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ORIGINAL RESEARCH

Total Psoas Area Index is Valuable to Assess Sarcopenia, Sarcopenic Overweight/Obesity and Predict Outcomes in Patients Undergoing Open Pancreatoduodenectomy

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Background and Aim: Sarcopenia has been proven to be a risk factor after pancreatoduodenectomy (PD). We aimed to evaluate if decreased psoas muscle area and density shown in CT scan, as measures for sarcopenia, were associated with postoperative major complications and adverse outcomes in patients who underwent PD.

Patients and Methods: We analyzed 152 consecutive patients who underwent open PD. Total psoas area and muscle attenuation were measured on CT images at the level of the third lumbar vertebra. Total psoas area index (TPAI) was calculated, the cut-off values of TPAI were estimated and validated. The relationship between radiographic characters and outcomes was analyzed.

Results: The optimal cut-off values of TPAI were 4.78 cm^2/m^2 for males and 3.46 cm^2/m^2 for females. The values were validated by outcomes with significant differences in the rate of major complications, re-operation, length of stay, and total cost. The prevalence of TPAI-defined sarcopenia and sarcopenic overweight/obesity was 38.8% and 17.1% in total. In multivariate logistic regression, rate of major complications was associated with TPAI [OR=0.605, 95% CI (0.414, 0.883), P=0.009], TPAI-defined sarcopenia [OR=8.256, 95% CI (2.890, 23.583), P=0.000] and sarcopenic overweight/obesity [OR=7.462, 95% CI (2.084, 26.724), P=0.002]; meanwhile, NRS2002-defined nutritional risk and GLIM-defined malnutrition did not show relationship with major complications.

Conclusion: Both sarcopenia and sarcopenic overweight/obesity determined by new TPAI cut-off values were associated with a higher rate of major complications and adverse outcomes in Chinese patients undergoing open PD whereas usual nutritional assessment was not.

Keywords: psoas muscle area index, CT scan, sarcopenia, sarcopenic obesity, pancreatoduodenectomy

Introduction

Open pancreatoduodenectomy (PD) is the first choice of treating diseases in the region of the duodenum and pancreatic head. It is a major operation that may cause a high rate of postoperative complications such as pancreatic fistula and hemorrhage, and lead to a prolonged hospital stay and extra financial burden.[1] Many risk factors were proved to relate to these adverse events, containing nutritional measurements like malnutrition, sarcopenia, body mass index, and so on.[2] However, an international survey showed that

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44% of surgeons did not do a preoperative nutritional consultation for their patients undergoing PD and no specific preoperative nutritional thresholds were used.[3]

Sarcopenia was defined as a "progressive and generalized skeletal muscle disorder" characterized by both loss of skeletal muscle mass and strength, which is proved to be a more independent poor prognostic factor than weight loss and body mass index (BMI) in patients undergoing major abdominal surgeries besides pancreatic surgery.[4,5] A recent European consensus definition of sarcopenia described computed tomography (CT) as the gold standard for estimating muscle mass and some research also showed that CT-determined sarcopenia linked to poor outcomes following pancreatic surgery.[6,7] Sarcopenic overweight/obesity is another clinical problem characterized by the coexistence of overweight or obesity and sarcopenia which has been proven to be a strong predictor of major complications after pancreatoduodenectomy.[8,9] So, the International Study Group of Pancreatic Surgery recommend assessment of both sarcopenia and sarcopenic obesity prior to pancreatic surgery.[10] However, currently, no universally established definitions, diagnostic criteria, and cutoffs of sarcopenia and sarcopenic obesity exist, and there has been no paper published in the pancreatic field in the Chinese population.[11]

In this study, we tried to solve two problems in order to provide some new evidence on radiographic sarcopenia and sarcopenic overweight/obesity: 1) determine and validate the cutoff values of total psoas area index (TPAI) to diagnose CT-determined sarcopenia and sarcopenic overweight/obesity; 2) evaluate the relationship between CT-determined sarcopenia, sarcopenic overweight/obesity, and the occurrence of major complications and adverse outcomes in Chinese patients undergoing open PD.

Patients and Methods

Participants and Basal Data

In total, 161 consecutive patients underwent open PD between January 2016 and December 2018 in the Department of Hepatobiliopancreatic Surgery in Beijing Hospital. Among the subjects, 152 cases had complete records of preoperative abdominal and pelvic CT imaging and were retrospectively reviewed. All the operations were done by the same surgeon group. The whole design of this study was shown in the flowchart in Figure 1.

Baseline variables such as age, gender, history of jaundice and treatment, diabetes, coronary artery disease, hypertension, heavy smoking, and drinking were extracted from original medical records. Preoperative blood tests such as hemoglobin (Hb), lymphocyte, and albumin (Alb) were recorded. Operative basal data included the method of pancreaticojejunostomy (invaginated or duct-to-mucous), pancreatic duct diameter, intraoperative blood loss, blood infusion, fluid infusion, and urine volume. Final pathology reports were used to divide the cases into two stratifications: pancreatic ductal adenocarcinoma or not and malignancy or not.

The study protocol conformed to the Helsinki declaration and was approved by the local ethics committee of Beijing Hospital including the usage and publication of these retrospectively analyzed data. Due to the blinded data and retrospective design, written informed consent was not considered necessary by the ethics committee (Approval letter No. 2018BJYYEC-196-02).

CT Image Analysis and CT-Determined Sarcopenia Definition

Measurements were performed on precontrast CT scans within two weeks before and after the operation. Since it was proven that the total psoas area at the third lumbar vertebra level correlated well with whole-body skeletal muscle mass, we chose two consecutive images at the middle third lumbar vertebral level to record the average psoas muscle cross-sectional area (total psoas area = left + right) and attenuation recorded the average result (Figure 2).[12] Then, the total psoas area index (TPAI) was calculated using the equation: TPAI = total psoas muscle area (cm^2)/ height (m^2).[13] The psoas muscle density (PMD) was defined as the mean muscle attenuation in Hounsfield units (HU).[14]

The CT scans were assessed by two observers. We analyzed 10 different randomly chosen patients to assess the agreements of the two observers by using intraclass correlation coefficients (ICC). The results were excellent for TPA [ICC=0.967, 95% CI (0.874, 0.992)] and for PMD [ICC=0.934, 95% CI (0.759, 0.983)].

Since no in-hospital mortality happened in the female cohort in our database, we performed receiver operating characteristic (ROC) curve analysis by taking the rate of major complications as an indicator for predictive validity to determine the optimal cutoff value of TPAI in both sexes.[8,15] Then, we defined "CT-determined sarcopenia" or "TPAI-defined sarcopenia" as less than and equal to the cut-off value of TPAI which we calculated in this study. Meanwhile, we took 24.0 kg/m^2 as the diagnosis criteria of

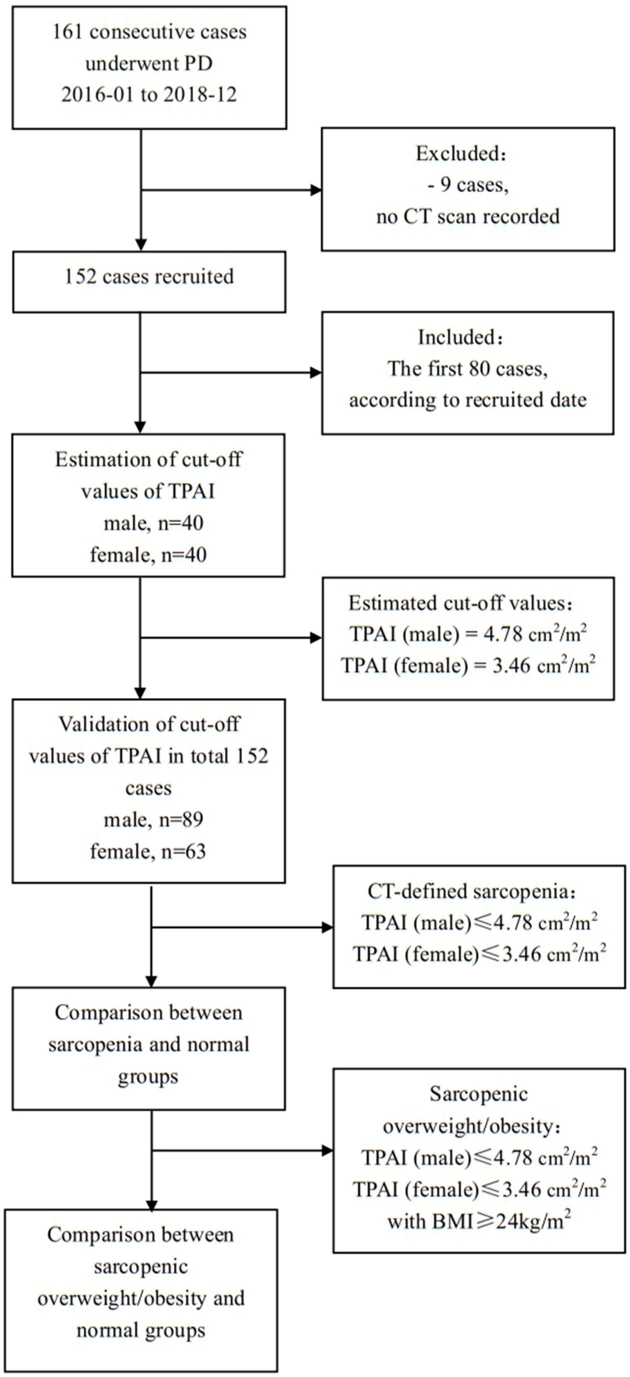

Figure 1 Flowchart of the study.

overweight, and 28 kg/m^2 as the diagnosis criteria of obesity in the Chinese population.[16] As in some published studies, sarcopenia with overweight and obesity was analyzed together and a significant association between sarcopenic overweight/obesity with adverse outcomes was proved.[9] So in our study, since the number of obesity was too small, we also put overweight and obesity together and defined the patients who were overweight/obese and fulfilled the criteria of CT-determined sarcopenia as "sarcopenic overweight/obesity."

Nutrition Status Measurements

The nutritional screening was done with NRS2002 within 24 hours after admission. NRS2002 contains three parts: nutritional status impairment, disease severity, and age. If the NRS2002 score is more than or equal to 3, it means "at nutritional risk."[17]

The GLIM criteria form the latest published tool to diagnose malnutrition and recommend a two-step model – screening and assessment.[18] The patients who were at nutritional risk by NRS 2002 would be assessed to diagnose malnutrition. The assessment step of GLIM criteria contains two parts: phenotypic criteria (three components: BMI, weight loss, and reduced muscle mass) and etiologic criteria (two components: reduced intake and disease burden), and fulfilling at least one component in each part is necessary to diagnose malnutrition. In our study, we used the new estimated cutoff values of TPAI in our study to assess the muscle mass reduction in the GLIM criteria.

In China, parenteral nutrition (PN) was still the most common route of postoperative nutrition support, and artificial nutrition was provided to all patients on postoperative day 2, often beginning with PN.[19] PN is defined as intravenous administration of a combination of amino acids, glucose, and fat meeting the recommendation of guidelines.[20] The transition from PN to enteral nutrition through tube feeding or oral nutrition supplement depended on the patients' condition. In any case, the guideline-recommended requirements of energy and protein were well guaranteed.

Clinical and Economic Outcome Measurements

Complications were recorded according to the Claviene–Dindo (CD) classification system (Minor: I–II; Major: III–V).[21] Postoperative pancreatic fistula (POPF) was defined and graded according to the 2016 ISGPS classification.[22] Nonfistulous complications contained cardiac and cerebrovascular events, hemorrhage (both intra-abdominal and gastrointestinal tract hemorrhage), biliary fistula, wound infection, and delayed gastric emptying. Postoperative length of hospital stay (LOS), in-hospital mortality, and total hospital costs were all recorded. Total hospital costs only contained the direct cost from the bill

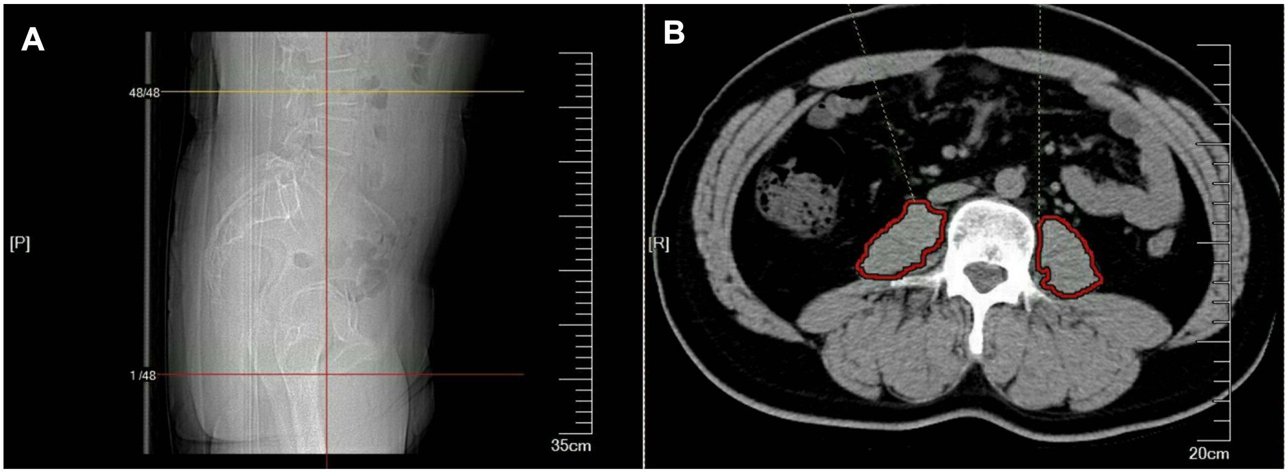

Figure 2 Computed tomographic images at the the middle third lumbar vertebral level. (**A**) Sagittal map. (**B**) Cross-sectional image and red circle shows the outline of psoas.

of hospitalization expenses regardless of the reimbursement of insurance, as in our previous published paper.[23]

Statistics Analysis

The data were collected and checked by two members of staff in our team. Quantitative data are expressed as the mean ±SD, while nominal data are expressed as a percentage. IBM SPSS Statistics (Ver. 20.0, IBM Corp., Armonk, NY, USA) was used to do the statistical analysis. Categorical data were analyzed using the chi-square test or Fisher exact test. Continuous data were tested by Student's unpaired *t*-test. The cutoff values of TPAI were calculated by maximizing sensitivity and specificity using the Youden index and the areas under the ROC curves were compared.

A logistic regression model was used to evaluate the relationship between risk factors and morbidity of major complications, which was expressed as an OR with 95% confidence intervals. We chose validated risk factors of major complications to be confounding variables to go with TPA, TPAI, PMD, sarcopenia, and sarcopenic overweight/obesity, such as age, BMI, history of diabetes, jaundice, PDAC, malnutrition, albumin, way of anastomosis, pancreatic duct diameter, and intraoperative bleeding.[24–26] *P*-values of less than 0.05 were considered statistically significant.

Results

Basal Data

In total, 152 consecutive patients were analyzed in this study with 89 males (58.5%). The mean age was 63.2 ±11.6 years (16.0–88.0). The mean BMI was 23.5±3.5 kg/m^2 (16.6–39.1), with no significant difference between the two genders. Table 1 displays the demographic data of all patients and different genders. For the comorbidity, it was obvious that men consumed more alcohol and cigarettes than women. The prevalence of nutritional risk and malnutrition was 69.7% and 56.6%, respectively; and 28.3% of cases suffered from pancreatic cancer. The male patients possessed more major complications, more re-operations, and higher costs than female patients, with statistical significance, and longer length of stay but without significance. Table 1 also showed that the TPA, TPAI, and PMD decreased after the operation with statistical significance.

Estimation and Validation of the Reference Values of TPAI

In total, 152 cases were enrolled between 2016 and 2018. According to recruited date, the first 40 consecutive male cases and the first 40 consecutive female cases were withdrawn to form estimation groups. Table 2 and Figure 3 display the results of ROC analysis that indicated TPAIs of 4.78 cm^2/m^2 for male patients and 3.46 cm^2/m^2 for female patients were the optimal cutoff points for predicting major complications with statistical significance.

Then, we did validation in total participants and divided the patients into sarcopenia and normal groups according to the cutoff point in three cohorts: all patients, males, and females (Table 3). In all three cohorts, the cutoff values showed excellent results in distinguishing major complications with significant differences. In total

Table 1 Demographic and Clinical Data

	All (n=152)	Male (n=89)	Female (n=63)	p#
Age, years	63.2±11.6	62.7±10.8	63.8±12.6	0.565
BMI, kg/m^2	23.5±3.5	23.5±2.8	23.4±4.4	0.894
Comorbidities, n(%)				
Diabetes	36 (23.7)	19 (21.3)	17 (27.0)	0.421
Hypertension	55 (36.2)	34 (38.2)	21 (33.3)	0.538
Cardiovascular disease	12 (7.9)	6 (6.7)	6 (9.5)	0.531
Smoking	59 (38.8)	56 (62.9)	3 (4.8)	0.000
Drinking	44 (28.9)	43 (48.3)	1 (1.6)	0.000
Jaundice	75 (49.3)	46 (51.7)	29 (46.0)	0.492
Nutrition status, n(%)				
NRS2002≥3	106 (69.7)	59 (66.3)	47 (74.6)	0.272
GLIM-defined malnutrition	86 (56.6)	47 (52.8)	39 (61.9)	0.265
Diagnosis, n(%)				
Malignance	123 (80.9)	73 (82.0)	50 (79.4)	0.706
PDAC	43 (28.3)	20 (22.7)	23 (36.5)	0.064
Lab results				
Hemoglobin, g/L	122.1±16.0	126.6±16.9	116.0±12.3	0.000
Albumin, g/L	38.1±4.7	38.1±5.0	38.0±4.3	0.851
Lymphocyte, ×10^9	2.27±9.41	2.77±12.3	1.58±0.56	0.444
Operation data				
Operation time, min	356.3±84.4	358.6±88.6	353.0±78.5	0.689
Intraoperative hemorrhage, mL	682.2±806.8	774.4±966.5	550.8±475.4	0.097
Duct-mucous anastomosis, n(%)	103 (67.8)	59 (66.3)	44 (69.8)	0.645
Pancreatic duct diameter, cm	3.10±2.12	2.75±1.92	3.59±2.20	0.175
CT characters				
Preoperative TPA, cm^2	13.4±5.0	16.0±4.5	9.7±3.0	0.000
Preoperative TPAI, cm^2/m^2	4.81±1.59	5.47±1.53	3.88±1.17	0.000
Preoperative PMD, HU	50.6±8.7	51.2±8.0	49.8±9.6	0.356
Postoperative TPA, cm^2	11.4±4.3*	13.7±3.9	8.4±2.7	0.000
Postoperative TPAI, cm^2/m^2	4.12±1.39*	4.69±1.34	3.36±1.04	0.000
Postoperative PMD, HU	46.2±8.6*	47.8±7.9	43.9±9.1	0.010
TPAI-defined sarcopenia, n(%)	59 (38.8)	31 (34.8)	28 (44.4)	0.231
Sarcopenic overweight/obesity, n(%)	26 (17.1)	14 (15.7)	12 (19.0)	0.950
Outcomes				
Major complications, n(%)	31 (20.4)	23 (25.8)	8 (12.7)	0.048
Re-operation, n(%)	14 (9.2)	12 (13.5)	2 (3.2)	0.030
In-hospital mortality, n(%)	5 (3.3)	5 (5.6)	-	-
LOS, day	27.7±18.4	28.3±19.3	27.0±17.2	0.681
Total hospital cost, USD	19,414.5±8349.0	20,834.1±9353.8	16,957.5±5593.1	0.032

Notes: #*P*-value of the comparison between two genders. **P*-values of the analysis between preoperative and postoperative CT measurements, all three *P*-values <0.01.
Abbreviations: BMI, body mass index; NRS, nutritional risk screening; GLIM, global leadership initiative malnutrition; PDAC, pancreatic ductal adenocarcinoma; CT, computed tomography; TPA, total psoas area; TPAI, total psoas area index; PMD, psoas muscle density; HU, Hounsfield units; LOS, length of stay; USD, United States Dollar.

and male groups, the differences between the re-operation rate, total cost, and length of stay were significant. Though significant differences were not found in the female group, the re-operation rate and length of stay were even higher than the no sarcopenia groups. So, the cutoff values were validated to be used to define sarcopenia.

Table 2 Estimation of the Cutoff Values of TPAI

	Male (n =89)	Female (n =63)
Major complication, n (%)	23 (25.8)	8 (12.7)
Estimated cut-off value in TPAI, cm^2/m^2	4.78	3.46
Area under the ROC curve	0.779, 95% CI (0.674, 0.885)	0.780, 95% CI (0.639, 0.920)
Sensitivity	0.739	0.875
Specificity	0.788	0.618
Youden Index	0.527	0.493
p-value	0.000	0.011

Abbreviations: TPAI, total psoas area index; ROC, receiver operating characteristic.

Sarcopenia and Sarcopenic Overweight/ Obesity

Based on the validated cut-off values of TPAI, the prevalences of CT-determined sarcopenia were 38.8% in total, 34.8% in males, and 44.4% in females (Table 1). According to the age, we divided the patients into age ≥65 and <65 groups. The prevalence of CT-determined sarcopenia was significantly higher in the elderly group (48.5% vs 31.4%, $p = 0.032$).

In our study, we used simple criteria to diagnose sarcopenic overweight/obesity: (1) BMI ≥24kg/m^2 and (2) TPAI ≤4.78 cm^2/m^2 for males or ≤3.46 cm^2/m^2 for females. According to this, the prevalences of sarcopenic overweight/obesity were 17.1% in total, 15.7% in males, and 19.0% in females, with no difference between the two genders (Table 1). Table 3 shows that the morbidity of major complications, the rate of re-operation, length of stay, and total cost were significantly higher in the sarcopenic overweight/obesity group than the normal group. The in-hospital mortality was worse in the sarcopenic overweight/obesity group, without statistical significance.

Logistic Regression Between Sarcopenia and Major Complications

Table 4 shows the univariate and multivariate logistic regression results for the risk of major complications. After adjusting for confounding variables calculated in univariate analysis (hemoglobin, albumin, method of anastomosis, diameter of pancreatic duct, and intraoperative hemorrhage), multivariate logistic regression analyses were done to evaluate TPA, TPAI, TPAI-defined sarcopenia, and sarcopenic overweight/obesity. The odds ratios of major complications were significantly associated with all four items. However, the traditional nutrition screening (NRS2002) and assessment (GLIM) tools were not proven to be associated with major complications.

Discussion

Sarcopenia is a clinical status with progressive loss of skeletal muscle mass, strength, and function, which may increase the risk of adverse outcomes. The prevalence of

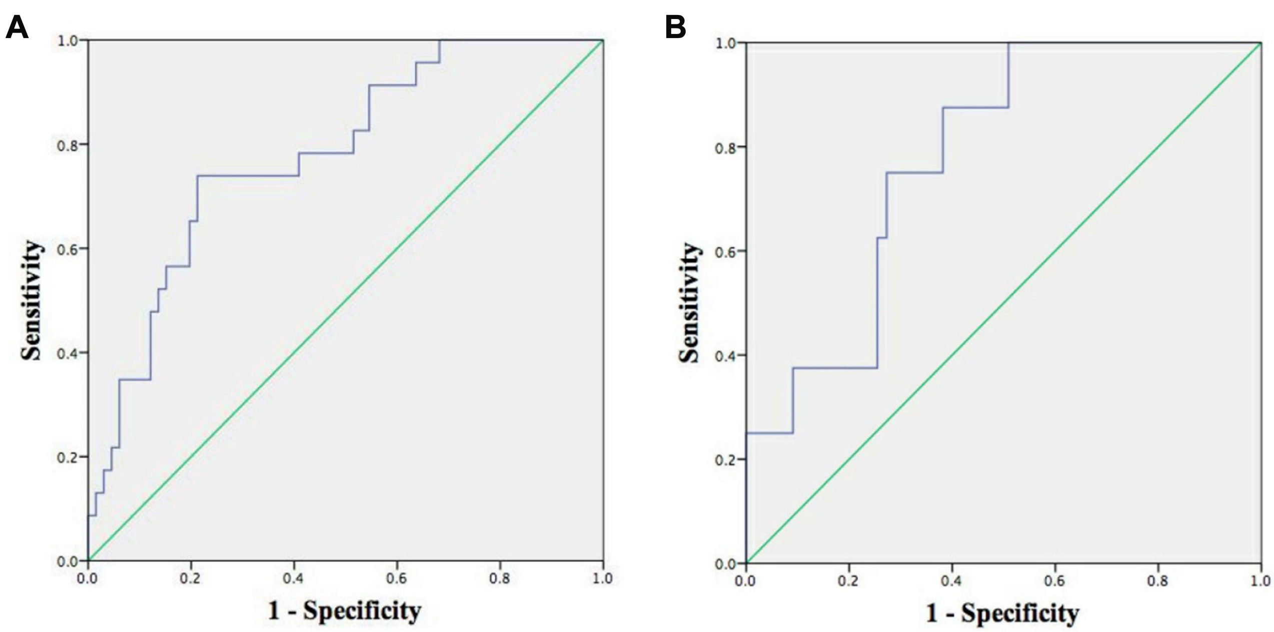

Figure 3 Receiver operating characteristic curves of TPAI for major complications. (**A**) For males. (**B**) For females.

Table 3 Comparison of Outcomes in Different Sarcopenic Cohorts

	Total, n = 152					Male, n = 89			Female, n = 63		
	Sarcopenia (n = 59)	Sarcopenic Overweight/ Obesity (n=26)	Normal (n = 93)	*P**	*P*#	TPAI ≤4.78 (n = 31)	TPAI>4.78 (n = 58)	*P*	TPAI ≤3.46 (n = 28)	TPAI>3.46 (n = 35)	*P*
Major complications, n(%)	24 (40.7)	11 (42.3)	7 (7.5)	0.000	0.000	17 (54.8)	6 (10.3)	0.000	7 (25.0)	1 (2.9)	0.025
Re-operation, n (%)	11 (18.6)	5 (19.2)	3 (3.2)	0.001	0.015	9 (29.0)	3 (5.2)	0.005	2 (7.1)	0 (0.0)	0.337
In-hospital mortality, n(%)	4 (6.8)	1 (3.8)	1 (1.1)	0.055	0.378	4 (12.9)	1 (1.7)	0.048	–	–	–
LOS, days	33.4±21.2	32.2±15.1	24.1±15.4	0.004	0.019	36.6±24.0	23.8±14.6	0.001	29.9±17.4	24.6±16.9	0.232
Total hospital cost, USD	22,761.8± 9158.5	25,190.5±7095.6	16,668.0± 6542.3	0.003	0.000	25,445.6± 9710.1	17,144.8± 7339.0	0.002	18,288.5± 6212.9	15,816.5± 4845.6	0.270

Notes: *Comparison between sarcopenia and normal groups. #Comparison between sarcopenic overweight/obesity and normal groups.
Abbreviations: TPAI, total psoas area index; LOS, length of stay; USD, United States Dollar.

sarcopenia is 5–10% in the elderly (>65 years old).[27] Sarcopenia can be either a primary syndrome such as in the elderly or secondary to malignancy, so screening of sarcopenia should be taken into consideration in all patients at risk. In our study, the prevalence of sarcopenia was 38.3% in all patients and 48.5%, in patients >65 years old, which were much higher figures than in the average population but similar to some pancreatic cohorts (48–65.3%).[28–30] We thought it was partly due to aging and pancreas-related problems, and the other reason was that the parameters chosen to diagnose sarcopenia were different between studies and might affect the prevalence.

There are many tools to diagnose and assess sarcopenia.[31] One core item is to evaluate muscle mass. Dual-energy X-ray absorptiometry and bioelectrical impedance analysis were both direct ways to assess body composition,[32] but they are complex and not widely available in many clinical settings. So, we need more easily available and practical parameters. A European consensus recommended CT and magnetic resonance imaging to be gold standards to evaluate reduced muscle mass, which was defined as "radiographic sarcopenia."[6] Radiographic sarcopenia has been proven to be associated with poor outcomes after pancreatectomy.[33,34] Many validated parameters in CT scan were published, including the parameters of muscle mass, such as skeletal muscle index (SMI), total psoas area (TPA), total psoas area index (TPAI), psoas muscle thickness, and parameters of muscle quality, such as muscle Hounsfield Units.[35–38] Some parameters were difficult to measure, and relied on the CT phase or were variable among researchers. So we chose TPAI, which was TPA adjusted for height, and was validated and easier to measure than total skeletal muscle. The ICC analysis in our study showed a high degree of consistency between different researchers.

Unfortunately, the cutoffs for diagnosing sarcopenia are not well defined. When using parameters of psoas, in some studies, sarcopenia was defined as less than the lowest tertile or quartile of total psoas area,[12] while, in others, some proposed definitions were used.[39] However, the standardized values must be adjusted based on population characteristics and whether the values can predict adverse clinical outcomes should be treated as a golden standard. So we performed receiver operating characteristic (ROC) curve analysis by taking the rate of major complications as an indicator for predictive validity to determine the optimal cutoff value of TPAI in both genders.[8] TPAI values of 4.78 cm^2/m^2 for male patients and 3.46 cm^2/m^2 for female patients were the optimal cut-off points for predicting major complications with statistical significance. And validation was done in a larger amount of patients (Table 3). So the diagnoses of TPA, TPAI, CT-determined sarcopenia, sarcopenic overweight/obesity, and GLIM-determined malnutrition were all based on these sex-specific values in our study. The multivariable regression analyses revealed the significant association between lower TPAI, sarcopenia, and more major complications, whereas the commonly used nutritional screening and assessment tools (NRS2002 and GLIM) were not significantly

Table 4 Association Between Different Covariates and Rate of Major Complications

	Univariate		Multivariate	
	OR (95% CI)	**p**	**OR (95% CI)**	**p**
Age, year	1.013 (0.978, 1.049)	0.476		
BMI, kg/m^2	1.077 (0.967, 1.199)	0.178		
Comorbidity of diabetes	1.740 (0.730, 4.149)	0.212		
Comorbidity of jaundice	1.555 (0.700, 3.452)	0.278		
Diagnosis of pancreatic cancer	0.681 (0.269, 1.722)	0.416		
Nutritional risk by NRS2002	0.619 (0.271, 1.411)	0.254		
GLIM-defined malnutrition	1.093 (0.494, 2.417)	0.827		
Hemoglobin, g/L	0.965 (0.940, 0.991)	0.010	0.958 (0.917, 1.000)	0.051
Albumin, g/L	0.900 (0.818, 0.990)	0.030	0.951 (0.814, 1.111)	0.526
Duct-mucous anastomosis	0.417 (0.186, 0.935)	0.034	0.486 (0.153, 1.548)	0.222
Intraoperative hemorrhage, mL	1.001 (1.000, 1.002)	0.003	1.001 (1.000, 1.002)	0.048
Pancreatic duct diameter, cm	0.707 (0.343, 1.455)	0.346		
Preoperative PMD, HU	1.004 (0.959, 1.051)	0.862		
Preoperative TPA, cm^2	0.999 (0.998, 1.000)	0.024	0.999 (0.998, 1.000)	0.065
Preoperative TPAI, cm^2/m^2	0.621 (0.451, 0.854)	0.003	0.605 (0.414, 0.883)	0.009
TPAI-defined sarcopenia	8.424 (3.327, 21.333)	0.000	8.256 (2.890, 23.583)	0.000
Sarcopenic overweight/obesity	9.010 (3.014, 26.928)	0.000	7.462 (2.084, 26.724)	0.002

Abbreviations: NRS, nutritional risk screening; GLIM, global leadership initiative malnutrition; TPAI, total psoas area index; PMD, psoas muscle density; HU, Hounsfield units.

associated. Moreover, due to surgical attack, though guideline-recommended nutrition support was administrated, there was still a sharp reduction of muscle mass, manifesting as the decrease of TPA, TPAI, and muscle attenuation.

Sarcopenic obesity is a subset of sarcopenia. It possesses the characters of both loss of skeletal muscle mass and an increase in adipose tissue mass which is often defined as increased BMI.[40] Currently, the definitions, diagnostic criteria, and cutoffs are not universally established, which significantly affected the prevalence and sensitivity study for any disease risk prediction.[11] So in our study, we put overweight and obesity together and made simple criteria to diagnose sarcopenic overweight/obesity: (1) BMI $\geq$24kg/m^2 and (2) TPAI $\leq$4.78 cm^2/m^2 for males or $\leq$3.46 cm^2/m^2 for females. The prevalence was 17.1% in total patients. Multivariable analysis showed that it was an independent predictor of increased rate of major complications. Our result is similar to Okumura's study of pancreaticoduodenectomy for PDAC, in which the sarcopenic obesity group had higher major complications (OR 3.2, p=0.008),[39] but in his study, the obesity was assessed by visceral to subcutaneous adipose tissue area obtained from CT images.

Muscle quality can also be quantified on imaging. Muscle Hounsfield units measured on CT scans can be used to predict muscle density, which represents the intra-muscular adipose infiltration.[41] It has been shown to correlate with adverse outcomes in patients undergoing pancreatic surgery,[7,42] but in our study, we did not find an association between lower muscle density and worse outcomes. But PMD decreased significantly after the operation, which represented higher fat infiltration in muscle or myosteatosis because of the inflammation-induced consumption of muscle protein and fat deposition.[43]

There are some limitations in our study: 1) It was a retrospective observational study in a single center. 2) We had a relatively small sample size, so it is difficult to do further analysis by stratification and difficult to perform standard external validation of the cutoff values of TPAI. 3) Although it is ideal to determine the cutoff values in the normal population, in our study we determined cutoff values in a certain population based on ROC curves. So it is important to validate whether our cutoff values are adequate to define low muscle mass.

However, to our knowledge, the present study is the first assessment of the prognostic significance of CT-determined sarcopenia in patients undergoing PD in the Chinese population. A larger, prospective, and multicenter study is necessary to verify our results in the future.

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Disclosure

The authors declare that the article is original, is not under consideration for publication anywhere else and has not been previously published. The authors declare no conflicts of interest, or financial disclosures.

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