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The Impact of Sarcopenia on Postoperative Course following Pancreatoduodenectomy: Single-Center Experience of 110 Consecutive Cases

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Complications · Hepato-pancreato-biliary surgery · Pancreas · Sarcopenia

Abstract
Background: Despite that mortality following pancreatoduodenectomy (PD) has gradually dropped during the past few decades, the incidence of postoperative complications remains high, ranging from 30–60%. Many studies have been focused on identification of perioperative risk factors for morbidity, and in recent years, sarcopenia has been pointed out as a valid predictor of postoperative complication. ***Materials and methods:*** Perioperative data from 110 consecutive patients who underwent PD were retrieved, and the presence of sarcopenia was assessed by the measurement of Hounsfield unit average calculation on preoperative CT scans. Postoperative complications were graded according to Clavien-Dindo classification, and the morbidity burden was assessed by comprehensive complication index (CCI) calculation. ***Results:*** Sarcopenia was associated with advanced age (72 vs. 66 years; $p = 0.014$) and lower preoperative albumin levels (3.5 vs. 3.7 g/dL; $p = 0.010$); it represented an independent risk factor for clinically relevant complications (relative risk: 1.71; $p = 0.015$) and was related to a higher rate of Grade C postoperative pancreatic fistula (50.0 vs. 11.4%; $p = 0.005$) and a higher CCI (47.6 vs. 29.6; $p = 0.001$). ***Conclusions:*** Sarcopenia represents a valid indicator of increased morbidity risk and may play a central role in preoperative risk stratification, allowing the selection of patients who may benefit from prehabilitation programs.

Introduction

Despite recent advances in surgical technique and perioperative care, which has led to a decrease in postoperative mortality to less than 5% in highly specialized pancreatic centers [1, 2], morbidity rate after pancreatoduodenectomy (PD) remains a challenge for pancreatic surgeons, ranging from 30 to 60% [3].

In recent years, growing age of surgical population, along with a better understanding of the pathophysiology of aging, has led to the introduction of the concept of frailty, which has been proven to exert a significant impact on postoperative outcomes in many branches of abdominal surgery [4], including pancreatic surgery.

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Sarcopenia has been identified as a valid marker of frailty [5] that might be evaluated through different methods [6], and growing evidence of its impact on postoperative complication following pancreatic surgery has emerged from recent studies [7–10].

The aim of our study was to retrospectively evaluate the incidence of sarcopenia and its impact on postoperative complications in a single-center cohort of 110 consecutive patients who underwent PD from 2010 to 2017.

Materials and Methods

Study Overview, Data, and Perioperative Management

The study protocol followed the ethical guidelines of the 1975 Declaration of Helsinki (as revised in Brazil in 2013). Local ethical committees' review of the protocol deemed that formal approval was not required owing to the retrospective, observational, and anonymous nature of this study. Results are reported according to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)] [11].

The study aim was to evaluate the prevalence of sarcopenia in our study population and its impact on postoperative complications.

All adult patients (age ≥ 18 years) who underwent PD for benign (chronic pancreatitis, intraductal papillary mucinous neoplasm, ampullary adenoma, or gastrointestinal stromal tumor) or malignant (pancreatic ductal adenocarcinoma, distal bile duct cancer, ampullary cancer, or neuroendocrine tumor) disease from 2010 to 2017 were evaluated for this study.

All data were retrieved from a single university-affiliated, hepato-pancreato-biliary (HPB) teaching center prospective database and anonymized prior to analysis. Age, sex, height, weight, and body mass index (BMI) were recorded for all patients; all comorbid conditions were retrieved in order to calculate the Charlson comorbidity index [12], as well as the preoperative American Society of Anesthesiologists (ASA) score [13].

Other preoperative variables included in the analysis were preoperative leukocytes count, hemoglobin, platelet count, serum amylase, serum protein, and albumin levels.

Preoperative CT scans were retrieved and blindly analyzed in order to calculate the Hounsfield unit average calculation (HUAC) for all patients, as described after.

All patients were explored through a median laparotomy extended from the xiphoid to the umbilicus, and a standard Whipple PD with Child reconstruction was performed in all cases. The pancreatic texture, as well as dilation of the main pancreatic duct, was subjectively established by a leading surgeon and was not directly measured but referred to as dilated or not dilated.

An end-to-side, double-layer pancreaticojejunostomy was routinely performed, beginning with a posterior layer of nonabsorbable (Prolene 4/0) seromuscular, separate stitches securing the jejunum to the pancreas; the duct-to-mucosa anastomosis was then performed after an enterotomy in the jejunum, with interrupted, nonabsorbable separate stitches (Prolene 5/0). An internal pancreatic duct stent (Bracci type) was routinely placed and secured to the jejunal mucosa; the anastomosis was completed with the anterior layer of seromuscular sutures between the anterior aspect of the jejunum and the pancreatic capsule, similar to the description by the Heidelberg group [14].

An end-to-side hepaticojejunostomy was carried out 10–15 cm distal to the pancreatic anastomosis, and finally, an end-to-side antecolic gastrojejunostomy was realized 30 cm distal to the hepaticojejunostomy. Nutritional jejunostomy was never used.

Two abdominal closed-suction drains were routinely positioned, one next to the biliojejunal anastomosis and one close to the pancreatojejunal anastomosis, and drainage amylase levels were measured on postoperative days 1, 3, 5, and 7.

Perioperative intravenous (IV) antibiotic prophylaxis in accordance with international guidelines on antimicrobial prophylaxis in surgery [15] was routinely performed; the majority of patients received IV cefazolin (2 g) 30 min before the cutaneous incision, with intraoperative doses repeated every 3 h.

Octreotide was routinely administered during the postoperative course until the patient could again take nourishment. All patients received gastric decompression through an intraoperatively positioned nasogastric tube, which was usually removed on postoperative day 4, with subsequent oral intake. Postoperative fluid intake ranged from 2,500 to 3,000 mL/24 h, with correction for the nasogastric tube and drain loss; nasoenteral feeding was not routinely administered.

Postoperative pancreatic fistula (POPF) was diagnosed and graded according to the latest International Study Group of Pancreatic Surgery (ISGPS) classification [16], biliary fistula was diagnosed and graded according to the International Study Group for Liver Surgery (ISGLS) classification [17], postpancreatectomy hemorrhage (PPH) was graded according to the ISGPS classification [18], and delayed gastric empty was diagnosed and graded according to the ISGPS classification [19].

All postoperative complications were graded according to the Clavien-Dindo classification [20] and incorporated in the comprehensive complication index (CCI) [21].

Sarcopenia Definition and Imaging Study

Sarcopenia is defined as syndrome characterized by progressive and generalized loss of both skeletal muscle mass and quality (strength or performance) [6].

Several methods have been described in order to quantify the loss of muscle mass and strength, ranging from impedance analysis to cross-sectional CT or MRI imaging study or hand-grip strength measurement through a dynamometer [22].

Because of the retrospective nature of this study, we were not able to test muscle strength in our series of patient; we therefore choose to evaluate both muscle mass and quality through a blinded revision of the preoperative CT scan conducted by a senior radiologist, aimed to define HUAC of the psoas muscle at the level of L3.

The HUAC of the psoas muscles is a measure of muscle density and fatty infiltration. Both the right and left psoas are evaluated, and their average is used for the final HUAC calculation.

Right Hounsfield Unit Calculation (RHUC) = (Right Hounsfield Unit × Right Psoas Area)/(Total Psoas Area), left Hounsfield Unit Calculation (LHUC) = (Left Hounsfield Unit × Left Psoas Area)/(Total Psoas Area), and HUAC = (Right Hounsfield Unit Calculation + Left Hounsfield Unit Calculation)/2 [9].

Sarcopenia was defined as a HUAC value within the lowest gender specific quartile, similar to other studies despite different measurement tools [5, 8, 23].

Table 1. Association between sarcopenia and selected patient characteristics and demographics (n = 110)

	No sarcopenic patients (n = 74)	Sarcopenic patients (n = 36)	p^1	Total (n = 110)
Gender, *n* (%)				
Female	32 (66.7)	16 (33.3)	0.90	48 (43.6)
Male	42 (67.7)	20 (32.3)		62 (56.4)
Age (median, IQR), years	66 (57–72)	72 (65–76)	**0.014**	68 (59–75)
Weight (median, IQR), kg	68 (64–75)	69 (60–76)	0.90	69 (60–76)
BMI (median, IQR), kg/m^2	24 (23–26)	25 (23–28)	0.09	24 (23–27)
Serum proteins (median, IQR), g/dL	6.3 (5.9–6.8)	6.3 (5.8–6.8)	0.44	6.3 (5.8–6.8)
Missing	2	3		5
Serum albumin (median, IQR), g/dL	3.7 (3.6–3.8)	3.5 (3.4–3.8)	**0.01**	3.6 (3.5–3.8)
Blood losses (median, IQR), mL	300 (200–500)	400 (200–700)	0.33	300 (200–500)
Missing	6	4		10
Operative time (median, IQR), min	370 (327–424)	372 (341–420)	0.86	370 (331–420)
Pancreatic texture, *n* (%)				
Normal	32 (42.8)	16 (44.4)	0.99	48 (44.0)
Soft	13 (17.8)	6 (16.7)		19 (17.5)
Fibrous	28 (38.4)	14 (38.9)		42 (38.5)
Missing	1	0		
Wirsung dilation, *n* (%)				
Yes	42 (57.5)	22 (61.1)	0.88	64 (58.7)
No	31 (42.5)	14 (38.9)		45 (41.5)
Missing	1	0		
Pathology, *n* (%)				
Pancreatic carcinoma or pancreatitis	44 (59.5)	21 (58.3)	1.00	65 (59.1)
Other	30 (40.5)	15 (41.0)		45 (40.9)
Charlson comorbidity index*, *n* (%)				
<4	19 (25.7)	6 (16.7)	0.21	25 (22.7)
4	15 (20.3)	9 (25.0)		24 (21.8)
5	23 (31.1)	7 (19.4)		30 (27.3)
>5	17 (23.0)	14 (38.9)		31 (28.2)
ASA score, *n* (%)				
1	11 (14.9)	3 (8.3)	0.15	14 (12.7)
2	50 (67.6)	21 (58.3)		71 (64.6)
3	13 (17.6)	12 (33.3)		25 (22.7)
Weight loss, *n* (%)				
No	35 (54.7)	17 (56.7)	1.00	52 (55.3)
Yes	29 (45.3)	13 (43.3)		42 (44.7)
Missing	10	6		16
Preoperative biliary drainage, *n* (%)				
No	38 (52.1)	17 (47.2)	0.79	55 (50.5)
Yes	35 (47.9)	19 (52.8)		54 (49.5)
Missing	1	0		1

All statistically significant values were put in bold. IQR, interquartile range; BMI, body mass index. * Categorized by quartiles. [1] χ^2 p value for categorical variables, Wilcoxon p value for continuous variables.

Statistical Analysis

Continuous data were reported as median and interquartile ranges (IQR) and categorical data as counts and percentages (%). The association between the presence of sarcopenia and selected features was estimated using the χ^2 test; Fisher's exact test was used for categorical variables and the Wilcoxon test for continuous variables. Univariate and multivariate log-binomial regression models were fitted to evaluate whether risk factors were associated with the risk of postoperative complications. The presence of sarcopenia and risk factors that were statistically associated with the risk of postoperative complications were considered in multivariate analyses. A p value <0.05 was considered statistically significant for all analyses. All the analyses were performed with the use of SAS software, version 9.4 (SAS Institute, Cary, NC, USA).

Results

Patients' Demographics and Clinical Characteristics

Demographics and clinical characteristics of the 110 patients are shown in Table 1. Sixty-two (56.4%) patients were males, the median age was 68 years (IQR: 59–75 years), and the median BMI was 24.41 kg/m^2 (IQR: 22.57–26.74 kg/m^2). Thirty-one (28.2%) patients exhibited a Charlson comorbidity index higher than 5, and 25 (22.7%) had an ASA score more than 2. The median HUAC was 16.40 HU (IQR: 14.46–18.90 HU); the lower HUAC quartile cutoff was 16.37 HU for males and 14.21 HU for females; 36 (32.72%) patients were defined as sarcopenic. Fifty-three patients (48.2%) received preoperative biliary drainage. Sarcopenic patients were elderly and presented with lower preoperative albumin levels.

Intraoperative Data

The median operative time was 370 min (IQR: 190–720 min), median estimated intraoperative blood loss was 300 mL (IQR: 50–200 mL), and 25 (22.7%) patients received a median of 2 units of packed blood cells (IQR: 1–6 units).

The gland texture was firm in 42 (38.5%) cases and soft in 19 (17.4%) patients; no abnormal findings concerning pancreatic texture appeared in the remainder 49 (45.1%). The main pancreatic duct was dilated in 64 (58.2%) patients.

Postoperative Outcomes

Table 2 depicts postoperative outcomes of the surgical procedure. The median length of stay was 26 days (IQR: 17–41 days), and 37 (33.6%) patients experienced a clinically relevant complication (Clavien score > 2), with a median CCI of 36.2 (IQR: 20.9–46.8). Table 3 depicts the postoperative morbidity. Twenty-four (21.8%) patients underwent relaparotomy (13 POPF Grade C, 8 PPH Grade B/C, 1 biliary fistula Grade C and 2 gastroenteroanastomotic leaks); the 30- and 90-day mortality was 4.5% (5 patients) and 9.1% (10 patients), respectively. The seeding complications leading to postoperative death were represented by a Grade C POPF in 7 patients, a gastroenteroanastomosis leak in 2 cases, and an acute respiratory distress syndrome (ARDS) in 1 patient. There were 5 (4.5%) 30-day readmissions: 2 for an intestinal occlusion medically treated, 1 for fever medically treated, 1 for acute bleeding from a gastroduodenal-artery pseudoaneurysm that received endovascular treatment, and 1 for an enterocutaneous fistula treated conservatively.

Analysis of Postoperative Morbidity

Table 3 presents the results of log-binomial regression analysis, evaluating the association between clinically relevant complications and selected risk factors. On univariate analysis, a 5 kg/m^2 increase in BMI was associated with a 1.26-fold increase in relative risk (RR) of clinically relevant complications (p value: 0.005), the presence of sarcopenia was associated with a 3.79-fold increase in RR of clinically relevant complications (p value <0.001), and an ASA score of 3 was associated with a 3.59-fold increase in RR of clinically relevant complications (p value <0.001). Statistically significant risk factors were included in multivariate analysis, and the presence of sarcopenia was the only risk factor that retained a statistically significant 1.71-fold increase in RR of clinically relevant complications (p value: 0.015).

Distribution of Postoperative Morbidity

Table 4 depicts the distribution of postoperative complications between the sarcopenic and nonsarcopenic populations. Sarcopenic patients showed a higher frequency of Grade C fistulas (50.0 vs. 11.4%) and a higher CCI (47.60 vs. 29.6).

Discussion

Sarcopenia is a widely accepted surrogate marker of frailty [22], and several studies have suggested a potential relation with worse postoperative and oncological outcomes following pancreatic surgery [5, 8–10, 24, 25].

Our analysis of sarcopenia highlighted its prevalence in elderly, which is consistent with observations from other studies [8].

Notably, despite its association with frailty, patient age did not showed significant correlation with clinically relevant postoperative complications in our series; this observation confirms the general belief that pancreatic surgery could be safely proposed to elderly patients in specialized HPB centers, as reported by other authors [26, 27].

The observed association between sarcopenia and slightly reduced (−0.2 g/dL in sarcopenic group) preoperative albumin levels, although statistically significant, does not seem clinically relevant, as the median albumin levels within the sarcopenic group were between the normal range.

Our results highlighted an association between greater BMI, higher ASA score, the presence of sarcopenia, and an increased risk of clinically relevant complications on

Table 2. Postoperative outcomes and morbidity

	Total (n = 110)
Clinically relevant complication, *n* (%)	
Yes	37 (33.6)
No	73 (66.4)
Postoperative complication Clavien score, *n* (%)	
0	16 (14.5)
I	4 (3.6)
II	53 (48.2)
IIIa	10 (9.1)
IIIb	6 (5.5)
IVa	11 (10.0)
V	10 (9.1)
Comprehensive complication index (median, IQR)	36.2 (20.9–46.8)
Thirty-day mortality, *n* (%)	
Yes	5 (4.5)
No	105 (95.5)
Ninety-day mortality, *n* (%)	
Yes	10 (9.1)
No	100 (90.9)
Postoperative pancreatic fistula, *n* (%)	
None	57 (51.8)
Biochemical leak	20 (18.2)
Grade B	20 (18.2)
Grade C	13 (11.8)
Biliary fistula, *n* (%)	
None	108 (98.2)
Grade A	0 (0.0)
Grade B	1 (0.9)
Grade C	1 (0.9)
Gastro-entero anastomosis leak, *n* (%)	
None	106 (96.4)
Clavien 1, 2	0 (0.0)
Clavien ≥3	4 (3.6)
Postpancreatectomy hemorrhage, *n* (%)	
None	89 (80.9)
Grade A	1 (0.9)
Grade B	12 (10.9)
Grade C	8 (7.3)
Delayed gastric empty, *n* (%)	
None	68 (61.8)
Grade A	23 (20.9)
Grade B	13 (11.8)
Grade C	6 (5.5)
Superficial/deep incisional surgical site infection, *n* (%)	
None	77 (69.1)
Clavien 1, 2	32 (29.1)
Clavien ≥3	2 (1.8)
Organ/space infection, *n* (%)	
None	71 (87.7)
Clavien 1, 2	7 (8.6)
Clavien ≥3	3 (3.7)
Not-applied[1]	29
Sepsis, *n* (%)	
Total	43 (39.1)
POPF related	29 (26.5)
Biliary fistula related	4 (3.6)
Organ/space infection related	5 (4.5)
Gastro-entero anastomosis leak related	1 (0.9)
Other causes	4 (3.6)
Cardiological complication, *n* (%)	
None	107 (97.3)
Clavien 1, 2	1 (0.9)
Clavien ≥3	2 (1.8)
Respiratory complication[2], *n* (%)	
None	83 (75.5)
Clavien 1–2	15 (13.6)
Clavien ≥3	12 (10.9)
Acute kidney injury[3], *n* (%)	
None	95 (86.4)
Clavien 1, 2	1 (0.9)
Clavien ≥3	14 (12.7)
Urinary tract infection, *n* (%)	
None	100 (90.9)
Clavien 1, 2	10 (9.1)
Clavien ≥3	0 (0.0)
Other complication, *n* (%)	
None	97 (88.2)
Clavien 1, 2	9 (8.2)
Clavien ≥3	4 (3.6)

IQR, interquartile range. [1] Abdominal collections related to an underlying POPF, biliary fistula or gastro-entero anastomosis leak were excluded. [2] All the 12 respiratory complications (pleural effusion, pneumonia, ARDS) occurred in the setting of planned (3/12) or unplanned (9/12) ICU admission; 9 of these complications occurred after a grade C POPF, and *only 3 developed independently from a concurrent surgical complication*. [3] All the 14 AKIs occurred in the setting of planned (2/12) or unplanned (10/12) ICU admission, 1 of these AKIs occurred after a grade B POPF, 10 followed a grade C POPF, another 1 developed in the setting of a grade C biliary fistula, and *only 2 actually occurred independently from an underlying surgical complication.*

univariate analysis, whereas only sarcopenia retained a statistically significant impact on multivariate analysis.

The role of obesity as a risk factor for postoperative complications following pancreatic surgery has been long debated; some studies pointed out how obesity was associated with increased postoperative morbidity [28, 29], but this finding was questioned by other investigators [30,31]. The impact of visceral adiposity on postop-

Table 3. Analysis of association between clinically relevant complications and selected risk factors

Variable	Univariable models					Multivariable model[1]		
	n/*N*	%	RR	IC 95%	*p*	RR	IC 95%	*p*
All patients	37/110	33.6						
Age, years								
+10 years			1.13	0.88–1.44	0.33			
BMI, kg/m^2								
+5 kg/m^2			1.26	1.07–1.49	**0.005**	0.99	0.78–1.28	0.990
Serum protein, g/dL								
+1 g/dL			0.92	0.64–1.31	0.63			
Serum albumin, g/dL								
+1 g/dL			0.45	0.16–1.27	0.13			
Preoperative white blood cells, mm^3								
+1,000 mm^3			1.07	0.99–1.13	0.10			
Serum amylase, U/L								
+20 U/L			0.97	0.86–1.08	0.57			
Preoperative Hb, g/dL								
+1 g/dL			0.97	0.82–1.14	0.70			
Blood losses, mL								
+100 mL			1.02	0.96–1.09	0.49			
Operative time, min								
+60 min			1.07	0.92–1.26	0.38			
Presence of sarcopenia								
No	13/74	17.6	1.00			1.00		
Yes	24/36	66.7	3.79	2.20–6.54	**<0.001**	1.71	1.11–2.65	**0.015**
Charlson comorbidity index								
<4	7/25	28.0	1.00					
4	6/24	25.0	0.85	0.24–3.06	0.81			
5	9/30	30.0	1.10	0.34–3.56	0.87			
>5	15/31	48.4	2.41	0.79–7.40	0.12			
ASA score								
1–2	18/85	21.2	1.00			1.00		
3	19/25	76.0	3.59	2.25–5.72	**<0.001**	1.72	0.99–3.00	0.060
Chronic pancreatitis								
No	33/99	33.3	1.00					
Yes	4/11	36.4	1.09	0.48–2.55	0.84			
Weight loss								
No	17/52	32.7	1.00					
Yes	18/42	42.9	1.31	0.78–2.21	0.31			
Missing	2/16							
Preoperative biliary drainage								
No	17/55	30.9	1.00					
Yes	19/54	35.2	1.14	0.67–1.95	0.64			
Missing	1/1							
Pancreatic texture								
Normal	15/48	31.2	1.00					
Fibrous	11/42	26.2	0.84	0.43–1.62	0.60			
Soft	10/19	52.6	1.68	0.93–3.06	0.09			
Missing	0/1							
Wirsung dilation								
No	18/45	40.0	1.00					
Yes	19/64	29.7	0.74	0.44–1.25	0.26			
Missing	0/1							

All statistically significant values were put in bold. RR, relative risk. [1] Variables with a p value < 0.05 were entered in multivariate model.

Table 4. Analysis of association between sarcopenia and specific complications*

	Presence of sarcopenia		*p*
	no (*n* = 74)	yes (*n* = 36)	
Postoperative pancreatic fistula, *n* (%)			
Yes	19 (25.7)	14 (38.9)	0.16[1]
No	55 (74.3)	22 (61.1)	
POPF grade, *n* (%)			
C	4 (11.4)	9 (50.0)	**0.005**[2]
BL, B	31 (88.6)	9 (50.0)	
Biliary fistula, *n* (%)			
Yes	2 (2.8)	0 (0.0)	1.00[2]
No	69 (97.2)	29 (100.0)	
Delayed gastric empty, *n* (%)			
Yes	13 (18.3)	6 (20.0)	0.84[1]
No	58 (81.7)	24 (80.0)	
Postpancreatectomy hemorrhage, *n* (%)			
Yes	10 (13.5)	10 (27.8)	0.07[1]
No	64 (86.5)	26 (72.2)	
Deep/incisional surgical site infection, *n* (%)			
Yes	1 (1.4)	1 (2.8)	0.55[2]
No	73 (98.6)	35 (97.2)	
Organ/space infection, *n* (%)			
Yes	1 (1.4)	2 (5.6)	0.25[2]
No	73 (98.6)	34 (94.4)	
Sepsis, *n* (%)			
Yes	1 (1.8)	1 (4.5)	0.49[2]
No	54 (98.2)	21 (95.5)	
Cardiological complication, *n* (%)			
Yes	1 (1.4)	1 (2.8)	0.55[2]
No	73 (98.6)	35 (97.2)	
Respiratory complication, *n* (%)			
Yes	0 (0.0)	2 (5.6)	0.10[2]
No	74 (100.0)	34 (94.4)	
Acute kidney injury, *n* (%)			
Yes	0 (0.0)	2 (5.6)	0.10[2]
No	74 (100.0)	34 (94.4)	
Urinary tract infection, *n* (%)			
No	74 (–)	36 (–)	NA
Other complication, *n* (%)			
Yes	72 (97.3)	34 (94.4)	0.60[2]
No	2 (2.7)	2 (5.6)	
Comprehensive complication index (median, IQR)	29.60 (29.60–36.20)	47.60 (36.20–62.50)	**0.001**[3]

IQR, interquartile range. * Clinically relevant complications (Clavien score ≥3). [1] χ^2 *p* value. [2] Fisher's exact test *p* value. [3] Wilcoxon *p* value.

erative complications has been recognized in past imaging-based studies [32], and recently, the association of visceral obesity with sarcopenia on automated preoperative imaging analysis has been proven to be a relevant indicator of increased risk of perioperative morbidity and mortality after pancreatic surgery [5, 8–10, 24, 25, 33]. It must be noted that despite its impact on postoperative complications on univariate analysis, BMI did not retain a statistically significant correlation with postoperative complications in our series and was not differently distributed between the sarcopenic and nonsarcopenic groups.

The presence of sarcopenia was associated with a 3.79-fold increase in RR of clinically relevant complications on univariate analysis and was the sole risk factor to retain a statistically significant 1.71-fold increase in RR of postoperative complications on multivariate analysis.

In our analysis on the different distributions of clinically relevant complications between sarcopenic and nonsarcopenic patients, we highlighted a higher rate of Grade C POPF in the sarcopenic population. Considering its role as a marker of frailty and impaired response to exogenous stress, it seems reasonable for sarcopenic patients to experience a lower self-recovery rate, with a more frequent necessity of surgical treatment.

The CCI of sarcopenic patients was significantly higher compared to the nonsarcopenic group, depicting a more complicated postoperative course.

These data confirm the observation from other studies in which sarcopenia was advocated as a useful tool for identifying patients at higher risk of postoperative complications [23, 24, 33].

The main limitation of our study is represented by its retrospective nature, which did not allow us to test other important sarcopenia indexes such as grip strength, walking speed, or levels of exhaustion. We tried to overcome this obstacle by choosing to evaluate the muscle density using the HUAC, which entails both muscle mass and quality.

Despite other studies used automated software in order to obtain quantitative measurements of muscle mass from cross-sectional images [23–25, 33], the manual measurement of HUAC is easy to perform and reproduce. It must be noted that many different methods for sarcopenia measurement have been described in retrospective surgical papers aimed to investigate the association between sarcopenia and surgical and oncological outcomes, and no universally accepted cutoffs are available.

The scarce numerosity of study population could lead to an increased risk of type II error. Finally, as any retrospective study, there is a large potential of selection bias in our patient population.

In conclusion, sarcopenia represents an independent risk factor for the development of clinically relevant postoperative complications and can be easily identified through the measurement of HUAC on preoperative imaging analysis.

The presence of sarcopenia, coupled with other characteristics such as higher ASA score, higher BMI, or multiple comorbidities, allows surgeons to identify patients at higher risk of postoperative complications and activate prehabilitation programs aimed to improve skeletal muscle hypertrophy and increase in lean muscle mass [34].

Previous studies demonstrated that prehabilitation is associated with an improved functional recovery among patients undergoing colorectal surgery [35].

Such policies could find even wider applications in the near future when neoadjuvant chemotherapy would possibly play a central role in the management of patients affected by pancreatic ductal adenocarcinoma even in resectable neoplasms [36].

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Statement of Ethics

The study protocol followed the ethical guidelines of the 1975 Declaration of Helsinki (as revised in Brazil in 2013). All individuals enrolled in our study signed an informed consent for anonymous data management and publications. Local ethical committees' review of the protocol deemed that formal approval was not required owing to the retrospective, observational, and anonymous nature of this study.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Study conception and design: L.C., S.D.S., V.B. Acquisition of data: L.C. Analysis and interpretation of data: L.C., S.D.S., F.B., V.B. Drafting of manuscript: L.C. Critical revision: L.C., S.D.S., A.L., R.D.C., F.B., A.M., V.B., L.G.D.C.

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