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Retrospective study comparing 30-day surgical outcomes of pancreaticoduodenectomy for pancreatic head adenocarcinoma in patients with and without malnutrition defined by the GLIM criteria

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Abstract

This single-center study conducted in Turkey aims to assess the impact of preoperative nutritional status based on global leadership initiative on malnutrition criteria on 30-day postoperative surgical outcomes in patients undergoing pancreaticoduodenectomy (PD) for pancreatic head adenocarcinoma. A retrospective analysis was conducted on patients who underwent PD. Patients were classified into 2 groups based on preoperative nutritional assessments of global leadership initiative on malnutrition criteria: malnourished (n = 23; 46%) and nonmalnourished (n = 27; 54%). Preoperative data, including demographics, comorbidities, intraoperative data, final pathological results, and postoperative 30-day outcomes, including overall and major (Clavien-Dindo > II) complications, length of hospital stay (LOS), and 30-day mortality rates, were recorded and compared. A total of 50 patients were included in the study. Demographics, American Society of Anesthesiologists scores, and comorbidities were similar between the groups ($P > .05$). The mean Clavien-Dindo grade was 3 in the malnourished group and 2 in the nonmalnourished group ($P = .001$). Malnourished patients had a significantly higher rate of major complications (73.9%) compared to nonmalnourished patients (14.8%)($P = .001$). The median LOS was similar between the 2 groups. The rate of postoperative transfusions was higher in the malnourished group ($P = .033$). Postoperative 30-day mortality was significantly higher in the malnourished group (26.1%) compared to the nonmalnourished group (0%) ($P = .006$). Multivariate logistic regression analysis confirmed that malnutrition was an independent predictor of postoperative major complications (OR: 16.3, 95% CI: 3.9–66.8, $P = .001$). Preoperative malnutrition is a strong predictor of 30-day postoperative major complications and mortality following PD in patients with pancreatic head adenocarcinoma.

Abbreviations: AJCC = American Joint Committee on Cancer, ASA = American Society of Anesthesiologists, BMI = body mass index, CA = carbohydrate antigen, CI = confidence interval, CKF = chronic kidney failure, CRP = C-reactive protein, CR-POPF = clinically relevant postoperative pancreatic fistula, CT = computed tomography, CVD = cardiovascular disease, DGE = delayed gastric emptying, DM = diabetes mellitus, DP = distal pancreatectomy, ERCP = endoscopic retrograde cholangio-pancreaticography, ESPEN = European Society of Parenteral and Enteral Nutrition, GI = gastrointestinal, GLIM = global leadership initiative on malnutrition, HL = hyperlipidemia, ISGPF = International Study Group of Pancreatic Fistula, LOS = length of stay, MLNR = mlymph node ratio, MRI = magnetic resonance imaging, NET = neuroendocrine tumors, OR = odds ratio, PD = pancreaticoduodenectomy, PDAC = pancreatic ductal adenocarcinoma, POPF = postoperative pancreatic fistula, POPH = postoperative pancreatic hemorrhage, RBC = red blood cell, SD = standard deviation, TP = total pancreatectomy.

Keywords: body mass index, complication, hypoalbuminemia, malnutrition, Pancreatic cancer, pancreaticoduodenectomy

Informed Consent Statement Informed consent was obtained from the patients or their first-degree relatives for inclusion in the study and the use of their data anonymously in this retrospective study. Prior to the study, each participant was provided with detailed information regarding the surgical procedure, associated risks, potential complications, expected benefits, and estimated mortality rates. In addition, they were informed about the use of their anonymized medical data in medical research, and written informed consent was obtained before the surgeries were performed.

The authors have no funding and conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Committee approval was obtained from the Başkent University Institutional Review Board (Project Approval Number: KA23/156) on April 20, 2023.

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1. Introduction

Malnutrition plays a critical role in global health, affecting both medical outcomes and cost-effectiveness. Over 20% of hospitalized patients are malnourished, which leads to longer hospital stays, increased complications, and worse medical and financial outcomes.[1,2] This highlights the need for serious attention to the issue.

Various biochemical, radiological, and anthropometric techniques are used to asses malnutrition, including measurements of prealbumin, albumin, transferrin, body mass index (BMI), and muscle mass using imaging techniques like computed tomography and magnetic resonance imaging. Nutritional screening tools such as MUST, SNAQ, NRS 2002, and MST, along with assessment tools like ESPEN Criteria, SGA, and Global Leadership Initiative on Malnutrition (GLIM) Criteria, are commonly employed.[3]

Hypoalbuminemia, a nonspecific marker, can result from trauma, chronic inflammation, and malignancies, with its etiology being multifactorial. It has been identified as a risk factor for complications following pancreatic resections.[4] Similarly, low BMI and albumin levels preoperatively are associated with higher postoperative complications in gastrointestinal (GI) cancer patients.[5–7]

Unlike other GI cancers, few studies have examined the effects of preoperative nutritional status in pancreatic cancer patients.[4,8–10] Distal pancreatectomy (DP), pancreaticoduodenectomy (PD-Whipple Procedure), and total pancreatectomy (TP) are surgical approaches to the pancreatic lesions.[11] PD is one of the most complicated abdominal surgeries. Compared to PD, DP, and TP are relatively shorter and safer surgical techniques because DP does not involve reconstruction and requires less dissection, and TP does not require pancreaticojejunal anastomosis. Pancreatic ductal adenocarcinoma (PDAC) is the primary indication for PD, alongside neuroendocrine tumors (NET), pancreatic cystic lesions, and other conditions. Metabolic and endocrine results of PD also have negative effects on the postoperative period in addition to the procedure's surgical effects. Due to knotty postoperative courses and complex anastomoses, patients usually need to have nutritional support. Therefore, the nutritional status of patients who will undergo PD due to PDAC is crucial for the postoperative period.

The primary aim of this retrospective study from a single center in Turkey, was to evaluate the impact of malnutrition, diagnosed based on low albumin levels (<3.5 g/dL) and low BMI (<18.5 kg/m^2) in the preoperative period according to the GLIM criteria, on 30-day short-term surgical outcomes in patients who underwent pancreaticoduodenectomy (PD-Whipple procedure) for pancreatic head pancreatic ductal adenocarcinoma (PDAC).[12] Secondarily, we aimed to identify factors influencing the development of major postoperative complications (Clavien-Dindo (CD) grade > II) within 30 days in this patient cohort.[13]

2. Materials and methods

2.1. Participants

The medical records for pancreatic resections performed in Başkent University Ankara Hospital, between 01.01.2017 and 31.12.2021, were investigated retrospectively. Patients who have undergone TP and DP or additional surgical procedure with pancreaticoduodenectomy (PD), patients undergone albumin replacement therapy, patients with permanent pathological diagnosis except for pancreatic ductal adenocarcinoma (PDAC), and patients with any kind of liver disease were excluded from this trial. Patients with any missing data were excluded. Only patients who underwent pancreaticoduodenectomy for pancreatic ductal adenocarcinoma were included (Figs. 1–4). Also, patients were included only if at least a 1-year follow-up could be conducted. All procedures were performed by the same team with an open surgical technique. Patients were classified into 2 groups based on preoperative nutritional assessments: malnourished and nonmalnourished. Albumin level <3.5 g/dL was defined as hypoalbuminemia.[4] Patients with hypoalbuminemia and BMI under 18.5 kg/m^2 were classified as malnutrition.[4]

2.2. Evaluation of nutritional status

In assessing patients' nutritional status, the GLIM criteria, published in 2019, represent a widely used and accepted tool

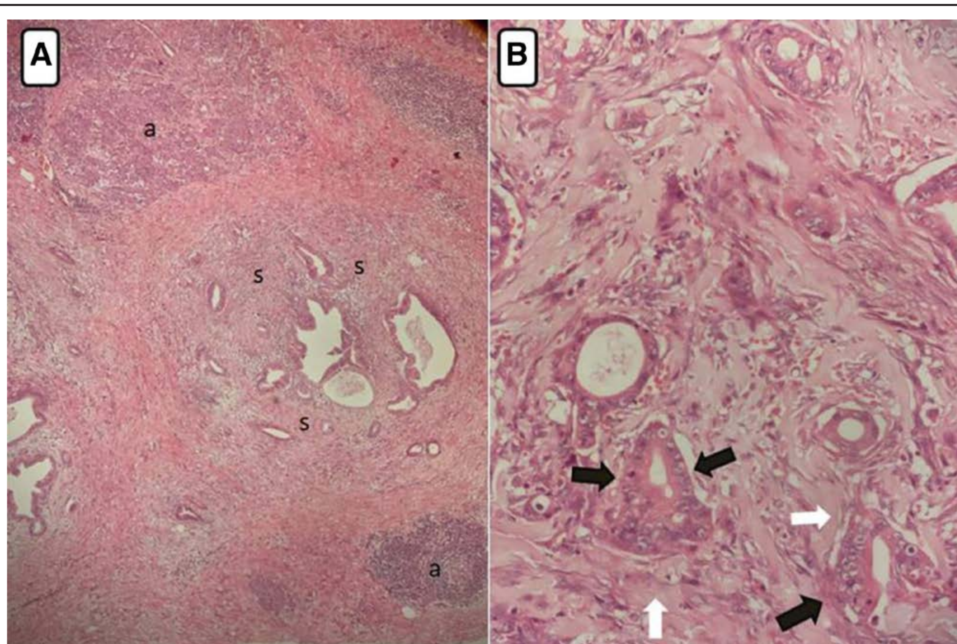

Figure 1. Histopathologic analysis. (A) Neoplastic lesion adjacent to pancreatic acini (a). Infiltrating well-formed ductal structures surrounded by desmoplastic stroma (s); Hematoxylin and eosin. Magnification ×40. (B) Abortive tubular structures composed of pleomorphic neoplastic cells (black arrows). White arrows: desmoplastic stroma; hematoxylin and eosin. Magnification ×200.

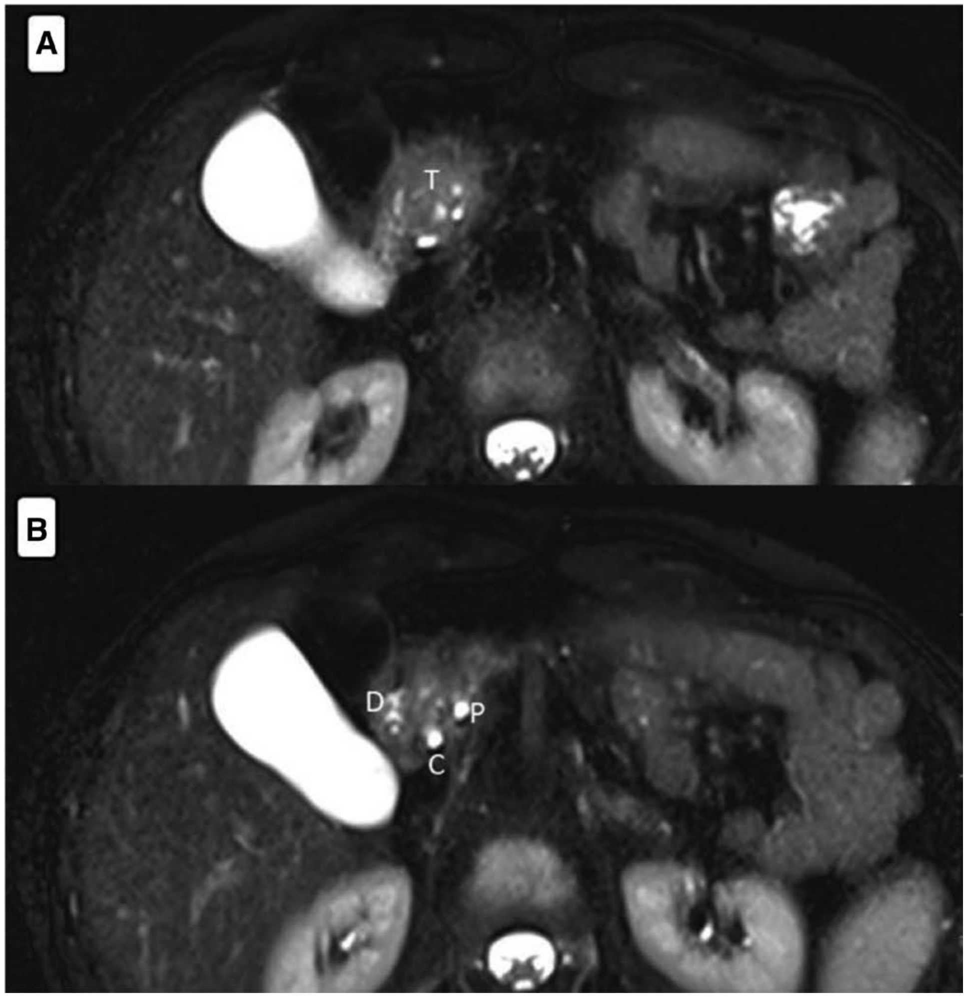

Figure 2. T2-weighted fat-saturated magnetic resonance imaging (MRI) of a 54-yr-old male patient. (A) A 3 cm tumor (T) located in the head of the pancreas, with no evidence of vascular invasion. (B) Adjacent tissues to the tumor; P: Dilated pancreatic duct, C: Common bile duct (CBD), D: Duodenum (Siemens Magnetom Avanto 1.5T MRI scanner, 1.5 Tesla field strength).

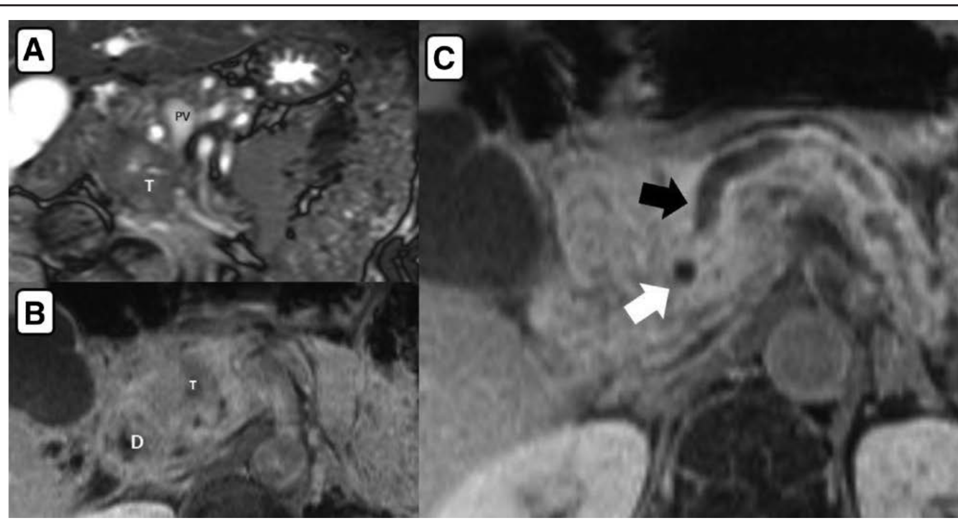

Figure 3. Magnetic resonance imaging (MRI) of a 61-yr-old male patient. (A) A 4 cm tumor (T) located in the head of the pancreas without evidence of vascular invasion. (B) Adjacent tissues surrounding the tumor (T); D: duodenum. (C) black arrow: dilated pancreatic duct; white arrow: CBD (Siemens Magnetom Avanto 1.5T MRI scanner, 1.5 Tesla field strength).

for malnutrition diagnosis.[12] According to the GLIM criteria for the diagnosis of malnutrition, 2 key components must be assessed: phenotypic and etiologic factors. The phenotypic criteria include weight loss, low BMI, and reduced muscle mass. The etiologic criteria are based on the presence of a chronic disease or inflammation (cancer, etc), which can impair

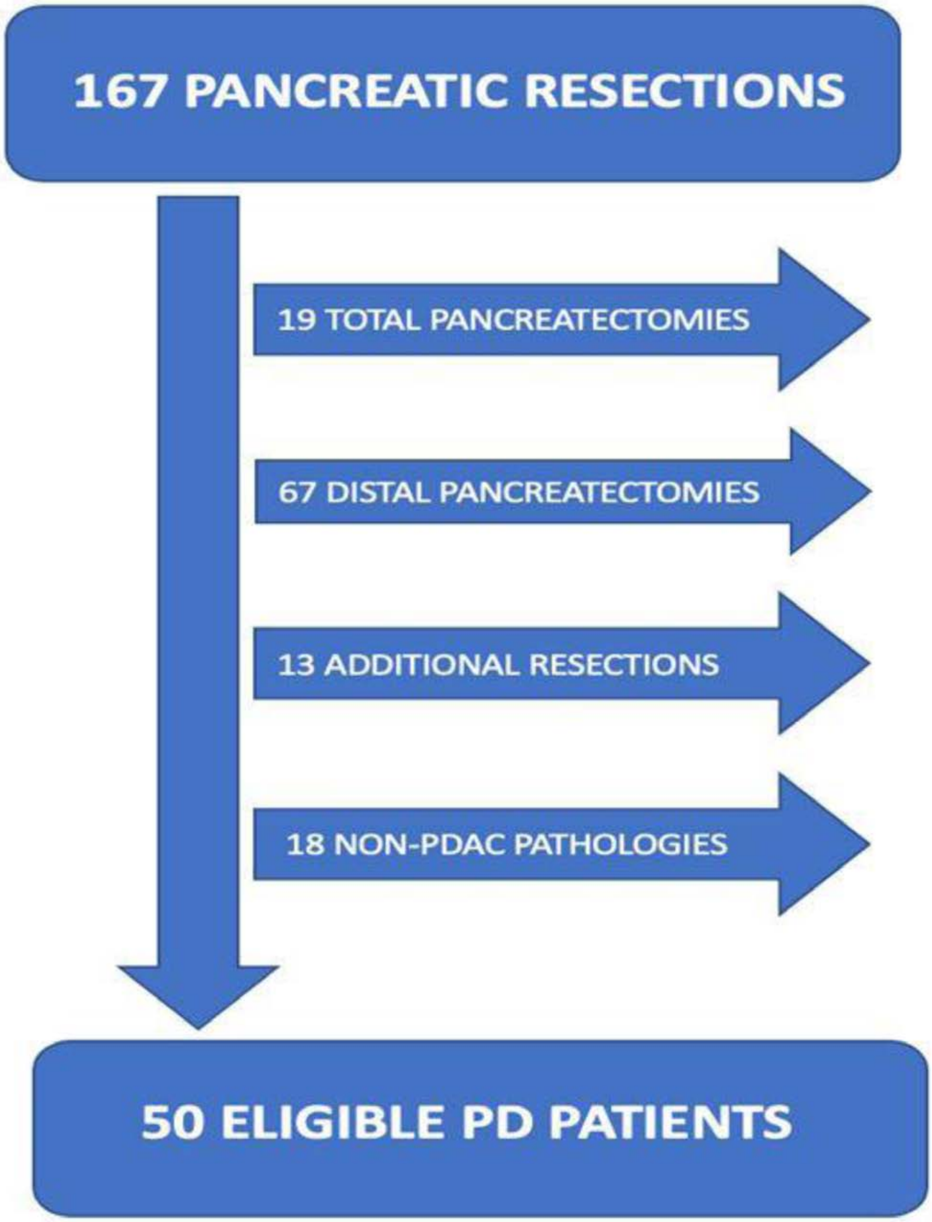

Figure 4. Flow chart depicting the patient selection process for the study. A retrospective analysis was performed on 167 patients who underwent pancreatic resection, of whom 50 met the inclusion criteria and were enrolled in the study.

nutritional status. A diagnosis of malnutrition can be established if at least 1 criterion from either the phenotypic or etiologic factors is met, ensuring an adequate evaluation of the patient's condition.

To classify patients according to the GLIM criteria for malnutrition, we selected the phenotypic criterion of low BMI (<18.5 kg/m^2) and the biochemical criterion of low albumin (<3.5 g/dL). Additionally, as all patients had a diagnosis of cancer, this fulfilled the etiologic criterion of chronic disease (cancer) as per the GLIM guidelines.[12] Therefore, based on these criteria, we classified the patients into malnourished and nonmalnourished groups.

2.3. Preoperative, intraoperative, and postoperative parameters

We analyzed the age and sex distributions as demographics. To compare patients' performance and functional status, we used the American Society of Anesthesiologists (ASA) score. Preoperative diagnoses of diabetes mellitus, cardiovascular disease (CVD), hyperlipidemia (HL), chronic kidney failure, and hypothyroidism were compared. Smoking and acetylsalicylic acid usage were analyzed. Preoperative C-reactive protein (CRP), carbohydrate antigen 19 to 9 (CA19-9), total bilirubin levels, and biliary drainage with endoscopic retrograde cholangiopancreaticography or external biliary catheter in the preoperative period were also compared.

Operation duration in minutes, intraoperative transfusion requirements and vascular resection requirements, hospital stay in days, and red blood cell transfusion in packages were also analyzed. Postoperative complications were graded using the CD classification.[13] Major complications were marked as CD grade III or higher. Postoperative pancreatic fistula (POPF) cases were marked based on the International Study Group of Pancreatic Fistula classification.[14] Both grades B and C were defined as clinically relevant postoperative pancreatic fistula;

CR-POPF. Delayed gastric emptying (DGE) and postoperative pancreatic hemorrhage (POPH) cases were marked based on the International Study Group of Pancreatic Surgery.[15,16] The pathological evaluations were based on the criteria stated in the 7th edition of the American Joint Committee on Cancer. Tumor differentiation and surgical margin positivity rates were also compared. We compared the malignant lymph node count to the total harvested lymph node count and defined it as the malignant lymph node ratio.

2.4. Statistical analysis

Descriptive statistics were employed to summarize baseline characteristics, including demographic and preoperative data. Continuous variables such as age and operation duration were presented as mean ± standard deviation or median (min–max). Categorical variables, such as sex, presence of comorbidities, and complication rates, were expressed as frequencies (n) and percentages (%). The Shapiro–Wilk test was used to assess the normality of the data distribution for continuous variables.

Univariate analyses were performed to identify significant associations between preoperative nutritional status (malnourished vs nonmalnourished) and postoperative outcomes such as complications, mortality, and length of hospital stay (LOS). Independent t-tests or Mann–Whitney *U* tests were used to compare continuous variables between malnourished and nonmalnourished groups. Chi-square tests or Fisher exact tests were used to compare categorical variables.

A multivariate logistic regression analysis was performed to control for potential confounding factors and identify independent predictors of postoperative major complications and mortality. Predictor variables that were significant in the univariate analysis ($P < .10$) were included in the multivariate model. These included ASA score, total bilirubin levels, transfusion requirements, operation duration. The results were reported as OR with 95% CI. A *P*-value < .05 was considered statistically significant.

All statistical analyses were conducted using IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk). A 2-tailed *P*-value of <.05 was considered statistically significant for all analyses.

2.5. Institutional review board approval

Ethics Committee approval was obtained from the Başkent University Institutional Review Board (Project Approval Number: KA23/156) on April 20, 2023. Informed consent was obtained from the patients or their first-degree relatives for inclusion in the study and the use of their data anonymously in this retrospective study. Prior to the study, each participant was provided with detailed information regarding the surgical procedure, associated risks, potential complications, expected benefits, and estimated mortality rates. In addition, they were informed about the use of their anonymized medical data in medical research, and written informed consent was obtained before the surgeries were performed.

3. Results

3.1. General outcomes

Table 1 outlines the baseline characteristics of the patients. The mean age was 68.9 ± 11.2. There were 20 females (40%) and 30 males (60%). The mean age was comparable between the malnourished and nonmalnourished groups (68.9 ± 13.3 years vs 69 ± 9.3 years, $P = .978$). Males represented 26.1% of the malnourished group compared to 51.9% in the nonmalnourished group ($P = .086$). Other comorbidities such as diabetes mellitus, cardiovascular disease, and chronic kidney failure were distributed similarly across the groups.

3.2. Postoperative outcomes

As seen in Table 2, the median operation duration did not differ significantly between the 2 groups (490 minutes vs 470 minutes, $P = .853$). The mean CD score was higher in the malnourished group ($P = .001$). Furthermore, malnourished patients experienced a significantly higher rate of major complications (73.9%) compared to the nonmalnourished group (14.8%) ($P = .001$). Major complications were categorized according to the CD classification, with malnourished patients more likely to suffer from CD grade ≥ III complications ($P = .001$).

Transfusion requirements were also significantly higher in malnourished patients (4 units vs 2 units, $P = .033$). Postoperative pancreatic fistula (POPF) and DGE were more frequent in the malnourished group ($P = .077$ for POPF and $P = .776$ for DGE).

Six patients (26.1%) in the malnourished group died within 30 days post-surgery, whereas no patients in the nonmalnourished group experienced mortality ($P = .006$) (Table 2). Of the deceased patients, 3 succumbed to intraabdominal sepsis, 2 to cardiac complications, and 1 to pneumonia. The median length of hospital stay was 12 days for both groups, with no significant difference observed ($P = .417$).

3.3. Pathological outcomes

Histopathological evaluations revealed no significant differences between the 2 groups in terms of T stage, nodal status, malignant lymph node ratio, tumor grade, and surgical margin positivity (Table 3).

Given the significant difference in major complication rates between the 2 groups, factors influencing these complications were analyzed (Table 4). Multivariate logistic regression, including age, gender, ASA score, and nutritional status, confirmed malnutrition as an independent predictor of major postoperative complications (OR: 16.3, 95% CI: 3.9–66.8, $P = .001$) (Fig. 5, Table 4).

4. Discussion

The present retrospective study revealed that malnourished patients who underwent pancreaticoduodenectomy due to pancreatic head adenocarcinoma have significantly higher rates of postoperative complications and mortality compared to those with adequate nutritional status. Furthermore, as a result of our logistic regression analysis, we concluded that malnutrition is an independent risk factor for the development of postoperative major complications in this patient group.

The higher incidence of major complications in malnourished patients compared to nonmalnourished patients aligns with numerous studies in the field of pancreatic surgery.[17–19] Zhang and colleagues, from China, enrolled 12,785 patients from the National Database and revealed increased overall complications following PD for pancreatic cancer.18 In particular, the malnourished group had higher DGE, LOS, and infection rates.18 Jin and colleagues, from China, enrolled 511 patients with ampullary carcinoma who underwent PD, and showed that the malnourished group had higher DGE, LOS, overall, and major complication (CD ≥ III) rates.[19] Lee and colleagues, from the USA, enrolled 4216 pancreatic resections with the diagnosis of pancreatic cancer in a propensity score-matched analysis. The malnourished group was shown to have higher complication and mortality rates.[9] The pathophysiological explanation behind this association lies in the impaired immune response and delayed wound healing typically seen in malnourished patients. In the present study, while overall complication rates were higher in our malnourished group, pancreatectomy-specific

Table 1

Demographics and preoperative data of the groups.

	Malnutrition		
	Yes (n = 23.46%)	**No (n = 27.54%)**	***P*-value**
Age (yr, mean, SD)	68.9 (±13.3)	69 (±9.3)	.978
Sex			
Male	6 (26.1%)	14 (51.9%)	.086
Female	17 (73.9%)	13 (48.1%)	
ASA score			
I	1 (4.3%)	0 (0%)	.460
II	12 (52.2%)	17 (63%)	
III	10 (43.5%)	10 (37%)	
Diabetes mellitus (n, %)			
0	10 (43.5%)	15 (56.6%)	.571
1	13 (56.5%)	12 (43.4%)	
Cardiovascular disease (n, %)			
0	11 (47.8%)	14 (51.9%)	1
1	12 (52.2%)	13 (48.1%)	
Hyperlipidemia (n, %)			
0	13 (56.5%)	19 (70.4%)	.382
1	10 (43.5%)	8 (29.6%)	
Smoking (n, %)			
0	15 (65.2%)	16 (59.3%)	.773
1	8 (34.8%)	11 (40.7%)	
Chronic kidney failure (n, %)			
0	22 (95.7%)	25 (92.6%)	1
1	1 (4.3%)	2 (7.4%)	
Acetyl salicylic acid usage (n, %)			
0	10 (43.5%)	12 (43.4%)	1
1	13 (56.5%)	15 (56.6%)	
Hypothyroidism (n, %)			
0	19 (82.6%)	25 (92.6%)	.395
1	4 (17.4%)	2 (7.4%)	
CA19-9 (U/mL)	289 (1–11.110)	231 (1–19.426)	.904
CRP (mg/L)	6 (2–27)	5 (2–24)	.322
Preoperative biliary drainage			
0	15 (65.2%)	17 (63%)	1
1	8 (34.8%)	10 (37%)	
Total bilirubin (mg/dL)	4 (0.5–13)	1.3 (0.4–18)	**.017**

Bold value indicates statistically significant differences ($P < .05$).
ASA = American Society of Anesthesiologists, CA19-9 = carbohydrate antigen 19-9, CRP = C-reactive protein, SD = standard deviation.

complication (POPF, POPH, DGE) rates were similar in both groups. Kim et al have demonstrated that malnourished patients experience higher overall complications and an increased incidence of pancreatic fistula following pancreaticoduodenectomy.[20] Kanda et al also highlighted the importance of lower albumin levels in predicting worse postoperative outcomes for pancreatic cancer.[21] Furthermore, Kanda et al suggested that a low BMI is an independent risk factor for pancreatic fistula in the postoperative period.[21] On the other hand, Aydin et al have demonstrated that the Prognostic Nutritional Index is a risk factor for CR-POPF in patients undergoing PD.[22]

The significant mortality rate observed in the malnourished group compared to the nonmalnourished group highlights the life-threatening impact of malnutrition. This result is consistent with the findings of Lee et al identified malnutrition as an independent predictor of early mortality after pancreatic resection.[9] The reasons for the higher mortality rates include not only the increased likelihood of complications such as sepsis and organ failure but also the reduced physiological reserves needed to withstand the stress of major surgery when the preoperative ASA scores and ages were similar in both groups (Table 1).

Although no significant difference in the length of hospital stay was found between malnourished and nonmalnourished patients in this study, previous studies suggest that malnutrition often leads to prolonged recovery times[9,23] In a large sample-sized study by Zhang and colleagues, malnourished patients undergoing PD had a median hospital stay that was 5.6 days longer than their nonmalnourished counterparts, likely due to higher rates of complications and delayed recovery.[18] This prolonged recovery not only impacts patient outcomes but also increases healthcare costs and the burden on medical resources. The low number of participants in our study seems to be the reason for the inadequacy of showing differences between the groups in terms of LOS.[24]

Several studies emphasize the importance of preoperative and postoperative nutritional interventions in improving surgical outcomes in pancreatic and gastrointestinal cancers. A meta-analysis by Yang et al concluded that preoperative immunonutrition, particularly formulas enriched with arginine, omega-3 fatty acids, and nucleotides, significantly reduced the incidence of postoperative infections in pancreatic surgery.[25] In pancreatic surgery, both preoperative and postoperative nutritional supplementation protocols, including the use of enteral or parenteral nutrition for malnourished patients, have been shown to decrease the rate of infectious complications and LOS in hospitals.[26]

Another important aspect of preoperative nutritional management is the timing and method of nutritional support. ESPEN guidelines recommend that preoperative nutritional supplementation for 5 to 7 days before surgery in malnourished patients results in better postoperative outcomes, including lower rates of infectious complications and shorter hospital stays.[27] Given the significant impact of malnutrition on surgical outcomes, early identification and treatment of at-risk patients should be a priority in preoperative management.

Table 2

Operative data and postoperative complications of the groups.

	Malnutrition		
	Yes (n = 23. 46%)	**No (n = 27.54%)**	***P*-value**
Operation time (min)	490 (330–630)	470 (360–570)	.853
Intraoperative transfusion requirement (n, %)			
0	16 (69.6%)	22 (81.5%)	.508
1	7 (30.4%)	5 (18.5%)	
Intraoperative vascular resection requirement (n, %)			
0	19 (82.6%)	24 (88.9%)	.689
1	4 (17.4%)	3 (11.1%)	
LOS (d)	12 (7–37)	12 (5–26)	.417
Clavien-Dindo (CD) score	3 (0–5)	2 (0–4)	**.001**
Major complication (CD > II) (n, %)			
0	6 (26.1%)	21 (85.2%)	**.001**
1	17 (73.9%)	4 (14.8%)	
Major complication distribution (CD > II) (n, %)			
3	7 (30.4%)	3 (11.1%)	**.002**
4	4 (17.4%)	2 (7.4%)	
5	6 (26.1%)	0 (0%)	
Postoperative transfusion (package)	4 (0–13)	2 (0–6)	**.033**
DGE (n, %)			
0	11 (47.8%)	11 (40.7%)	.776
1	12 (52.2%)	16 (59.3%)	
POPH (n, %)			
0	20 (87%)	27 (100%)	.090
1	3 (13%)	0 (0%)	
POPF (n, %)			
0	18 (78.3%)	14 (51.9%)	.077
1	5 (21.7%)	13 (48.1%)	
CR-POPF (n, %)			
B	2 (8.6%)	5 (18.5%)	.189
C	1 (4.3%)	0 (0%)	
Mortality; 30-d (n, %)	6 (26.1%)	0 (0%)	**.006**

Bold values indicate statistically significant differences ($P < .05$).

CR-POPF = clinically relevant postoperative pancreatic fistula, DGE = delayed gastric emptying, LOS = length of stay, Min = minutes, POPF = postoperative pancreatic fistula, POPH = postoperative pancreatic hemorrhage.

Table 3

Pathological findings of the groups.

	Malnutrition		
	Yes (n = 23.46%)	**No (n = 27.54%)**	***P*-value**
T stage (n, %)			
I	1 (4.3%)	1 (3.7%)	.371
II	8 (34.8%)	13 (48.1)	
III	12 (52.2%)	11 (40.7%)	
IV	2 (8.7%)	2 (7.4%)	
Tumor differentiation			
Well	9 (39.1%)	6 (22.2%)	.390
Moderate	9 (39.1%)	15 (56.5%)	
Poor	5 (21.7%)	6 (22.2%)	
Perineural invasion (n, %)			
0	3 (13%)	1 (3.7%)	.322
1	20 (87%)	26 (96.3%)	
Vascular invasion (n, %)			
0	8 (37.5%)	4 (14.8%)	.183
1	15 (62.5%)	23 (85.2%)	
N Stage (n, %)			
0	9 (39.1%)	3 (11.1%)	.069
I	9 (39.1%)	15 (55.6%)	
II	5 (21.7%)	9 (33.3%)	
Total LN (mean)	20 (13–78)	22 (14–45)	.452
Malignant LN (mean)	1 (0–13)	2 (0–18)	.119
MLNR (mean)	7 (0–40)	10 (0–70)	.346
Surgical margin positivity			
0	20 (87%)	23 (85.2%)	.432
1	3 (13%)	4 (14.8%)	

LN = lymph node, MLNR = malignant lymph node ratio.

Table 4

Univariate analysis and the logistic regression analysis of the factors affecting the postoperative major complications (Clavien-Dindo > II).

	Univariate			Multivariate	
	Major complication				
	Yes (n = 21; 42%)	No (n = 29; 58%)	*P*-value	Odds ratio (95% CI)	*P*-value
Age (yr)	67.6 (±13.4)	69.9 (±9.4)	.460	–	.121
Male (n, %)	15 (71.4%)	15 (51.7%)	.243	–	.319
Malnutrition (n, %)	17 (81.7%)	6 (20.7%)	**.001**	16.3 (3.9–66.8)	**.001**
ASA score					
I	1 (4.8%)	0 (0%)	.122	-	.999
II	9 (42.9%)	20 (69%)		–	
III	11 (52.4%)	9 (31%)		–	
CA19-9 (U/mL)	293 (1–11.110)	185 (1–19.426)	.934	–	–
CRP (mg/L)	6 (2–20)	5 (2–27)	.789	–	–
Diabetes mellitus	13 (61.9%)	12 (41.4%)	.252	–	–
Total bilirubin (mg/dL)	4.2 (0.4–12.5)	1.7 (0.4–21)	.301	–	.936
Operation time (minute)	505 (330–630)	465 (340–570)	.132	–	–
CV disease	10 (47.6%)	15 (51.7%)	1	–	–
Acetyl salicylic acid usage	12 (57.1%)	16 (55.2%)	1	–	–
Preoperative biliary drainage	6 (28.6%)	12 (41.4%)	.388	–	–

Bold values indicate statistically significant differences ($P < .05$).
ASA = American Society of Anesthesiologists, CA19-9 = carbohydrate antigen 19-9, CI = confidence interval, CRP = C-reactive protein, CV = cardiovascular.

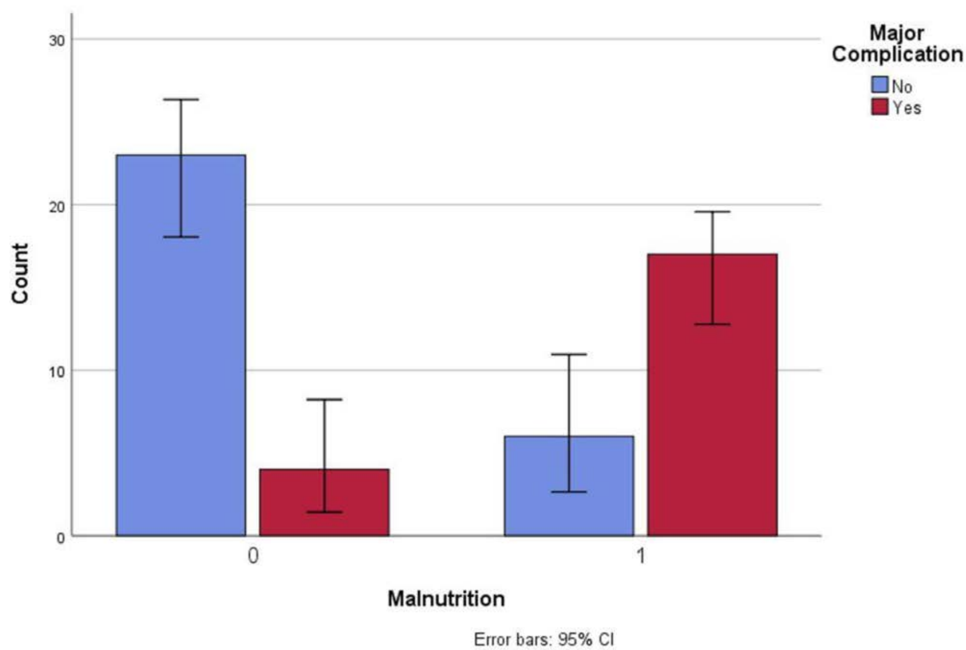

Figure 5. Multivariate logistic regression analysis showing the association of malnutrition with major postoperative complications.

In addition to nutritional support, multimodal prehabilitation programs, which combine nutrition, physical conditioning, and psychological support, have been shown to improve outcomes in patients undergoing major surgery. Bundred and colleagues found that patients who participated in a prehabilitation program had fewer postoperative complications and a faster return to normal function following pancreatic resections for pancreatic cancer.[28] This highlights the need for a comprehensive approach to preoperative care, particularly in high-risk patients such as those with pancreatic cancer.

Moving forward, prospective studies are needed to further explore the optimal nutritional interventions for patients undergoing PD. There is also a need for more research on the role of multimodal prehabilitation in this patient population, including the integration of nutritional, physical, and psychological support. Additionally, personalized nutritional interventions based on specific biomarkers, such as serum albumin and CRP levels, may offer a more tailored approach to improving surgical outcomes in malnourished patients.

Our study has several notable limitations. First and foremost, the fact that it is a retrospective study with data from a single center is the most significant limitation. Within the retrospectively collected data, the absence of information regarding the patient's oral intake restrictions and whether they experienced weight loss before surgery does not diminish the real importance of these parameters. It is clear that more comprehensive nutritional assessments could have been achieved if these parameters had been available. Furthermore, although the similar number of patients in both groups and the fact that all of them were diagnosed with pancreatic ductal adenocarcinoma might seem advantageous, 50 patients are insufficient for evaluating the outcomes of a complex surgical technique like pancreaticoduodenectomy for a critical disease such as pancreatic cancer. We believe that more reliable results could be obtained through prospective, multicenter studies with a larger number of patients.

This study reinforces the critical role of preoperative nutritional status in determining short-term surgical outcomes following pancreaticoduodenectomy for pancreatic cancer. Malnutrition significantly increases the risk of major complications and mortality. Although a gold standard nutritional assessment has not yet been established, the importance of utilizing existing comprehensive methods, especially before pancreaticoduodenectomy for pancreatic ductal adenocarcinoma, and preparing patients for surgery is evident. Early nutritional assessment and meticulous intervention are essential components of preoperative management and should be standard practice for pancreatic cancer patients. Future research should focus on optimizing preoperative nutritional strategies and exploring the benefits of multimodal prehabilitation programs.

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