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Abstract

Background

It is unclear which body composition affects postoperative pancreatic fistula (POPF) after pancreaticoduodenectomy. In the present study, we evaluated the relationship between nutritional factors, body composition, and POPF.

Methods

This was a prospective observational cohort study. Patients who underwent pancreaticoduodenectomy between March 2018 and July 2021 were included in this study. Preoperative body composition was measured using a bioelectrical impedance analyzer. In addition, the predictive factors for POPF were analyzed.

Results

The study included 143 patients. Among these patients, 31 had POPF (POPF group) and 112 did not (non-POPF group) after pancreaticoduodenectomy. For body composition, the percent body fat was significantly higher in the POPF group (26.90 vs 23.48, $P = 0.022$). Multivariate analysis revealed that alcohol consumption (odds ratio 2.71, $P = 0.028$), body mass index ≥ 25.0 kg/m^2 (odds ratio 3.43, $P = 0.01$), albumin level (odds ratio 2.65, $P = 0.028$), and percent body fat (odds ratio 1.06, $P = 0.032$) were significantly independent predictive factors for POPF. When the patients were divided into three groups based on their percent body fat (< 25, 25–35, and ≥ 35), POPF occurred more frequently in the group with ≥ 35 percent body fat (47.1%) than in the < 25 group (15.5%) ($P = 0.008$).

Conclusion

Pancreaticoduodenectomy could be performed if it is technically and oncologically appropriate, and predictive factors for POPF, such as percent body fat, should be considered before proceeding to surgery (ClinicalTrials.gov trial registration no. NCT5257434).

Introduction

Pancreaticoduodenectomy (PD) is a potentially curative treatment for both primary and secondary peri-ampullary neoplasms. In recent years, improvements in operative and anesthetic techniques, regionalization to high-volume centers, implementation of standardized recovery pathways, and better understanding and management of common complications have contributed to markedly improve short-term outcomes after PD [1, 2]. However, postoperative complications after PD remain an important issue, with a high incidence varying between 40% and 60% [3]. Postoperative pancreatic fistula (POPF) is the most common and severe complication due to leakage of pancreatic exocrine secretions at the pancreatic-enteric anastomosis, with reported rates ranging from 10%-28%. Furthermore, patients with POPF have approximately double the risk of mortality compared to those without POPF [4]. Therefore, to ensure access to PD and improve the quality of surgical care, the treating physician must consider both the risks associated with the PD procedure and patient characteristics.

Factors predicting the occurrence of POPF after PD for peri-ampullary neoplasms include numerous strategies, such as patient physiological status, pancreatic conditions, surgical technique, and surgeon experience [5]. Development of POPF seems inevitable in high-risk scenarios, whereas predicting the risk of developing clinically relevant POPF is extremely complex. Every clinical study and meta-analysis review is always technically biased by the surgeons. Pancreatic communities would like to know the true risk factors of POPF after PD on individual patient characteristics without this bias. A previous study demonstrated that high body mass index (BMI) was an independent predictive factor for POPF [6]. Recently, some articles related to pancreatectomy and body composition assessed using bioelectrical impedance analysis (BIA) have been reported [7, 8]. However, the body composition factors that affect POPF remain unclear.

Given the sparse reports on POPF after PD, more robust data are needed to help physicians assess and understand the impact of POPF on patient quality and postoperative management. Therefore, the purpose of our study was to determine the incidence rate of POPF after PD and to examine its short-term outcomes with a fixed expert pancreatic team, as well as to identify the risk factors of POPF after PD, especially with patient physiological characteristics using BIA.

Patients And Methods

Study population

All patients who underwent elective PD for peri-ampullary tumors between March 2018 and July 2021 at the Kochi Health Sciences Center were considered eligible for inclusion in this study. The inclusion criterion was the availability of preoperative contrast-enhanced computed tomography (CT) performed at this institution within 30 days of scheduled surgery. Our criteria for PD in patients with pancreatic tumors were neoplasms located at the head of the pancreas with no distant metastasis surgically resected, according to the consensus statement of the Society of Abdominal Radiology and the American Pancreatic Association [9]. They were also reviewed by a multi-disciplinary hepato-biliary-pancreatic tumor board at Kochi Health Sciences Center with treatment recommendations rendered from a consensus. Patient exclusion criteria included patients with a prior history of pancreatic surgery, a body weight loss of > 10% during the six months prior to surgery, the presence of distant metastases, or seriously impaired function of vital organs due to respiratory, renal, or heart disease. Patients were informed of the purpose and details of the study, and written consent was obtained prior to enrolment. The study was approved by the local ethics committee of the Kochi Health Sciences Center and was carried out in accordance with the Declaration of Helsinki (ClinicalTrials.gov trial registration no. NCT5257434).

Preoperative anthropometric and blood-chemistry measurements

Physical status and preoperative laboratory values were obtained within 2 weeks prior to the initiation of surgery. BMI was calculated by dividing the body weight in kilograms by the square of the height in meters. The prognostic nutritional index (PNI) was calculated based on the serum albumin and total lymphocyte count using the following equation: PNI = 10 × serum albumin (g/dL) + 0.005 × total lymphocyte count (/mL) [10]. In addition to BMI and factors related to body composition, previously established nutritional scores were calculated. These included controlling nutritional status (CONUT), Glasgow prognostic score (GPS), PNI, platelet lymphocyte ratio (PLR), and neutrophil-lymphocyte ratio (NLR) [11–14].

Bioelectrical impedance analysis

Body composition values were obtained from the electronic medical records of InBody® (InBody, Tokyo Japan) testing performed within 14 days of the scheduled surgery. InBody is a body composition analyzer that estimates segmental body composition (arms, trunk, and legs) at multiple frequencies (1, 5, 50, 250, 500, and 1000 kHz). The BIA analyzer displays extracellular water/total body water (ECW/TBW) as the water balance. The patients were instructed to grasp the handles of the analyzer in which the electrodes were embedded and to stand on electrodes that contacted the bottoms of their feet (two electrodes for each foot and hand). The analyzer independently measures ECW and intracellular water (ICW) [15]. Body fat mass was calculated as body weight minus fat-free mass [16]. The formula for percent body fat was calculated as body fat mass divided by body weight. Body cell mass (BCM) was calculated as the sum of ICW and protein.

The skeletal muscle index (SMI) was calculated as the sum of the muscles in the four extremities for the square of the height (kg/m^2) [17]. The items reported were percent body fat, ECW/TBW, and BMI. Sarcopenia was diagnosed by measuring muscle mass using a bioelectrical impedance analyzer. SMI was calculated as the sum of muscles in four extremities/$height^2$ (kg/m^2) < 7.0 in men and < 5.7 in women, based on the diagnostic criteria advocated by the Asian Working Group for Sarcopenia [17].

Pancreatico-enteric anastomotic technique

Reconstruction was performed using the modified Child’s technique. After the jejunal limb was brought up through the retrocolic root, pancreaticojejunostomy (sutured using a running monofilament synthetic absorbable suture, 5/0 or 6/0, for anastomosis of the main pancreatic duct to the jejunal mucosal layer and several interrupted sutures with a double-armed 4 – 0 monofilament synthetic absorbable suture of the pancreatic parenchyma to the jejunal seromuscular layer) was performed approximately 15 cm away from the end of the jejunal limb. No drainage tube was inserted into the main pancreatic duct, and the two drains were always placed close to the pancreatic anastomoses.

Assessments

Postoperative complications were classified according to the Clavien-Dindo classification [18]. POPF was diagnosed and graded according to the International Study Group on Pancreatic Fistula classification [19]. Only grade B and C fistulas were regarded as POPF in this study because grade A fistulas are of no clinical relevance. The primary outcomes of the current study were the rate of POPF after PD and the predictive factors of POPF after PD. The secondary outcome was to identify patient characteristics and nutritional status excluding surgeons' biases with a fixed expert pancreatic team that is prone to POPF, especially by using InBody®.

Statistical analysis

Continuous variables are described as medians and ranges. Categorical variables are presented as absolute numbers and percentages. Statistical analyses were performed using the Mann-Whitney U-test for continuous variables and Fisher's exact test for categorical variables. All statistically significant preoperative and perioperative variables were included in the model. By using Logistic regression models, the odds ratios and 95% confidence intervals (CI) were estimated. The strength of the linear relationship between the two variables was measured using Pearson correlation. All *P*-values reported are two-sided, with an alpha level of 0.05 considered statistically significant. Statistical analyses were performed using the EZR software (Saitama Medical Center, Jichi Medical University, Saitama, Japan).

Results

Patient selection

Elective PD was performed on 167 consecutive patients between March 2018 and July 2021 (Fig. 1). All patients underwent preoperative cancer-staging CT scan within a month of surgery. Patients who did not undergo preoperative BIA (n = 24) were excluded from this study. The remaining 143 patients were included in this analysis, with 31 having POPF (POPF group) and 112 without POPF (non-POPF group) after undergoing PD.

Overall patient characteristics

Patient characteristics and preoperative oncologic and nutritional statuses are shown in Table 1. The patient population was comprised of 95 males and 48 females with a median age of 72 years (range, 27–89 years). The pathological diagnoses were pancreatic cancer (PC) in 89 patients, cholangiocarcinoma in 21, ampullary cancer in 15, intraductal papillary mucinous neoplasm (IPMN) in nine, pancreatic neuroendocrine tumor in five, duodenal cancer in three, and duodenal gastrointestinal stromal tumor. The median CONUT score was 2 (range, 0–8), indicating mild malnutrition. For variables measured by BIA, the median abdominal circumference was 75.9 cm (range, 59.2-106.9). In body composition, TBW, protein, mineral, and body fat mass were 31.5 L (range, 20.4–49.9), 8.20 kg (range, 5.2–13.2), 2.81 kg (range, 1.93–4.51), and 14.0 kg (range, 1.4–48.1), respectively. The median value of SMI was 6.85 kg/m^2 (range, 4.48–9.18), and percent body fat was 25.01% (range, 7.55–52.39).

Table 1
Patient demographics and clinicopathological data

Factor	Overall (n = 143)
Demographics	
Age (median, range)	72.0 [27.0,89.0]
Sex, male/female	95/48
ASA-PS 1/2/3/4	5/106/31/1
BMI (kg/m2) (median, range)	22.15 [15.0,34.7]
Alcohol (%)	41 (29.5)
Smoking (%)	25 (17.6)
Comorbidities (%)	133 (93.0)
Chronic kidney disease	8 (5.6)
Diabetes mellitus	55 (38.5)
Brain disease	21 (14.7)
Cardiovascular disease	78 (54.5)
Liver disease	10 (7.0)
Pulmonary disease	24 (16.8)
Others	99 (69.2)
Disease (%)	
Pancreatic cancer	89 (62.2)
Cholangiocarcinoma	21 (14.7)
Ampulllary cancer	15 (10.4)
IPMN	9 (6.3)
P-NET	5 (3.5)
duodenal cancer	3 (2.1)
duodenal GIST	1 (0.8)

ASA-PS; American Society of Anestheologists-Physical Status, BMI; body mass index, IPMN; intraductal papillary mucinous neoplasm, P-NET; pancreatic neuroendocrine neoplasm, CEA, carcinoembryonic antigen, CA19-9; Carbohydrate antigen 19 − 9, CONUT; controlling nutritional status, GPS; Glasgow prognostic score, PN; prognostic nutritional index, PLR; platelet lymphocyte ratio,; NLR; neutrophil lymphocyte ratio, BIA; bioelectrical impedance analysis, ECW; extracellular water, ICW; intracellular water, TBW; total body water, SMI; skeletal mass index, POPF; postoperative pancreatic fistula.

Factor	Overall (n = 143)
CEA (ng/mL) (median, range)	2.4 [0.4,27.0]
CA19-9 (U/mL) (median, range)	28.5 [0.3,23623.2]
Nutritional variables(median, range)	
Albumin (g/dL)	3.9 [2.2,5.0]
Hemoglobin A1c (%)	6.1 [4.2,13.8]
CONUT	2.0 [0.0,8.0]
GPS (0/1/2)	91/33/17
PNI	46.0 [27.8,71.4]
PLR	89.9 [16.4,1050.0]
NLR	2.2 [0.2,24.5]
Variables measured by BIA (median, range)	
Abdominal circumference (cm)	75.9 [59.2, 106.9]
Arm circumference (cm)	28.0 [21.8, 38.2]
Mineral (kg)	2.8 [1.9, 4.5]
Bone mineral content (kg)	2.3 [1.5, 3.7]
Basal metabolic rate (kcal)	1283.2 [963.0, 1830.6]
ECW (L)	12.5 [8.3, 19.4]
ICW (L)	19.0 [12.1, 30.5]
TBW (L)	31.5 [20.4, 49.9]
ECW/ TBW	0.4 [0.4, 0.4]
Body cell mass (kg)	27.2 [17.3,43.7]
Protein (kg)	8.2 [5.2, 13.2]
Fat free mass (kg)	42.3 [27.5, 67.6]
Soft lean mass (kg)	40.0 [25.9, 63.9]

ASA-PS; American Society of Anestheologists-Physical Status, BMI; body mass index, IPMN; intraductal papillary mucinous neoplasm, P-NET; pancreatic neuroendocrine neoplasm, CEA, carcinoembryonic antigen, CA19-9; Carbohydrate antigen 19 − 9, CONUT; controlling nutritional status, GPS; Glasgow prognostic score, PN; prognostic nutritional index, PLR; platelet lymphocyte ratio,; NLR; neutrophil lymphocyte ratio, BIA; bioelectrical impedance analysis, ECW; extracellular water, ICW; intracellular water, TBW; total body water, SMI; skeletal mass index, POPF; postoperative pancreatic fistula.

Factor	Overall (n = 143)
Skeletal muscle mass (kg)	22.7 [13.8, 37.8]
SMI (kg/m2)	6.9 [4.5,9.2]
Body fat mass (kg)	14.0 [1.4, 48.1]
Trunk fat mass (kg)	6.8 [0.3, 20.5]
Obesity degree (%)	101.0 [68.2, 165.3]
Percent body fat (%)	25.0 [7.6,52.4]
Surgical variables (median, range)	
Operation time (min)	320 [202,567]
Estimated blood loss (mL)	330 [25,4940]
Portal vein resection (%)	20 (14.0)
Blood transfusion (%)	25 (17.5)
Soft pancreatic texture (%)	78 (54.5)
Pancreatic duct (mm)	3.0 [1.0,10.0]
Fistula risk score	5 [0,10]
Complications (%)	
Mortality	3 (2.1)
Clavien-Dindo ≥ 3	36 (25.2)
POPF grade B	31 (21.7)
POPF grade C	0 (0)
Intra-abdominal abscess	5 (3.5)
Bile leakage	3 (2.1)
Bleeding	3 (2.1)
Delayed gastric emptying	2 (1.4)
Pneumonia	1 (0.7)

ASA-PS; American Society of Anestheologists-Physical Status, BMI; body mass index, IPMN; intraductal papillary mucinous neoplasm, P-NET; pancreatic neuroendocrine neoplasm, CEA, carcinoembryonic antigen, CA19-9; Carbohydrate antigen 19 – 9, CONUT; controlling nutritional status, GPS; Glasgow prognostic score, PN; prognostic nutritional index, PLR; platelet lymphocyte ratio,; NLR; neutrophil lymphocyte ratio, BIA; bioelectrical impedance analysis, ECW; extracellular water, ICW; intracellular water, TBW; total body water, SMI; skeletal mass index, POPF; postoperative pancreatic fistula.

Factor	Overall (n = 143)
Postoperative course (median, range)	
Resuming food intake, postoperative day	6.0 [3.0,34.0]
Length of drain placement, days	12.0 [6.0,96.0]
Length of hospital stay, days	18.0 [8.0,136.0]
Medical expenses, US$	19978 [14233,88533]
ASA-PS; American Society of Anestheologists-Physical Status, BMI; body mass index, IPMN; intraductal papillary mucinous neoplasm, P-NET; pancreatic neuroendocrine neoplasm, CEA, carcinoembryonic antigen, CA19-9; Carbohydrate antigen 19 – 9, CONUT; controlling nutritional status, GPS; Glasgow prognostic score, PN; prognostic nutritional index, PLR; platelet lymphocyte ratio,; NLR; neutrophil lymphocyte ratio, BIA; bioelectrical impedance analysis, ECW; extracellular water, ICW; intracellular water, TBW; total body water, SMI; skeletal mass index, POPF; postoperative pancreatic fistula.	

The operation time was 320 min (range, 202–567) and the estimated blood loss was 330 (range, 25-4940). Twenty patients (14.0%) underwent portal vein resection. Soft pancreatic texture was observed in 78 patients (54.5%), the median pancreatic duct diameter was 3.0 mm (range, 1.0–10.0), and the median fistula risk score was 5 (range, 0–10). Complications with Clavien- Dindo grade ≥ 3 were found in 36 patients (25.2%), where 31 of these patients (21.7%) were POPF grade B. None of the patients in our cohort had POPF grade C. Mortality occurred in three patients (2.1%) due to interstitial pneumonia, colonic ischemia followed by sepsis, and acute respiratory distress, respectively. Food intake was resumed on postoperative day 6 (range, 3–34) and the median length of hospital stay was 18.0 days (range, 8-136). The medical expenses were 19,978 US dollars (range, 14,233 – 88,533).

Comparison of clinicopathological characteristics between POPF and non-POPF groups

Depending on the occurrence of POPF, the patients were divided into two groups: the POPF group (n = 31) and the non-POPF group (n = 112). A comparison of the clinicopathological characteristics between the two groups is shown in Table 2. There were no significant differences in age (71.0 vs 72.0 years, *P* = 0.63), sex (male/female, 23/8 vs. 72/40, *P* = 0.39), and ASA-PS ≥ 3 (29.0 vs. 20.5%, *P* = 0.34). In the POPF group, significantly more patients with a BMI of ≥ 25.0 kg/m^2 were seen than in the non-POPF group (41.9% vs 17.9%, *P* = 0.01). In addition, alcohol consumption was higher in the POPF group than in the non-POPF group (48.4% vs. 24.1%, *P* = 0.01). No significant difference was found between the two groups for any comorbidity. A significantly lower rate of patients with PC was observed in the POPF group (54.2% vs 67.0%, *P* = 0.03).

Table 2
Comparison of clinicopathologic characteristics between POPF and non-POPF

Factor	POPF (n = 31)	Non-POPF (n = 112)	*P*
Patient demographics (median, range)			
Age	71.0 [45.0, 89.0]	72.0 [27.0, 89.0]	0.63
Sex, male/female	23/8	72/40	0.39
ASA-PS ≥ 3 (%)	9 (29.0)	23 (20.5)	0.34
BMI ≥ 25.0 kg/m^2	13 (41.9)	20 (17.9)	0.01
Alcohol (%)	15 (48.4)	26 (24.1)	0.01
Smoking (%)	5 (16.1)	20 (18.0)	1.00
Comorbidities (%)	30 (96.8)	103 (92.0)	0.69
Chronic kidney disease	1 (3.2)	7 (6.2)	1.00
Diabetes mellitus	11 (35.5)	44 (39.3)	0.84
Brain disease	7 (22.6)	14 (12.5)	0.16
Cardiovascular disease	20 (64.5)	58 (51.8)	0.23
Liver disease	1 (3.2)	9 (8.0)	0.69
Pulmonary disease	7 (22.6)	17 (15.2)	0.41
Disease (Pancreatic neoplasms/Others)	13/13	85/32	0.03
CEA (ng/mL)	2.6 [0.9, 7.3]	2.3 [0.4, 27.0]	0.45
CA19-9 (U/mL)	24.4 [0.4, 1330.0]	33.5 [0.3, 23623.2]	0.11
Nutritional variables (median, range)			
Albumin (g/dL)	4.2 [2.7, 4.9]	3.8 [2.2, 5.0]	0.01
Choline esterase	275 [150, 461]	254 [100, 514]	0.13
Hemoglobin A1c (%)	5.0 [5.1, 7.7]	5.7 [3.8, 13.3]	0.93
CONUT	2.0 [0.0, 7.0]	2.0 [0.0, 8.0]	0.82
GPS 0/1/2	20/8/2	71/25/15	0.59

ASA-PS; American Society of Anestheologists-Physical Status, BMI; body mass index, IPMN; intraductal papillary mucinous neoplasm, P-NET; pancreatic neuroendocrine neoplasm, CEA, carcinoembryonic antigen, CA19-9; Carbohydrate antigen 19 − 9, CONUT; controlling nutritional status, GPS; Glasgow prognostic score, PN; prognostic nutritional index, PLR; platelet lymphocyte ratio,; NLR; neutrophil lymphocyte ratio, BIA; bioelectrical impedance analysis, ECW; extracellular water, ICW; intracellular water, TBW; total body water, SMI; skeletal mass index, POPF; postoperative pancreatic fistula.

Factor	POPF (n = 31)	Non-POPF (n = 112)	*P*
PNI	48.3 [32.0, 60.1]	45.3 [27.8, 71.4]	0.03
PLR	88.9 [32.7, 256.6]	95.3 [16.4, 1050.0]	0.95
NLR	2.7 [1.4, 6.8]	2.2 [0.2, 24.5]	0.09
Variables measured by BIA			
Abdominal circumference (cm)	78.7 [62.4, 106.9]	75.6 [59.2, 104.4]	0.01
Arm circumference (cm)	29.8 [22.7, 38.2]	27.7 [21.8, 36.4]	0.01
Mineral (kg)	3.0 [2.2, 4.1]	2.8 [1.9, 4.5]	0.23
Bone mineral content (kg)	2.5 [1.7, 3.5]	2.3 [1.5, 3.7]	0.24
Basal metabolic rate (kcal)	1331.4 [999.9, 1689.0]	1266.3 [963.0, 1830.6]	0.23
ECW (L)	13.0 [8.3, 18.0]	12.5 [8.3, 19.4]	0.38
ICW (L)	20.0 [13.1, 27.2]	18.5 [12.1, 30.5]	0.19
TBW (L)	32.9 [21.4, 45.2]	30.8 [20.4, 49.9]	0.26
ECW/ TBW	0.4 [0.4, 0.4]	0.4 [0.4, 0.4]	0.06
Body cell mass (kg)	28.6 [18.7, 38.9]	26.5 [17.3, 43.7]	0.19
Protein (kg)	8.6 [5.6, 11.7]	8.0 [5.2, 13.2]	0.20
Fat free mass (kg)	44.5 [29.2, 61.1]	41.5 [27.5, 67.6]	0.24
Soft lean mass (kg)	42.0 [27.4, 57.7]	39.3 [25.9, 63.9]	0.24
Skeletal muscle mass (kg)	24.0 [15.0, 33.4]	22.1[13.8, 37.8]	0.19
SMI (kg/m2)	6.7 [4.5, 9.2]	7.1 [4.8, 8.8]	0.17
Sarcopenia (%)	9 (29.0)	39 (34.8)	0.67
Body fat mass (kg)	14.6 [3.2, 48.1]	13.3 [1.4, 36.8]	0.03
Trunk fat mass (kg)	6.6 [0.3, 18.1]	8.1 [2.1, 20.5]	0.01
Obesity degree (%)	102.8 [79.6, 165.3]	100.9 [68.2, 160.4]	0.08
Percent body fat (%)	26.9 [11.9, 49.5]	23.5 [7.6, 52.4]	0.02

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Factor	POPF (n = 31)	Non-POPF (n = 112)	*P*
Surgical variables (median, range)			
Operation time (min)	324.0 [237.0, 482.0]	311.5 [202.0, 567.0]	0.13
Estimated blood loss (mL)	490.0 [100.0, 1570.0]	322.5 [25.0, 4940.0]	0.32
Portal vein resection (%)	5 (16.1)	15 (13.4)	0.77
Blood transfusion (%)	6 (19.4)	19 (17.0)	0.79
Soft pancreatic texture (%)	21 (67.7)	57 (50.9)	0.11
Pancreatic duct (mm)	1.5 [1.0, 7.0]	3.0 [1.0, 10.0]	< 0.01
Fistula risk score	6 [0, 10]	4 [0, 9]	< 0.01
Complications (%)			
Mortality	1 (3.2)	2 (1.8)	1.00
Clavien-Dindo ≥ 3	29 (93.5)	7 (6.2)	< 0.01
Intra-abdominal abscess	2 (6.5)	3 (2.7)	0.30
Bile leakage	1 (3.2)	2 (1.8)	0.52
Bleeding	3 (9.7)	0 (0.0)	0.01
Delayed gastric emptying	1 (3.2)	1 (0.9)	0.39
Pneumonia	1 (3.2)	0 (0.0)	0.22
Postoperative course (median, range)			
Resuming food intake, postoperative day	11.0 [4.0, 34.0]	5.0 [3.0, 14.0]	< 0.01
Length of drain placement, days	27.0 [8.0, 96.0]	11.0 [6.0, 35.0]	< 0.01
Length of hospital stay, days	30.0 [17.0, 136.0]	17.0 [8.0, 62.0]	< 0.01
Medical expenses, US$	23300 [17031, 88533]	19042 [14233, 46489]	< 0.01

ASA-PS; American Society of Anestheologists-Physical Status, BMI; body mass index, IPMN; intraductal papillary mucinous neoplasm, P-NET; pancreatic neuroendocrine neoplasm, CEA, carcinoembryonic antigen, CA19-9; Carbohydrate antigen 19 − 9, CONUT; controlling nutritional status, GPS; Glasgow prognostic score, PN; prognostic nutritional index, PLR; platelet lymphocyte ratio,; NLR; neutrophil lymphocyte ratio, BIA; bioelectrical impedance analysis, ECW; extracellular water, ICW; intracellular water, TBW; total body water, SMI; skeletal mass index, POPF; postoperative pancreatic fistula.

Regarding nutritional variables, albumin level (4.15 vs 3.80, $P = 0.01$) and PNI (48.3 vs 45.3, $P = 0.03$) were significantly higher in the POPF group. However, nutritional variables such as choline esterase ($P = 0.125$), CONUT ($P = 0.82$), and GPS ($P = 0.59$) were not significantly different between the two groups. Among the variables measured by BIA, abdominal circumference was larger in the POPF group (78.7 vs 75.6, P = 0.01). No significant differences in body composition were observed for mineral (P = 0.23), TBW (P = 0.259), and protein (P = 0.20). However, factors related to body fat were significantly more abundant in the POPF group; for example, percent body fat was higher in the POPF group (26.90 vs 23.48, P = 0.02).

There were no significant differences in the operation time (P = 0.13), estimated blood loss (P = 0.32), portal vein resection rate (P = 0.77), or pancreatic texture (P = 0.11). However, the diameter of the pancreatic duct was smaller in the POPF group (1.5 vs 3.0 mm, P < 0.01). In accordance with that, the fistula risk score was higher in the POPF group (6 vs 4, P = 0.001). The rate of complications with Clavien-Dindo ≥ 3 was higher in the POPF group (93.5% vs 6.2%, P < 0.01) due to the occurrence of POPF. Similarly, significantly higher rates of bleeding, delayed food intake resumption, and longer drain placement length were observed in the POPF group (9.7% vs 0%, P = 0.01; 11.0 vs 5.0 days, P < 0.01; and 27.0 vs 11.0 days, P < 0.01, respectively). In accordance with this, a longer hospital stay was found in the POPF group (30.0 vs 17.0 days, P < 0.01), which caused higher medical expenses (23,300 vs. 19,042 US dollars, P < 0.01).

Predictive factors for POPF

Of the 31 patients (21.7% of all patients) who developed POPF grade B, predictive factors for POPF are shown in Table 3. Multivariate analysis was performed using a logistic regression model. The pancreatic duct diameter was negatively correlated with POPF (odds ratio 0.586, P = 0.01). Conversely, alcohol consumption (odds ratio 2.71, P = 0.03), BMI ≥ 25.0 kg/m^2 (odds ratio 3.43, P = 0.01), and albumin level (odds ratio 2.65, P = 0.03) were significant predictive factors for POPF. For factors measured by BIA, abdominal circumference (odds ratio 1.05, P = 0.02), arm circumference (odds ratio 1.15, P = 0.04), body fat mass (odds ratio 1.07, P = 0.03), trunk fat mass (odds ratio 1.15, P = 0.02), and percent body fat (odds ratio 1.06, P = 0.03) were independent predictive factors for POPF.

Table 3
Multivariate analysis for predictive factors of POPF

Factor	Odds ratio	(95% CI)	*P*
Patient demographics			
Alcohol (%)	2.71	(1.11–6.61)	0.03
Body mass index ≥ 25.0 kg/m^2	3.43	(1.34–8.74)	0.01
Disease and surgery			
Disease other than pancreatic neoplasms	1.00	(1.00–1.00)	0.14
Pancreatic duct mm	0.59	(0.40–0.86)	0.01
Nutritional status			
Albumin (g/dL)	2.65	(1.11–6.30)	0.03
Prognostic nutrition index	1.06	(0.99–1.13)	0.09
Factors measured by BIA			
Abdominal circumference (cm)	1.05	(1.01–1.10)	0.02
Arm circumference (cm)	1.15	(1.01–1.31)	0.04
Body fat mass (kg)	1.07	(1.01–1.14)	0.03
Trunk fat mass (kg)	1.15	(1.03–1.29)	0.02
Percent body fat (%)	1.06	(1.00-1.12)	0.03

POPF; postoperative pancreatic fistula, CI; confidence interval, BIA, bioelectrical impedance analysis.

BMI and percent body fat as predictive factors for POPF

The correlation between BMI and the POPF rate is shown in Fig. 2A. Patients were divided into three groups based on their BMI values (< 20, 20–25, and ≥ 25). The higher the BMI values, the more likely POPF was to occur ($P = 0.026$). Especially, the BMI ≥ 25 group had a significantly higher rate of POPF (39.4%) compared with the BMI < 20 and 20–25 groups (15.8%, $P = 0.03$; 16.7%, $P = 0.015$; respectively).

Similarly, when the patients were divided into three groups based on their percent body fat (< 25, 25–35, and ≥ 35), the correlation between percent body fat and POPF rate is shown in Fig. 2B. POPF was more likely to occur as the percent body fat increased ($P = 0.02$). In fact, POPF occurred more frequently in the group with ≥ 35 percent body fat (47.1%) than in the group with < 25 percent body fat (15.5%) ($P = 0.01$).

Correlation between BMI and percent body fat

Considering the above results, it was suspected that a higher percent body fat contributed to a higher BMI. This can be explained by the fact that body fat mass is one of the components of body weight. The correlation between BMI and percent body fat is shown in Fig. 2. In fact, it revealed strong positive correlation (r = 0.716, 95% CI: 0.625–0.788, P < 0.01) between both factors.

Discussion

In this study, percent body fat measured using BIA was identified as a predictive factor for POPF. Interestingly, to our knowledge, this is the first report to compare detailed nutritional indicators for POPF, including those assessed using BIA. In fact, other nutritional factors, including sarcopenia, and established scoring systems such as CONUT, GPS, and PNI were not predictive factors, except for BMI and albumin level. In addition, only fat-related factors, such as abdominal circumference, body fat mass, and percent body fat, were predictive factors for POPF. In other words, body water, minerals, and proteins, including muscle, were not predictive of POPF. These findings suggest that body fat assessment using BIA should be a preoperative evaluation in patients undergoing PD.

This study showed that higher BMI and percent body fat were predictive factors for POPF. Today, these parameters are easily and rapidly obtained using BIA. They can also be used at home. Previously, it was reported that a higher BMI was related to the incidence of POPF, as revealed in this study [20]. However, BMI only indicated a relationship between body weight and height. Higher BMI did not exclude individuals with high body weight due to muscularity or edema. In other words, it did not reveal the body composition that affected POPF. Therefore, this needed to be clarified, and we investigated this problem. The results revealed that percent body fat was an independent predictive factor of POPF. In fact, the value measured by BIA is affected by circadian variations and differences between the instruments. To avoid these problems, all patients underwent BIA in the morning using the same instrument (InBody 720®) in our study.

Poor nutritional status was a risk factor for anastomotic leakage in intestinal anastomoses. For example, a PNI ≤ 40 is a contraindication for anastomosis [21]. However, hypernutritional status (i.e., body fat) was correlated with POPF. In obese patients, efficient autophagy is suppressed and inflammation in the pancreas is promoted [22], and visceral fat is regarded as a source of proinflammatory cytokines [23]. This may have led to an increased POPF rate.

Previously reported FRS and its components, such as the pathology of PC and IPMN, soft pancreatic texture, and pancreatic diameter were predictive factors for POPF [24]. They could not be manipulated by the surgeons' efforts. However, nutritional status, such as percent body fat, could be improved preoperatively. Therefore, this study has significant clinical implications. Obese patients can undergo interventions such as prehabilitation to improve their body composition. However, it is unclear whether rapidly improving percent body fat would contribute to a better outcome for POPF. In summary, preoperative nutritional evaluation using BIA is useful in patients undergoing PD.

In our cohort, alcohol consumption was a predictive factor of POPF. For alcohol, postoperative infections, cardiopulmonary complications, and bleeding episodes dominate the list of complications [25]. The endocrine stress response to surgery is significantly increased in drinkers during and immediately after the operative procedure, especially during pancreatic surgery. This is most marked in the changes in the concentrations of epinephrine, norepinephrine, and cortisol, which may aggravate existing alcohol-induced organ dysfunction resulting from POPF with the failure of pancreatic-enteric anastomosis. The most frequent complications that required treatment were infection, bleeding episodes, and wound healing. More studies are needed to clarify the most beneficial intervention program and the duration of preoperative alcohol intervention, whereas pathophysiological studies indicate an effect of short-term abstinence, since some organ dysfunction improved 1–2 weeks after alcohol consumption was halted [26].

Our study had several important limitations. The single-center study design resulted in a small sample size. The total number of patients undergoing PD was 143, which was relatively small. This indicates the low statistical power of the results. However, we had minimal missing data regarding clinicopathological characteristics, which were comparable to those of other studies. In addition, extensive data collection was conducted to ensure the accuracy of the database. Another limitation is the study design. We studied and described the perioperative factors and short-term outcomes. This did not refer to long-term outcomes after discharge. Therefore, we could not determine the operative indications without considering them. However, we believe that our results will improve our understanding of the association between POPF and nutritional status such as percent body fat.

In conclusion, while PD can be performed if it is technically and oncologically appropriate, predictive factors for POPF, such as percent body fat, should be considered before proceeding to surgery.

Declarations

Compliance with Ethical Standards:

Funding: No financial disclosures.

Conflict of interest: The authors declare that they have no competing interests.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

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Figures

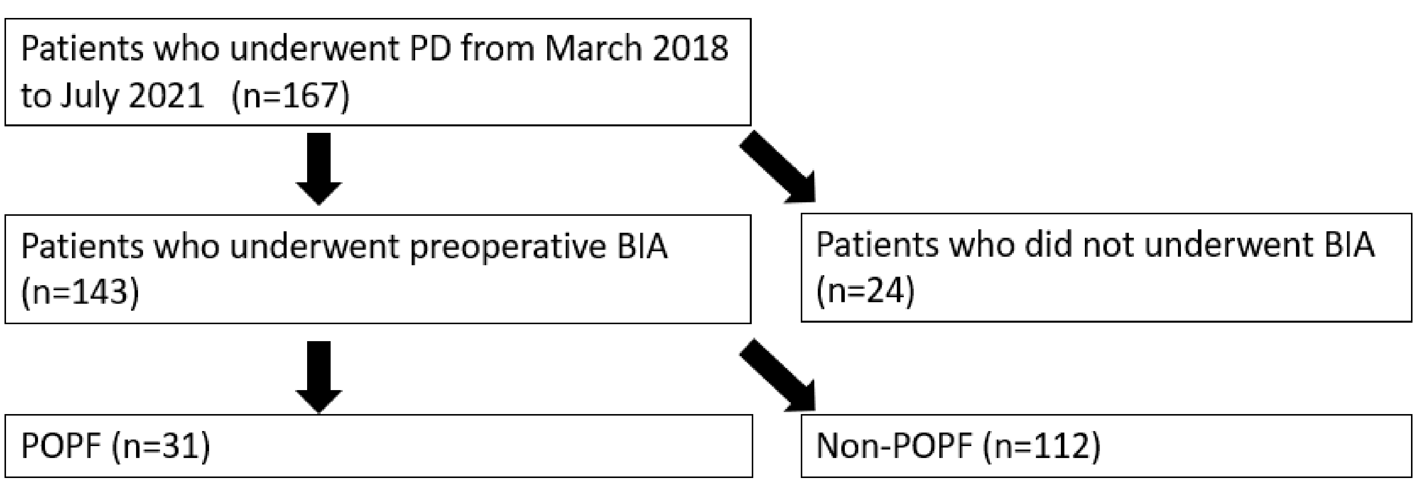

Figure 1

Flow diagram for patient selection. PD, pancreaticoduodenectomy; BIA, body impedance analysis, POPF; postoperative pancreatic fistula.

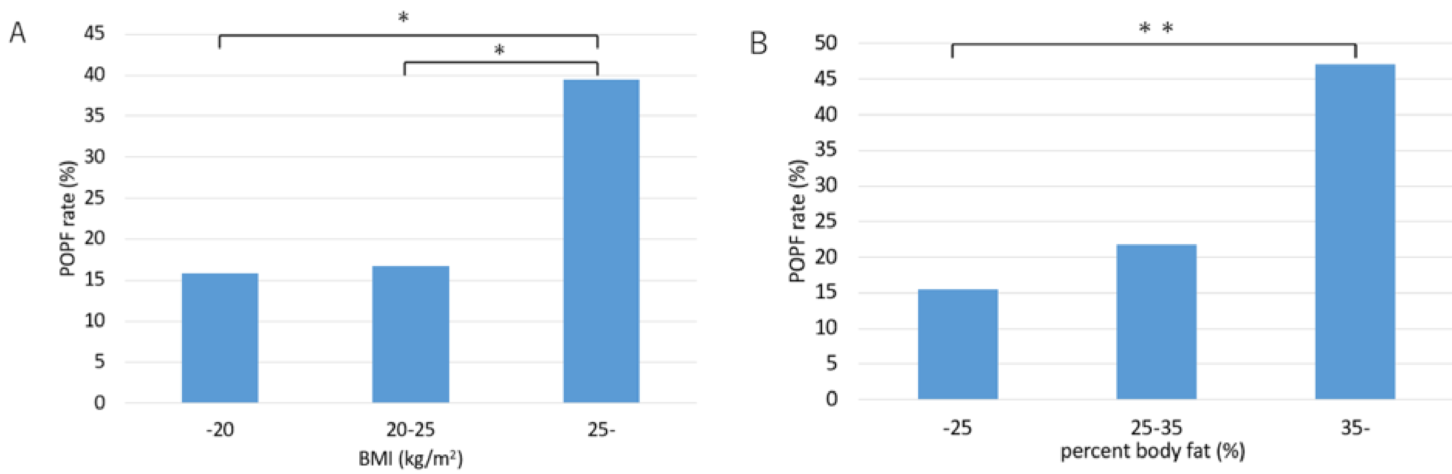

Figure 2

A. Correlation between BMI and POPF rate (*P<0.05).

B. Correlation between percent body fat and POPF rate (**P<0.01).

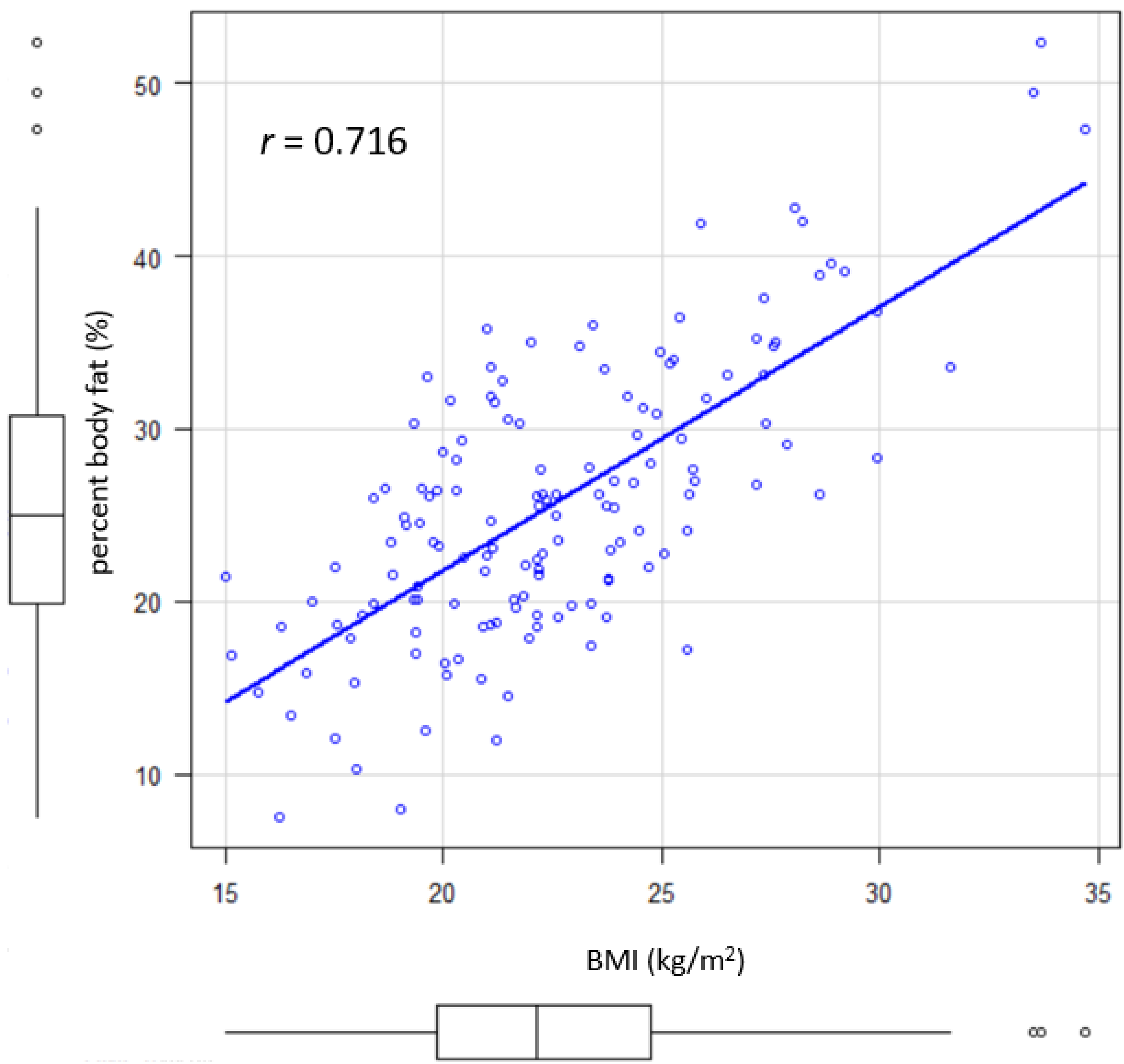

Figure 3

Correlation between BMI and percent body fat. It revealed strong positive correlation (r= 0.716, P<0.01) between both factors.