



Predictive value of sarcopenia and visceral obesity for postoperative pancreatic fistula after pancreaticoduodenectomy analyzed on clinically acquired CT and MRI

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Received: 31 May 2018 / Revised: 6 September 2018 / Accepted: 21 September 2018 / Published online: 7 November 2018

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Abstract

Objective To evaluate predictive values of sarcopenia and visceral obesity measured from preoperative CT/MRIs for postoperative pancreatic fistula (POPF) after pancreaticoduodenectomy in patients with periampullary malignancies.

Methods From the prospectively constructed surgical registry, we included adult patients treated with pancreaticoduodenectomy. Based on CT/MRIs, body morphometric analysis was performed to evaluate the visceral obesity and sarcopenia, based on the areas of visceral fat and skeletal muscle measured at the L3 vertebrae level. We retrieved various perioperative factors from registry. As outcomes of postoperative complications, we evaluated POPF and major complications based on the Clavien–Dindo classification. Multivariate logistic regression analyses were performed.

Results From a total of 284 patients (163 males, 121 females) who met the inclusion/exclusion criteria, POPF, major complications, and 60-day mortality occurred in 52 (18.3%), 34 (12.0%), and 6 (2.1%), respectively. Sarcopenia and visceral obesity were noted in 123 (75.5%) and 66 (40.5%) of men and 68 (56.2%) and 53 (43.8%) of women, respectively. Combination of sarcopenia and obesity (sarcopenic obesity) was noted in 31.9% (52/163) of men and in 26.4% (32/121) of women. In multivariate logistic regression analyses, sarcopenic obesity was the only independent predictor for POPF (OR 2.65, 95% CI 1.43–4.93), and the vascular resection during pancreaticoduodenectomy was the only independent predictor for severe complications (OR 3.75, 95% CI 1.61–8.70).

Conclusion Sarcopenic obesity might be highly predictive for POPF. Body morphometric analysis in preoperative CT/MRI combined with assessment of perioperative clinical features may help to identify high-risk patients and determine perioperative management strategies.

Key Points

- *Sarcopenic obesity might be predictive for postoperative pancreatic fistula after pancreaticoduodenectomy.*
- *The vascular resection during pancreaticoduodenectomy might be predictive of major complications.*
- *Body morphometric analysis might be helpful for identifying high-risk patients.*

Keywords Muscle weakness · Sarcopenia · Pancreaticoduodenectomy · Postoperative complications · Treatment outcome

Minji Jang and Hyung Woo Park contributed equally to this work.

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s00330-018-5790-7>) contains supplementary material, which is available to authorized users.

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Abbreviations

ASA	American Society of Anesthesiologists
BIA	Bioelectrical impedance analysis
BMI	Body mass index
CT	Computed tomography
DEXA	Dual energy x-ray absorptiometry
EWGSOP	European working group on sarcopenia in older people
HU	Hounsfield unit
ISGPR	International Study Group on Pancreatic Fistula
MPD	Main pancreatic duct
MRCP	Magnetic resonance cholangiopancreatography
PACS	Picture archiving and communication system
POPF	Postoperative pancreatic fistula
SFA	Subcutaneous fat area
SI	Signal intensity
TAMA	Total abdominal muscle area
VFA	Visceral fat area

Introduction

Pancreaticoduodenectomy is an important curative treatment for periampullary malignancies; however, it is hampered due to the relatively high level of complications [1]. The postoperative mortality has improved over the last several decades, although there is still a relatively high mortality rate of 2–5%. The postoperative morbidity has remained high at approximately 30–45% [2–4]. In the era of the world population aging, the number of elderly patients with multiple comorbidities is increasing, which may increase the risk of postoperative complications after pancreaticoduodenectomy [5]. Accordingly, the preoperative evaluation of risk factors to predict postoperative complications has gained emphasis. Of the postoperative complications, the postoperative pancreatic fistula (POPF) is a unique and significant complication of pancreaticoduodenectomy, thus is assessed separately from other major complications, such as bleeding, infection, or death.

In general, many risk factors, including pancreatic fatty degeneration, pancreatic duct dilatation, and comorbidities, such as alcoholism, coagulopathy, or cardiovascular/renal disease, are regarded as increasing the postoperative complications after pancreaticoduodenectomy [6, 7]. Recently, more general physical factors, such as sarcopenia and visceral obesity, have gained emphasis as predictors for postoperative complications after pancreaticoduodenectomy [8].

Although there is a lack of worldwide agreement on the definition of sarcopenia, the most commonly used definition is established by the European Working Group on Sarcopenia in Older People (EWGSOP) [9]. The EWGSOP recommends using the presence of both low muscle mass and low muscle function (strength or performance) for the diagnosis of sarcopenia. Sarcopenia may result in physical impairment

and adversely impacting the surgical outcome after pancreaticoduodenectomy [10]. Sarcopenia is regarded as a prognostic factor in various cancer patients treated with major surgery or chemotherapy even beyond the field of pancreatic cancer [11–13]. In a recent meta-analysis, the pre-therapeutic sarcopenia was more related with digestive cancers, such as esophageal, gastric, pancreas cancers, probably due to the close link between digestive dysfunction and undernutrition [14]. In addition, the combination of sarcopenia and visceral obesity, termed sarcopenic obesity, is more problematic when it worsens the surgical outcome [15].

Currently, advances in medical imaging may allow the extraction of body morphometric information, such as muscle and visceral fat in the body [9, 16]. Therefore, research projects to evaluate risk factors or predictors, including sarcopenia, and visceral obesity to predict postoperative complications have been increasing; however, more evidence is still required in order to obtain a consensus and to incorporate body morphometric information into clinical practice [1, 10, 17–20]. In that regard, we aimed to evaluate predictive values of sarcopenia and visceral obesity measured from preoperative CT/MRIs for postoperative pancreatic fistula (POPF) after pancreaticoduodenectomy in patients with periampullary malignancies.

Materials and methods

Our institutional review board approved this retrospective observational study based on prospectively determined surgery registry, and they waived the requirement for informed consent. This study is reported according to the Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD) guidelines [21].

Patients

The patients eligible to be included in the study were those treated with pancreaticoduodenectomy for periampullary malignancies. This study is based on a registry of patients who underwent pancreaticoduodenectomy for any reason between 2005 and 2016. Between 2005 and 2016, two pancreatobiliary surgeons had performed all pancreaticoduodenectomy using the same surgical procedure. During this period, the standard surgical procedure is an open pancreaticoduodenectomy with subtotal stomach-preserving pancreaticoduodenectomy with the reconstruction of gastrojejunostomy using an antecolic route. In our hospital, the Surgery Department has prospectively constructed a comprehensive registry, which contains the demographic characteristics of patients, preoperative evaluation results, surgical methods and outcomes, pathologic data, and the postoperative course and outcomes. In the registry,

we consecutively included patients based on the following inclusion and exclusion criteria.

The inclusion criteria were as follows: (a) patients who were treated with pancreaticoduodenectomy for periampullary malignancies, i.e., pancreas cancer, ampulla of Vater cancer, duodenal cancer, and distal common bile duct cancer, with a curative intent between January 2005 and December 2016 in Ulsan University Hospital; (b) patients without other active cancer; (c) patients > 18 years of age; and (d) patients who underwent preoperative CT or MRI within 1 month before pancreaticoduodenectomy. We excluded patients whose preoperative CT or MRI was obtained 1 month or more before pancreaticoduodenectomy as well as patients without follow-up data.

Acquisition of CT and MRI

Various CT units were used over a 10-year period; these included a Sensation 16, Definition flash, or SOMATOM Definition AS + scanner (Siemens Healthineers). Unenhanced-, arterial-, and portal venous phase dynamic CT images were obtained for all patients. For contrast enhancement, 100–120 mL of 300 mg I/mL iopromide (Xenetix 300; Guerbet) was administered intravenously at a rate of 3–4 mL/s using an automatic power injector through an 18-gauge intravenous cubital line, followed by a 20-mL saline flush at the same flow rate. Arterial-phase images were obtained using a 10–15-s delay after the attenuation of the aorta at the thoracolumbar junction had reached 100 Hounsfield units (HUs). Portal venous-phase images were obtained using a fixed 75-s delay after contrast injection. Coronal reformations of portal venous-phase images have routinely been performed at a slice thickness of 5 mm for all CT scans at our institution since 2010. The scan parameters were as follows: beam collimation, 16×0.75 , 32×0.6 , or 64×0.6 mm; beam pitch, 1; gantry rotation time, 0.5 s; field of view to fit; 120 kVp; and an automatic exposure control system (CARE Dose 4D, Siemens Healthineers).

Two MR units were used over a 10-year period, i.e., a 1.5 T scanner (Achieva, Philips Healthcare) and a 3.0 T scanner (Magnetom Skyra, Siemens Healthineers). The MRI was performed mostly using the MR cholangiopancreatography (MRCP). The MRCP on Achieva machine was performed using the following sequences: breath-hold T2-weighted turbo spin echo (TSE) images with fat saturation, T2-weighted single-shot TSE (SSH-TSE), T1-weighted fast field echo (FFE) with dual-echo, breath-hold T1-weighted high-resolution isotropic volume examination (THRIVE), and three-dimensional MRCP sequences. The MRCP on Magnetom Skyra machine was performed using the following sequences: dual-echo T1-weighted breath-hold gradient-echo sequence, T2-weighted TSE with fat saturation, T2-weighted half-Fourier acquisition single-shot turbo-spin

echo (HASTE), and MRCP using a breath-hold thick-slab single-shot rapid acquisition with relaxation enhancement (RARE) sequence. For contrast-enhanced imaging, an extracellular gadolinium-based contrast agent (Dotarem®, gadoterate meglumine, Guerbet) was injected at a dose of 0.2 ml/kg of body weight.

Medical data collection

The demographic information, including patient age, sex, weight, height, body mass index (BMI), and comorbidities, i.e., diabetes mellitus or hypertension, were recorded. Preoperative evaluation information, including the American Society of Anesthesiologists (ASA) grade, prior open abdominal surgery history, prior pancreatitis history, and the presence of neoadjuvant treatment, was collected. Factors related to surgery were recorded, including the type of surgical procedure, operation time, i.e., from the start to recovery from anesthesia, operative blood loss, and the histologic diagnosis.

For the outcome of postoperative complications, we recorded the occurrence of POPF and pancreaticoduodenectomy-specific postoperative complications as well as the postoperative death at 60 days. Regarding the definition of POPF, we adopted the recent consensus definition of the International Study Group on Pancreatic Fistula (ISGPF) criteria [22]. We regarded a POPF as when the ISGPF grade is B or C. Postoperative complications other than POPF were recorded and graded according to the Clavien–Dindo classification [23]. Complications requiring surgical, endoscopic, or radiologic intervention, requiring intensive care or causing death were considered as major (grade III–V) complications. The rationale to adopt the postoperative mortality rate at 60 days rather than at 30 days was based on a prior study [17] in which the decrease in perioperative mortality within the 60-day interval was deemed to be more critical than the 30-day interval for improving the overall patient survival rate.

Preoperative imaging variables

All CT and/or MRI images were retrieved from the Picture Archiving and Communication System (PACS) at our institution. A clinically trained radiologist (M.J.J.) analyzed the CT or MRI images, and another radiologist (J.H.) double-checked the results.

The main pancreatic duct (MPD) diameter, which is a known risk factor for POPF [24], was measured at the section where the maximal ductal dilatation was noted on CT or MRI, whichever was better for visualizing. A diameter ≥ 6 mm was regarded as a MPD dilatation.

The sarcopenia was evaluated on abdominal CT or MRI using the Asan-J software, which was developed based on Image J (NIH, Bethesda, MD, USA). Two consecutive axial

CT images at the level of the inferior endplate of L3 lumbar vertebra were processed and then averaged for each patient. If there was not available CT, e.g., CT taken in an outside hospital, we used MRI. Using the Asan-J software, the total abdominal muscle area (TAMA) (cm^2), including all muscles on the selected axial images, i.e., psoas, paraspinals, transversus abdominus, rectus abdominus, quadratus lumborum, and internal and external obliques, were demarcated using predetermined thresholds for the HU on CT or the signal intensity (SI) on precontrast, T1-weighted MRI. The visceral fat area (VFA) (cm^2) and the subcutaneous fat area (SFA) (cm^2) were also demarcated using the adipose tissue thresholds on CT/MRI (Fig. 1).

The TAMA was normalized to stature by dividing the muscle area by the patient's height squared, and which is termed the TAMA index ($\text{TAMAI} = \text{TAMA} (\text{cm}^2)/\text{height} (\text{m}^2)$). Sarcopenia was defined using the sex-specific cutoff values, i.e., $\leq 52.4 \text{ cm}^2/\text{m}^2$ in males and $\leq 38.5 \text{ cm}^2/\text{m}^2$ in females [25]. According to a prior study, visceral obesity was defined as $\text{VFA} > 136 \text{ cm}^2$ in men and $> 95 \text{ cm}^2$ in women [26]. The VFA/TAMAI ratio was also calculated for all patients as an index for sarcopenic obesity. The cut-off value for diagnosing sarcopenic obesity was 3.2, according to Pecorelli et al's study results [1].

Statistical analysis

Normality was assessed by the inspection of frequency histograms or by using the Kolmogorov-Smirnov test. Continuous data were reported as the mean with standard deviation, and categorical data were presented as proportions. As a univariate analysis for comparison between the groups, continuous variables were compared using the Student's *t* test and categorical variables were analyzed, as appropriate, using the χ^2 test or Fisher's exact test, hereafter referred to as univariate comparison analysis.

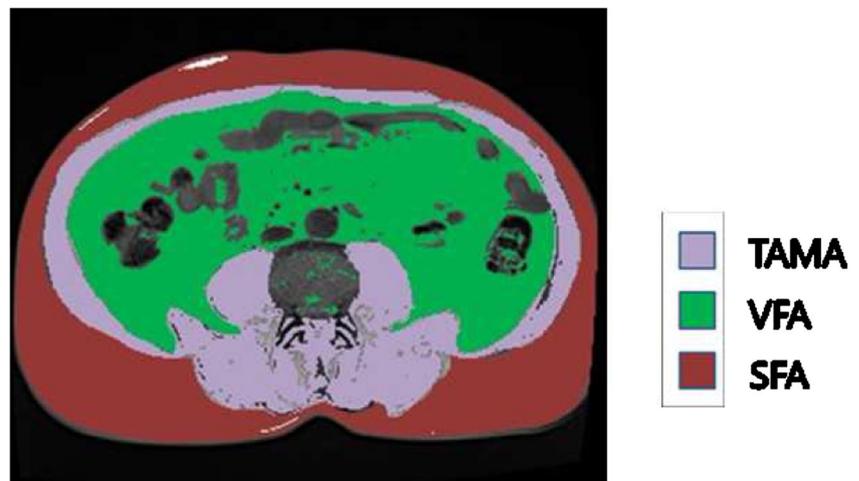
In order to assess the independent contribution of each variable to POPF, major complications, and the 60-day mortality rate, univariate and multivariate logistic regression analyses were performed with the inclusion of candidate predictors, which were significant at $p < 0.200$ in the univariate comparison analyses. The backward stepwise elimination method was used to determine the final, significant predictors. Multicollinearity was assessed by inspecting the correlation matrices of independent variables and by calculating the variance inflation factor (VIF). VIF values greater than 10 were regarded as indicating serious multicollinearity. The discriminative power of the logistic model equations was determined by constructing a receiver operating characteristic (ROC) curve and by calculating the C-statistic. In order to determine the goodness-of-fit of the models, the Hosmer–Lemeshow test was used to assess whether the model differed significantly from a perfect prediction model. Statistical analyses were performed using SPSS® version 21 (IBM, Armonk, NY, USA).

Results

Patients

In the surgical registry in our institution, there were 317 eligible patients who underwent pancreaticoduodenectomy for periampullary malignancies between 2005 and 2016. Among these patients, 284 consecutive patients were selected based on the inclusion/exclusion criteria for this study. The reasons for exclusion were preoperative CT or MRI taken 30 days before their surgery ($n = 30$) and a lack of follow-up ($n = 3$). In the 284 included patients, there was no missing data regarding study outcomes or the main variables considered in the analysis.

Fig. 1 Body morphometric evaluation for abdominal fat and muscle areas. At the level of the inferior endplate of L3 vertebra, the axial CT image is segmented into the total abdominal muscle area (TAMA), visceral fat area (VFA), and superficial fat area (SFA)



The patient characteristics and preoperative imaging variables are summarized in Table 1. In our study population, POPF with ISGPF grade B/C occurred in 18.3% of the

Table 1 Demographic and basic characteristics of patients

Characteristics	Data
Age (years)*	62.6 ± 10.0
Sex ratio (M:F)	163:121
Weight (kg)*	61.2 ± 10.6
Height (m)*	1.62 ± 0.21
Body mass index (kg/m ²)*	23.8 ± 6.3
ASA grade	
1–2	273 (96.1%)
3–4	11 (3.9%)
Comorbidity	
Hypertension	123 (43.3%)
Diabetes	105 (37.0%)
Types of cancers	
Pancreatic cancer	78 (27.5%)
Bile duct cancer	76 (26.8%)
Ampulla of Vater cancer	58 (20.4%)
IPMN	21 (7.4%)
Neuroendocrine tumor	3 (1.1%)
Others	48 (16.9%)
Neoadjuvant treatment	5 (1.8%)
Prior open surgery history	60 (21.1%)
Prior pancreatitis history	41 (14.4%)
Operation time (hour)*	9.6 ± 2.1
Operative blood loss (ml)*	799.7 ± 486.1
Vascular resection	35 (12.3%)
Postoperative pancreatic fistula (ISGPF grade)	
None and A	232 (81.7%)
B and C	52 (18.3%)
Complications (Clavien-Dindo grade)	
I–II	250 (88.0%)
III–IV	34 (12.0%)
Postoperative mortality within 60 days	6 (2.1%)
MPD dilatation	41 (14.4%)
VFA (cm ²)*	110.9 ± 61.5
TAMAI (cm ² /m ²)*	43.8 ± 14.6
VFA/TAMAI ratio*	2.67 ± 1.81
Sarcopenia	191 (67.3%)
Visceral obesity	119 (41.9%)
Sarcopenic obesity	84 (29.6%)

Values in parentheses are percentages unless otherwise indicated

ASA American Society of Anesthesiologists, IPMN intraductal papillary mucinous neoplasm, ISGPF International Study Group for Pancreatic Fistulas, MPD main pancreatic duct, VFA visceral fat area, TAMAI total abdominal muscle area index

*Values are mean ± standard deviation

patients (52/284), and the major complication with Clavien-Dindo grade III/IV occurred in 12.0% of them (34/284). The 60-day postoperative mortality occurred rarely and in only 2.1% (6/284) of these patients.

According to the predefined sex-specific cut-offs, the sarcopenia was more common in men (75.5%, 123/163) compared to women (56.2%, 68/121) with statistical significance ($p = 0.001$). Visceral obesity was similarly observed in men (40.5%, 66/163) and women (43.8%, 53/121) ($p = 0.662$). Sarcopenic obesity also did not differ between men (31.9%, 52/163) and women (26.4%, 32/121) ($p = 0.387$). The data of variables stratified by sex is presented in the [supplementary table](#).

Prediction models for outcomes

In univariate comparison analyses, the variables which may have a potential to predict outcomes differ in the outcomes of POPF, major complications, and the 60-day mortality, as shown in Table 2. Between patients without and with POPF, the proportions of patients with visceral obesity (38.4% vs. 57.7%, $p = 0.011$) and sarcopenic obesity (25.4% vs. 48.1%, $p = 0.001$) differed significantly (Fig. 2). Between patients without and with major complications, only the proportion of patients who underwent vascular resection differed significantly (10.0% vs. 29.4%, $p = 0.001$). However, there was no significant variable for the 60-day mortality rate.

The univariate logistic regression analyses also revealed that visceral obesity (OR 2.19, 95% CI 1.19–4.03, $p = 0.012$) and sarcopenic obesity (OR 2.65, 95% CI 1.43–4.93, $p = 0.002$) were significant predictors of POPF and the vascular resection (OR 3.75, 95% CI 1.61–8.74, $p = 0.002$) was a significant predictor for major complications (Table 3). However, there was no significant variable for the 60-day mortality rate.

In the multivariate logistic regression analysis (Table 3), sarcopenic obesity was the only independent predictor for POPF (OR 2.65, 95% CI 1.43–4.93), and with moderate discriminative power (C-statistic 0.611) and high goodness-of-fit of the model ($p = 0.758$). For major complications, the vascular resection remained as an independent variable to predict major complications (OR 3.75, 95% CI 1.61–8.70), and with moderate discriminative power (C-statistic 0.647) and high goodness-of-fit of the model ($p = 0.334$). For 60-day mortality, there was no significant predictor remaining in the multivariate logistic regression model. In fact, the 60-day mortality event was too infrequent ($n = 6$) in order to allow construction of a model.

Discussion

In our study, multivariate logistic regression demonstrated that sarcopenic obesity was a strong predictor for POPF (OR

Table 2 Univariate analyses of potential predictors associated with postoperative complications in patients who underwent pancreaticoduodenectomy

	Postoperative pancreatic fistula			Major complications		
	No (<i>n</i> = 232)	Yes (<i>n</i> = 52)	<i>p</i> value	No (<i>n</i> = 250)	Yes (<i>n</i> = 34)	<i>p</i> value
Age (years)*	62.4 ± 10.4	63.1 ± 7.9	0.619	62.3 ± 10.2	64.7 ± 8.5	0.191
Sex ratio (M:F)	129:103	34:18	0.197	142:108	21:13	0.583
BMI*	23.7 ± 6.9	24.3 ± 3.2	0.546	23.6 ± 3.5	25.7 ± 15.8	0.435
ASA grade						
1–2	222 (95.7)	51 (98.1)	0.742	240 (96.0)	33 (97.1)	0.301
3–4	10 (4.3)	1 (1.9)		10 (4.0)	1 (2.9)	
Comorbidities						
Diabetes mellitus	87 (37.5)	18 (34.6)	0.697	90 (36.0)	15 (44.1)	0.358
Hypertension	96 (41.4)	27 (51.9)	0.165	109 (43.6)	14 (41.2)	0.789
Neoadjuvant treatment	5 (2.2)	0 (0.0)	0.285	3 (1.2)	2 (5.9)	0.051
Prior open surgery history	49 (21.1)	11 (21.2)	0.996	55 (22.0)	5 (14.7)	0.328
Prior pancreatitis history	37 (15.9)	4 (7.7)	0.126	35 (14.0)	6 (17.6)	0.570
Operation time (hours)*	9.6 ± 2.1	9.3 ± 1.9	0.326	9.5 ± 2.0	9.8 ± 2.1	0.448
Operative blood loss (ml)*	816.0 ± 517.9	726.9 ± 299.1	0.233	785.3 ± 458.5	905.9 ± 653.6	0.175
Vascular resection	31 (13.4)	4 (7.7)	0.261	25 (10.0)	10 (29.4)	0.001
MPD dilatation	37 (15.9)	4 (7.7)	0.097	37 (14.8)	4 (11.8)	0.558
Sarcopenia	157 (67.7)	34 (65.4)	0.751	168 (67.2)	23 (67.6)	0.958
Visceral obesity	89 (38.4)	30 (57.7)	0.011	107 (42.8)	12 (35.3)	0.405
Sarcopenic obesity	59 (25.4)	25 (48.1)	0.001	75 (30.0)	9 (26.5)	0.672

Values in parentheses are percentages unless otherwise indicated

BMI body mass index, ASA American Society of Anesthesiologists, MPD main pancreatic duct

*Values are mean ± standard deviation

2.65), and which is one of the important complications following PD. In the univariate logistic regression analyses, both visceral obesity (OR 2.19) and sarcopenic obesity (OR 2.65) were predictive of POPF. These results suggest that radiologic quantification of body composition, such as depletion of muscle mass and excessive fat tissue, might be helpful for predicting POPF in patients following PD.

Regarding the visceral obesity, Pecorelli et al's study examined 202 patients treated with pancreatic resection for adenocarcinoma between 2010 and 2014 and found that visceral obesity was an independent predictor of POPF [1]. However, in their study, sarcopenia and sarcopenic obesity were not associated with POPF. Indeed, there has been controversy regarding the predictive value of sarcopenia for POPF. Our study results and Peng et al's study results demonstrated that sarcopenia alone had no impact on POPF [10]. In contrast, several studies have shown that sarcopenia is highly associated with POPF in patients undergoing pancreaticoduodenectomy [18–20]. Further research will be required in order to resolve these controversies.

Contrary to sarcopenia alone, sarcopenic obesity, which is the combination of excessive visceral fat and sarcopenia, has been gaining emphasis. The emerging concept of sarcopenic

obesity was previously introduced as an important risk factor for physical disability and as an objective feature of the frailty syndrome [15]. It has been consistently reported that the sarcopenic obesity is suggestive of a poor prognosis in cancer patients and is a predictor of postoperative complications [25, 27]. Our results also demonstrated that sarcopenic obesity remains a predictor in the final model of multivariate logistic regression, although visceral obesity was removed from the final model.

From the pathophysiologic point of view, cancer is in general a catabolic illness characterized as ongoing muscle loss and cachexia, which is driven by combination of reduced food intake, imbalanced metabolism, and inflammation. Cancers of digestive organs may have mechanical factors to reduce food intake more commonly than non-digestive cancers. Some cancers may cause systemic inflammation driven by cytokines, hormones, and neurotransmitters from the early stage of cancers. The pancreatic cancer commonly leads to severe muscle wasting from due to both mechanical factor as well as systemic inflammation [28]. Therefore, special care to prevent sarcopenia or cachexia should be taken to the patients with pancreatic cancer.

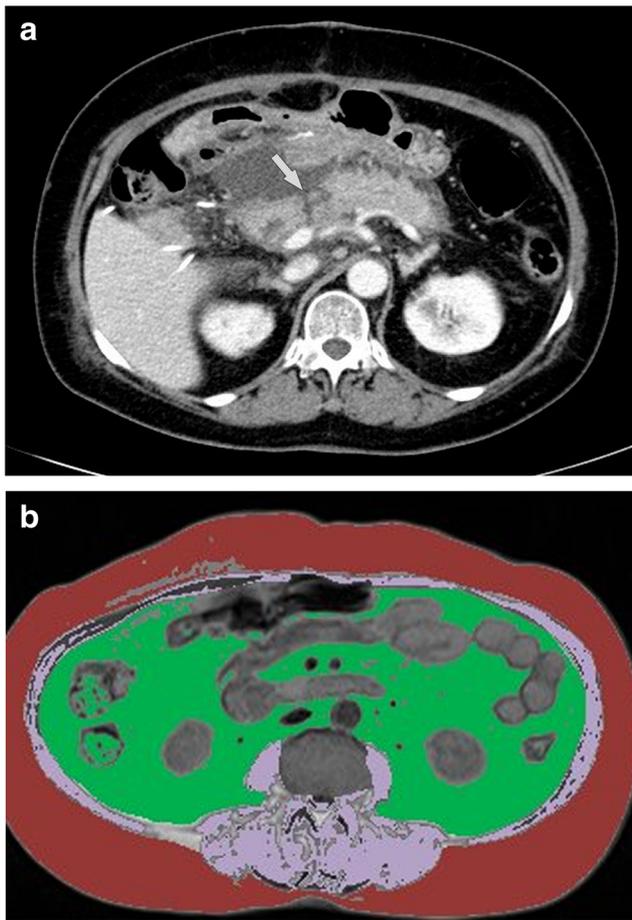


Fig. 2 A 69-year-old woman treated with pancreaticoduodenectomy for ampulla of Vater cancer. **a** Axial contrast-enhanced CT images taken 7 days following surgery show fluid collection around the pancreaticojejunal anastomosis (arrow). Postoperative pancreatic fistula was confirmed based on the amylase level in the drained fluid greater than three times the upper normal serum value. **b** On the preoperative axial CT, the patient shows sarcopenic obesity based on the measured VFA/TAMAI ratio of 5.7, and which is a risk factor predictive of postoperative pancreatic fistula

Excessive adipose tissue may lead to the production and secretion of pro-inflammatory adipocytokines, such as leptin, TNF- α , IL-1, and IL-6, which are associated with regulation of the immune reaction [29–32]. During the postoperative period, the pro-inflammatory adipocytokines can weaken the immune system and delay wound healing, therefore increasing the risk of postoperative complications, especially of POPF [33].

On univariate and multivariate analyses, we observed that vascular resection was the only predictive parameter of severe, surgery-related complications (grade III–V in the Clavien-Dindo classification) except for POPF. This result is in concordance of a recent meta-analysis and several large-scale studies, which demonstrated that pancreaticoduodenectomy with vascular resection is more likely associated with postoperative complications and

reoperations [34, 35]. Interestingly, in the majority of prior studies, the vascular resection has not been associated with POPF.

There have been efforts to establish a prediction model or prognostic score to predict postoperative complications after pancreaticoduodenectomy [6–8, 36]. Of these, Braga et al's study developed a prognostic score system, which can predict postoperative complications with moderate discriminative power (C-statistic index = 0.743) [6]. In addition, the estimation of physiologic ability and surgical stress (E-PASS) score has also been reported as a useful scoring system to evaluate morbidity after pancreaticoduodenectomy; however, the predictive power may be moderate [36, 37]. Currently, any clinical scoring systems currently do not contain body morphometric analysis, such as sarcopenia and visceral obesity. As recent studies have consistently demonstrated the prognostic/predictive value of body morphometric analysis for postoperative morbidity and mortality, we strongly believe that a novel scoring system including body morphometric analysis would be desirable.

The body morphometry-based prediction/prognostic model may help surgeons to understand the risk of POPF and determine perioperative management strategies to improve postoperative outcome. Either resistance exercise, amino acid-based nutritional supplement, or both appear to increase muscle protein metabolism and prevent sarcopenia [38]. Therefore, resistance exercise and nutritional supplement might be incorporated into the standard perioperative management, especially in high-risk patients.

Body morphometric imaging has advanced greatly and regarded to be more accurate to evaluate muscle and fat mass than non-imaging tests, such as physical anthropometry examinations, such as body mass index, skin-fold thickness or body circumference, and serum/urine biomarkers, such as C-terminal agrin fragment [39]. Among the various imaging modalities used to measure body fat and muscle, including dual-energy x-ray absorptiometry (DEXA), bioelectrical impedance analysis (BIA), and CT/MRI, CT/MRI is regarded as the most accurate and reliable method based on its very precise anatomic evaluation used to segment the areas of muscle and fat [39, 40]. However, the measurement methods in CT/MRI have not yet been standardized. First, the level of measurement differed in various research studies, although the L3 vertebral body level has been most commonly used. Second, the segmentation methods used to extract fat and muscle areas should be standardized. Current research uses various commercial or customized imaging-processing softwares; however, no effort has been made to validate those types of software using phantoms. In our study, we used the frequently used open-source software (Image J, NIH, Bethesda, MD, USA), and its threshold-based

Table 3 Univariate and multivariate logistic regression analysis results

Predictors	Univariate logistic regression			Multivariate logistic regression		
	OR	95% CI	<i>p</i> value	OR	95% CI	<i>p</i> value
For POPF						
Sex	0.663	0.354–1.242	0.199			
Hypertension	1.530	0.837–2.798	0.167			
MPD dilatation	0.412	0.141–1.210	0.107			
Prior pancreatitis history	0.439	0.149–1.292	0.135			
Visceral obesity	2.191	1.190–4.034	0.012			
Sarcopenic obesity	2.654	1.430–4.926	0.002	2.65	1.43–4.93	0.002
For major complications						
Age	1.027	0.987–1.068	0.191			
Neoadjuvant treatment	5.146	0.828–31.973	0.079			
Vascular resection	3.750	1.610–8.735	0.002	3.75	1.61–8.70	0.002
Blood loss	1.000	1.000–1.001	0.202			

OR odds ratio, CI confidence interval, POPF postoperative pancreatic fistula, MPD main pancreatic duct

segmentation function, although validation would still be required. We strongly believe that body morphometric imaging will become a major part of quantitative imaging and that global efforts to obtain an international consensus regarding standardized acquisition and analysis methods will be mandatory in the near future.

Despite the important findings reported in this study, some limitations should be discussed. First, this study is a relatively small study ($n = 284$) from a registry in a single tertiary medical center. The single center data might have limitations in generalizing our results. To validate our study and confirm the impact of sarcopenic obesity on POPF, a large, multicenter study would be necessary. Second, we could not evaluate muscle function, e.g., grip strength, speed of gait, or the level of patient exhaustion. The European Working Group on Sarcopenia in Older People (EWGSOP) suggested an algorithm for sarcopenia based on measurements of both muscle functional status and mass [9]. Future studies are expected to evaluate preoperative sarcopenia using various measuring methods. Third, the evolution of surgical procedures, device, and environment during the study period may influence our study results. However, in our institution, there has been no change in pancreaticobiliary surgeons and standard surgical procedures during study period. Finally, the 60-day mortality following pancreatic surgery ($n = 6$) was too small to allow determination of the statistical significance.

In conclusion, our study results indicate that preoperative sarcopenic obesity might be a strong and independent predictor for the development of POPF after pancreaticoduodenectomy. Vascular resection during pancreaticoduodenectomy might be strongly predictive of severe postoperative complications. These predictive values of body morphometric imaging and perioperative information should be considered in the management of patients treated with pancreaticoduodenectomy.

Funding This research was supported by a grant from Guerbet (No. GK-XTX-2017-34) and a grant (No. HI18C1216) from the Korea Health Industry Development Institute (KHIDI).

Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Jimi Huh.

Conflict of interest J.H. is a recipient of the grant from Guerbet.

K.W.K. is a recipient of the grant from the Korea Health Industry Development Institute (KHIDI).

The other authors have no conflict of interest.

Statistics and biometry One author (Kyung Won Kim) has significant statistical expertise.

Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Methodology

- Prospective
- Diagnostic or prognostic study
- Performed at one institution

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