ORIGINAL ARTICLE

Retrospective Study

Predictive value of preoperative albumin-bilirubin score and other risk factors for short-term outcomes after open pancreatoduodenectomy

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Abstract

BACKGROUND
Pancreatoduodenectomy represents a complex procedure involving extensive organ resection and multiple alimentary reconstructions. It is still associated with high morbidity, even in high-volume centres. Prediction tools including preoperative patient-related factors to preoperatively identify patients at high risk for postoperative complications could enable tailored perioperative management and improve patient outcomes.

AIM
To evaluate the clinical significance of preoperative albumin-bilirubin score and other risk factors in relation to short-term postoperative outcomes in patients after open pancreatoduodenectomy.

METHODS
This retrospective study included all patients who underwent open pancreatic head resection (pylorus-preserving pancreatoduodenectomy or Whipple resection) for various pathologies during a five-year period (2017-2021) in a tertiary care setting at University Medical Centre Ljubljana, Slovenia and

Cattinara Hospital, Trieste, Italy. Short-term postoperative outcomes, namely, postoperative complications, postoperative pancreatic fistula, reoperation, and mortality, were evaluated in association with albumin-bilirubin score and other risk factors. Multiple logistic regression models were built to identify risk factors associated with these short-term postoperative outcomes.

RESULTS
Data from 347 patients were collected. Postoperative complications, major postoperative complications, postoperative pancreatic fistula, reoperation, and mortality were observed in 52.7%, 22.2%, 23.9%, 21.3%, and 5.2% of patients, respectively. There was no statistically significant association between the albumin-bilirubin score and any of these short-term postoperative complications based on univariate analysis. When controlling for other predictor variables in a logistic regression model, soft pancreatic texture was statistically significantly associated with postoperative complications [odds ratio (OR): 2.09; 95% confidence interval (95%CI): 1.19-3.67]; male gender (OR: 2.12; 95%CI: 1.15-3.93), soft pancreatic texture (OR: 3.06; 95%CI: 1.56-5.97), and blood loss (OR: 1.07; 95%CI: 1.00-1.14) were statistically significantly associated with major postoperative complications; soft pancreatic texture was statistically significantly associated with the development of postoperative pancreatic fistula (OR: 5.11; 95%CI: 2.38-10.95); male gender (OR: 1.97; 95%CI: 1.01-3.83), soft pancreatic texture (OR: 2.95; 95%CI: 1.42-6.11), blood loss (OR: 1.08; 95%CI: 1.01-1.16), and resection due to duodenal carcinoma (OR: 6.58; 95%CI: 1.20-36.15) were statistically significantly associated with reoperation.

CONCLUSION
The albumin-bilirubin score failed to predict short-term postoperative outcomes in patients undergoing pancreatoduodenectomy. However, other risk factors seem to influence postoperative outcomes, including male sex, soft pancreatic texture, blood loss, and resection due to duodenal carcinoma.

Key Words: Pancreatoduodenectomy; Albumin; Bilirubin; Postoperative complications; Pancreatic fistula; Perioperative care

Core Tip: Pancreatoduodenectomy remains a challenging procedure with substantial potential for morbidity and mortality. Prognostic tools to preoperatively identify patients at high risk for postoperative complications could help tailor their perioperative management and optimize treatment outcomes. Due to its objectivity and simplicity being based on routine laboratory parameters, the albumin-bilirubin score can readily be implicated in clinical routine. We evaluated the clinical significance of preoperative albumin-bilirubin score in patients undergoing pancreatoduodenectomy in relation to short-term postoperative outcomes, namely, postoperative complications, pancreatic fistula, reoperation, and mortality. Additionally, other potential risk factors were assessed as well. In case of their recognition, the operating surgeon may opt for alternative management options to avoid unfavourable postoperative outcomes.

INTRODUCTION

Pancreatoduodenectomy is a standard surgical procedure for the treatment of benign and malignant lesions in the pancreatic head and periampullary region. It represents an important challenge for pancreatic surgeons due to its complexity involving extensive organ resection and multiple alimentary reconstructions[1]. Although perioperative mortality has decreased significantly over the years, the procedure is still associated with high morbidity, even in high-volume centres[1,2].

Various modalities, such as modification of anastomotic techniques, placement of pancreatic duct stents, and prophylactic use of somatostatin analogues, have been implemented to improve postoperative outcomes after pancreatoduodenectomy[3,4]. Still, postoperative course can be marked by several life-threatening complications which remain a major clinical problem, with postoperative pancreatic fistula (POPF) representing the main determinant of morbidity and mortality[2,5]. Understanding and recognition of potential complications are imperative to taking proper care of these complex patients. Therefore, prediction tools including preoperative patient-related factors could facilitate preoperative preparation and further optimize their management.

The albumin-bilirubin (ALBI) score was initially developed to assess the underlying liver (dys)function in patients with hepatocellular carcinoma and its impact on survival, demonstrating an even better predictive ability for long-term

survival than the conventional Child-Pugh score[6,7]. It offers a simple and entirely objective method containing only two variables, namely, serum bilirubin and albumin concentrations. In patients undergoing pancreatoduodenectomy, bilirubin levels reflect biliary stricture resulting from the tumour expansion with hyperbilirubinemia leading to abnormal liver function with consequent coagulopathy and decreased ability of albumin synthesis[8,9]. Therefore, surgery in patients with severe obstructive jaundice carries an increased risk of postoperative complications[10,11]. Furthermore, pancreatic exocrine insufficiency is a common condition in patients with tumour involving the pancreatic head[12]. It results in maldigestion and malabsorption of nutrients, thus contributing to malnutrition in these patients which is reflected by albumin levels[13]. Impaired nutritional status plays an important role in postoperative complications as it has been recognized to lead to protracted wound healing and increased susceptibility to infection[14,15]. Given all this, the ALBI score could be a useful tool to preoperatively identify patients at high risk for postoperative complications after pancreatoduodenectomy and could help tailor their perioperative management.

The aim of the present study was to evaluate the clinical significance of preoperative ALBI score in a cohort of patients undergoing pancreatoduodenectomy in relation to short-term postoperative outcomes, namely, postoperative complications, POPF, reoperation, and mortality. Additionally, we aimed to identify other risk factors associated with an increased risk for these adverse short-term postoperative outcomes.

MATERIALS AND METHODS

This retrospective study included all patients who underwent open pancreatic head resection (pylorus-preserving pancreatoduodenectomy or Whipple resection) for various pathologies during a five-year period (2017-2021) at the Department of Abdominal Surgery, University Medical Centre Ljubljana, Slovenia and the Department of General Surgery, Cattinara Hospital, Trieste, Italy. Patients' demographic data, preoperative laboratory results, intraoperative findings, and surgical outcomes were collected from electronic patient records. Short-term postoperative outcomes were evaluated in association with ALBI score and other risk factors. The study was performed in accordance with the Declaration of Helsinki.

Baseline characteristics
Preoperative clinical data included patient demographics, body mass index (BMI), American Society of Anesthesiologists (ASA) score, and preoperative levels of serum bilirubin and albumin. Preoperative blood tests were performed one day prior to the operation. ALBI score was calculated as follows: ALBI score = [$\log_{10}$ bilirubin (μmol/L) × 0.66] + [albumin (g/L) × -0.0852]. The ALBI score was assigned as grade 1 (ALBI score ≤ -2.60), grade 2 (-2.60 < ALBI score ≤ -1.39), and grade 3 (-1.39 < ALBI score), as proposed previously[6].

Operative technique
Either a classical Whipple or a pylorus-preserving pancreatoduodenectomy was performed depending on whether an oncological clearance could be achieved. All operations were carried out using an open approach and were performed by surgeons experienced in pancreatic surgery. The pancreatic texture was classified as either soft or hard based on the impression of the operating surgeon during surgery. Pancreatic duct size was retrieved from the operative record as measured by the operating surgeon during surgery. For reconstruction of the pancreatic remnant to the gastrointestinal tract, a duct-to-mucosa pancreaticojejunostomy, invaginating pancreaticojejunostomy, or pancreaticogastrostomy was performed. The final pathology was determined from histopathologic reports of the resected specimen.

Postoperative outcomes
In the postoperative period, all patients were treated according to a standardized postoperative protocol for pancreatic resections. Somatostatin or somatostatin analogues were administered at the operating surgeon's discretion. The drain fluid was checked for amylase content routinely on postoperative days 3 and 5. POPF was defined and graded according to the 2016 International Study Group for Pancreatic Surgery as any drain amylase value more than 3 times the upper limit of normal amylase level on or after postoperative day 3 associated with a clinically relevant change in management [5]. Therefore, POPF grades B and C were defined as clinically relevant and were included as the outcomes in the analysis. Postoperative complications within 90 d after the operation or during the overall hospital stay following pancreatoduodenectomy were recorded and graded according to the Clavien-Dindo classification[16]. Those with a Clavien-Dindo score of IIIb and higher were regarded as major complications. Mortality was defined as death within 90 d after the operation or death occurring during the overall hospital stay following pancreatoduodenectomy.

Statistical analysis
Categorical variables are presented as frequencies and percentages; continuous variables are expressed as median and interquartile ranges (IQR) as none of the continuous variables is normally distributed.

Association between the ALBI score as well as other risk factors and short-term postoperative outcomes (postoperative complications, POPF, reoperation, or death) was assessed by univariate logistic regression or likelihood ratio test, as appropriate. Multiple logistic regression models were built to identify risk factors associated with postoperative complications, POPF, and reoperation. About ten events per variable[17] rule of thumb was taken into consideration when deciding on the number of independent variables in the multiple logistic regression model. For this reason, no multiple regression model was built for the outcome of death. Only patients having no missing data on any of the predictor or outcome variables were included in the multiple regression analysis. Patients with complete data did not differ from

patients with missing data in POPF (P = 0.581), reoperation (P = 0.159), postoperative complications (P = 0.421), pathology in the pancreas (P = 0.324) or duodenum (P = 0.470), ASA score above 2 (P = 0.647), type of operation (P = 0.934), soft pancreatic texture (P = 0.476), gender (P = 0.799), BMI (P = 0.696), ALBI score (P = 0.727), age (P = 0.475), or blood loss (P = 0.334). The comparisons were done by chi-square test and Mann-Whitney U test.

Multiple linear regression model was used to investigate the relationship between risk factors and length of hospitalization. As distribution of the length of the hospitalization was highly positively skewed, the variable was logarithmized prior to the analysis. There was no multicollinearity (the highest variance inflation factor equalled 2.8). Also, residuals were approximately normally distributed and there was no heteroscedasticity (both examined graphically).

A two-sided P value < 0.05 was considered statistically significant. All statistical analyses were performed using the IBM Statistical Package for Social Sciences for Windows, version 28.0 (SPSS Inc., IBM Corporation, Armonk, NY, United States).

RESULTS

Patient characteristics
Data from 347 patients were collected. Patient characteristics are summarized in Table 1. Median patient age was 69 years (IQR: 61-76 years) and more than half of patients were male (55.6%). Median BMI was 25.2 kg/m^2 (IQR: 22.5-28.4 kg/m^2). More than half of patients had an ASA score of 3 (56.8%). Among 344 patients in whom an ALBI score was calculated, it was found that 50.3%, 42.4%, and 7.3% of patients corresponded to the ALBI grades of 1, 2, and 3, respectively.

Approximately half of patients underwent surgery due to pancreatic carcinoma (49%), while a smaller subset of patients had surgery due to ampullary carcinoma (13.6%), bile duct carcinoma (10.4%), neuroendocrine tumour (7.8%), IPMN (4.6%), and duodenal carcinoma (2.6%). Other indications accounted for 12.4% of operations. Altogether, in the majority (83%) of patients, the underlying pathology was a malignant tumour.

Pancreatic texture was classified as soft by the operating surgeon in more than half of cases (53.4%). Median size of the main pancreatic duct was 3 mm (IQR: 3-5 mm). Duct-to-mucosa pancreaticojejunostomy was created in most cases (69.5%). Median intraoperative blood loss was 400 mL (IQR: 300-563 mL).

Postoperative complications
Postoperative complications and major postoperative complications were observed in 52.7% and 22.2% of patients, respectively. Results of the univariate analysis indicated that the ALBI score was not statistically significantly associated with postoperative complications [odd ratio (OR): 1.14; 95% confidence interval (95%CI): 0.84-1.56], nor major postoperative complications (OR: 1.26; 95%CI: 0.89-1.78) (Tables 2 and 3). Postoperative complications were associated with five risk factors: Male gender (OR: 1.62; 95%CI: 1.05-2.48), BMI (OR: 1.06; 95%CI: 1.01-1.12), higher ASA score (P = 0.019), soft pancreatic texture (OR: 2.47; 95%CI: 1.56-3.91), and resection due to pancreatic carcinoma which was associated with a lower odds of developing postoperative complications (OR: 0.50; 95%CI: 0.33-0.77) (Table 2). The development of major postoperative complications was associated with seven risk factors: Male gender (OR: 1.85; 95%CI: 1.13-3.02), BMI (OR: 1.07; 95%CI: 1.02-1.13), ASA score 4 compared to ASA score 1 (OR: 27.00; 95%CI: 1.26-578.40), soft pancreatic texture (OR: 3.09; 95%CI: 1.79-5.34), blood loss (OR: 1.08; 95%CI: 1.02-1.14), and resection due to duodenal carcinoma (OR: 9.94; 95%CI: 2.03-48.77) and pancreatic carcinoma (OR: 0.48; 95%CI: 0.29-0.77) which was associated with a lower odds of developing major postoperative complications (Table 3).

Pancreatic fistula
A total of 23.9% of patients developed clinically relevant POPF; however, the ALBI score was not associated with the development of clinically relevant POPF (OR: 1.13; 95%CI: 0.78-1.62). Factors such as BMI (OR: 1.08; 95%CI: 1.02-1.15), soft pancreatic texture (OR: 5.77; 95%CI: 3.00-11.08), and resection due to bile duct carcinoma (OR: 2.91; 95%CI: 1.43-5.93) and duodenal carcinoma (OR: 6.78; 95%CI: 1.66-27.74) were associated with a higher odds of POPF while resection due to pancreatic carcinoma was associated with a lower odds of developing clinically relevant POPF (OR: 0.38; 95%CI: 0.23-0.64) (Table 4).

Reoperation
Reoperation was required in 21.3% of patients. Univariate analysis indicated that the ALBI score was not statistically significantly associated with reoperation (OR: 1.27; 95%CI: 0.87-1.85). Factors such as male gender (OR: 1.89; 95%CI: 1.10-3.26), BMI (OR: 1.07; 95%CI: 1.01-1.14), ASA score 4 compared to ASA score 1 (OR: 27.00; 95%CI: 1.26-578.35), soft pancreatic texture (OR: 3.25; 95%CI: 1.77-5.96), blood loss (OR: 1.07; 95%CI: 1.02-1.13), and resection due to duodenal carcinoma (OR: 7.94; 95%CI: 1.94-32.57) were associated with an increased odds for reoperation. Again, pancreatic carcinoma was associated with a lower odds for reoperation (OR: 0.49; 95%CI: 0.28-0.83) (Table 5).

Postoperative mortality
Mortality rate was 5.2%. The ALBI score was not statistically significantly associated with postoperative mortality (OR: 1.18; 95%CI: 0.59-2.34). Factors such as age (OR: 1.07; 95%CI: 1.01-1.14) and blood loss (OR: 1.07; 95%CI: 1.02-1.13) were statistically significantly associated with postoperative mortality (Table 6).

Table 1 Patient characteristics, *n* (%)	
Patient characteristic	***n* = 347**
Male gender	193 (55.6)
Age (yr), median (IQR)	69 (61-76)
BMI, median (IQR)	25.2 (22.5-28.4)
Bilirubin (μmol/L), median (IQR)	21 (10-84)
Albumin (g/L), median (IQR)	41 (38-44)
ALBI score, median (IQR)	-2.6 (-3.0 to -2.0)
ALBI grade	
1	173 (50.3)
2	146 (42.4)
3	25 (7.3)
ASA score	
1	10 (2.9)
2	136 (39.2)
3	197 (56.8)
4	4 (1.2)
Operation type	
PPPD	175 (50.4)
Whipple	172 (49.6)
Pathology	
Pancreatic carcinoma	170 (49.0)
Bile duct carcinoma	36 (10.4)
Duodenal carcinoma	9 (2.6)
Ampullary carcinoma	46 (13.6)
NET	27 (7.8)
IPMN	16 (4.6)
Other	43 (12.4)
Soft pancreatic texture, *n* (%) (*n* = 307)	164 (53.4)
Duct diameter (mm), median (IQR)	3 (3-5)
Anastomosis type	
PJA duct to mucosa	241 (69.5)
PJA invagination	94 (27.1)
PGA	12 (3.5)
Blood loss (ml), median (IQR)	400 (300-563)
Somatostatin use	185 (53.3)
Length of hospitalization (d), median (IQR)	14 (10-23)
Clavien-Dindo	
0	164 (47.3)
I	9 (2.6)
II	79 (22.8)
IIIa	18 (5.2)
IIIb	32 (9.2)

IV	27 (7.8)
V	18 (5.2)
Main reason of postoperative complications	
No complications	164 (47.3)
Pancreatic fistula	66 (19.0)
Haemorrhage	20 (5.8)
Biliary fistula	13 (3.7)
Abscess	38 (11.0)
Other	52 (15.0)
Pancreatic fistula	
0 and BL	264 (76.1)
B and C	83 (23.9)
Reoperation	74 (21.3)
Death	18 (5.2)

IQR: Interquartile range; BMI: Body mass index; ALBI: Albumin-bilirubin; ASA score: American Society of Anesthesiologists score; PPPD: Pylorus-preserving pancreatoduodenectomy; NET: Neuroendocrine tumour; IPMN: Intraductal papillary mucinous neoplasm; PJA: Pancreatico-jejunal anastomosis; PGA: Pancreatico-gastric anastomosis; BL: Biochemical leak.

Table 2 Factors associated with postoperative complications (univariate logistic regression), *n* **(%)**

	No postoperative complications (*n* = 164)	Postoperative complications (*n* = 183)	OR (95%CI)	*P* value
Male gender	81 (49.4)	112 (61.2)	1.62 (1.05-2.48)	0.027
Age (yr), median (IQR)	67 (60.5-74.5)	69 (63-76)	1.01 (0.99-1.03)	0.383
BMI, median (IQR)	24.6 (22.0-27.8)	25.4 (22.8-29.0)	1.06 (1.01-1.12)	0.014
ASA score				0.019[1]
1	8 (4.9)	2 (1.1)		
2	66 (40.2)	70 (38.3)		
3	90 (54.9)	107 (58.5)		
4	0 (0)	4 (2.2)		
ALBI score	-2.6 (-3.0 to -2.1)	-2.6 (-3.0 to -1.9)	1.14 (0.84-1.56)	0.404
Operation type				
PPPD	88 (53.7)	87 (47.5)	1	
Whipple	76 (46.3)	96 (52.5)	1.28 (0.84-1.95)	0.255
Somatostatin use	82 (50)	103 (56.3)	1.29 (0.84-1.97)	0.242
Soft pancreatic texture	60 (41.7)	104 (63.8)	2.47 (1.56-3.91)	< 0.001
Blood loss (mL), median (IQR)	400 (250-500)	400 (300-600)	1.05 (0.99-1.10)	0.088
Pathology				
Pancreatic carcinoma	95 (57.9)	75 (41.0)	0.50 (0.33-0.77)	0.002
Bile duct carcinoma	12 (7.3)	24 (13.1)	1.91 (0.92-3.96)	0.081
Duodenal carcinoma	1 (0.6)	8 (4.4)	7.45 (0.92-60.23)	0.060
Ampullary carcinoma	21 (12.8)	25 (13.7)	1.08 (0.58-2.01)	0.814
NET	12 (7.3)	15 (8.2)	1.13 (0.51-2.49)	0.760
IPMN	8 (4.9)	8 (4.4)	0.89 (0.33-2.43)	0.822

OR: Odds ratio; IQR: Interquartile range; BMI: Body mass index; ALBI: Albumin-bilirubin; ASA score: American Society of Anesthesiologists score; PPPD: Pylorus-preserving pancreatoduodenectomy; NET: Neuroendocrine tumour; IPMN: Intraductal papillary mucinous neoplasm.

Table 3 Factors associated with major postoperative complications (univariate logistic regression), *n* (%)			
	No or minor postoperative complications (*n* = 252)	Major postoperative complications (*n* = 95)	OR (95%CI)	*P* value
Male gender	130 (51.6)	63 (66.3)	1.85 (1.13-3.02)	0.014
Age (yr), median (IQR)	68 (61-76)	69 (63-76)	1 (0.98-1.03)	0.698
BMI, median (IQR)	24.8 (22.3-27.9)	26.6 (23.1-29.8)	1.07 (1.02-1.13)	0.012
ASA score				
1	9 (3.6)	1 (1.1)	1	
2	98 (38.9)	38 (40)	3.49 (0.43-28.49)	0.243
3	144 (57.1)	53 (55.8)	3.31 (0.41-26.78)	0.261
4	1 (0.4)	3 (3.2)	27 (1.26-578.35)	0.035
ALBI score	-2.6 (-3.0 to -2.0)	-2.6 (-3.0 to -1.9)	1.26 (0.89-1.78)	0.188
Operation type				
PPPD	131 (52)	44 (46.3)	1	
Whipple	121 (48)	51 (53.7)	1.25 (0.78-2.01)	0.347
Somatostatin use	130 (51.6)	55 (57.9)	1.29 (0.80-2.08)	0.294
Soft pancreatic texture	103 (46.2)	61 (72.6)	3.09 (1.79-5.34)	< 0.001
Blood loss (mL), median (IQR)	400 (250-500)	400 (300-700)	1.08 (1.02-1.14)	0.005
Pathology				
Pancreatic carcinoma	136 (54.0)	34 (35.8)	0.48 (0.29-0.77)	0.003
Bile duct carcinoma	22 (8.7)	14 (14.7)	1.81 (0.88-3.70)	0.105
Duodenal carcinoma	2 (0.8)	7 (7.4)	9.94 (2.03-48.77)	0.005
Ampullary carcinoma	36 (14.3)	10 (10.5)	0.71 (0.34-1.49)	0.359
NET	18 (7.1)	9 (9.5)	1.36 (0.59-3.14)	0.471
IPMN	11 (4.4)	5 (5.3)	1.22 (0.41-3.60)	0.722

OR: Odds ratio; IQR: Interquartile range; BMI: Body mass index; ALBI: Albumin-bilirubin; ASA score: American Society of Anesthesiologists score; PPPD: Pylorus-preserving pancreatoduodenectomy; NET: Neuroendocrine tumour; IPMN: Intraductal papillary mucinous neoplasm.

Length of hospitalization

Median length of hospitalization was 14 d (IQR: 10-23). The ALBI score was statistically significantly associated with the length of hospitalization with an increase of 13% for each increase in the ALBI score. Among other factors, BMI was associated with a 2% increase in the hospitalization length. Furthermore, pathology for which pancreatoduodenectomy was undertaken significantly affected the length of hospitalization with a 99% increase in case of duodenal carcinoma, 33% decrease in case of ampullary carcinoma, 36% decrease in case of pancreatic carcinoma, and 41% decrease in case of IPMN (Table 7).

Multiple logistic regression model

When controlling for other predictor variables in the logistic regression model, there was no statistically significant association between the ALBI score and postoperative complications, major postoperative complications, POPF, or reoperation (Table 8). Soft pancreatic texture was statistically significantly associated with postoperative complications (OR: 2.09; 95%CI: 1.19-3.67). Male gender (OR: 2.12; 95%CI: 1.15-3.93), soft pancreatic texture (OR: 3.06; 95%CI: 1.56-5.97), and blood loss (OR: 1.07; 95%CI: 1.00-1.14) were statistically significant predictors of major postoperative complications. Soft pancreatic texture was statistically significantly associated with the development of POPF (OR: 5.11; 95%CI: 2.38-10.95). Male gender (OR: 1.97; 95%CI: 1.01-3.83), soft pancreatic texture (OR: 2.95; 95%CI: 1.42-6.11), blood loss (OR: 1.08;

Table 4 Factors associated with postoperative pancreatic fistula (univariate logistic regression), *n* (%)

	No POPF (*n* = 264)	POPF (*n* = 83)	OR (95%CI)	*P* value
Male gender	140 (53)	53 (63.9)	1.56 (0.94-2.6)	0.085
Age (yr), median (IQR)	68 (61-75.5)	70 (64-76)	1.01 (0.99-1.03)	0.478
BMI, median (IQR)	24.8 (22.2-27.9)	26 (23.5-29.8)	1.08 (1.02-1.15)	0.008
ASA score				
1	9 (3.4)	1 (1.2)	1	
2	101 (38.3)	35 (42.2)	3.12 (0.38-25.51)	0.289
3	152 (57.6)	45 (54.2)	2.66 (0.33-21.6)	0.359
4	2 (0.8)	2 (2.4)	9 (0.52-155.24)	0.130
ALBI score	-2.6 (-3.0 to -2.0)	-2.6 (-3.0 to -1.9)	1.13 (0.78-1.62)	0.520
Operation type				
PPPD	129 (48.9)	46 (55.4)	1	
Whipple	135 (51.1)	37 (44.6)	0.77 (0.47-1.26)	0.298
Somatostatin use	135 (51.1)	50 (60.2)	1.45 (0.88-2.39)	0.148
Soft pancreatic texture	104 (44.4)	60 (82.2)	5.77 (3.00-11.08)	< 0.001
Blood loss (mL), median (IQR)	400 (250-560)	400 (300-600)	1.02 (0.98-1.05)	0.356
Pathology				
Pancreatic carcinoma	144 (54.5)	26 (31.3)	0.38 (0.23-0.64)	< 0.001
Bile duct carcinoma	20 (7.6)	16 (19.3)	2.91 (1.43-5.93)	0.003
Duodenal carcinoma	3 (1.1)	6 (7.2)	6.78 (1.66-27.74)	0.008
Ampullary carcinoma	34 (12.9)	12 (14.5)	1.14 (0.56-2.33)	0.712
NET	20 (7.6)	7 (8.4)	1.12 (0.46-2.76)	0.799
IPMN	11 (4.2)	5 (6.0)	1.47 (0.50-4.37)	0.484

POPF: Postoperative pancreatic fistula; OR: Odds ratio; IQR: Interquartile range; BMI: Body mass index; ALBI: Albumin-bilirubin; ASA score: American Society of Anesthesiologists score; PPPD: Pylorus-preserving pancreatoduodenectomy; NET: Neuroendocrine tumour; IPMN: Intraductal papillary mucinous neoplasm.

95%CI: 1.01-1.16), and resection due to duodenal carcinoma (OR: 6.58; 95%CI: 1.20-36.15) were statistically significantly associated with reoperation.

DISCUSSION

In this retrospective analysis evaluating short-term postoperative outcomes in patients undergoing pancreatoduodenectomy, preoperative ALBI score was not associated with postoperative complications, POPF, reoperation, or mortality.

The ALBI score was first introduced to assess liver function and predict survival in patients with hepatocellular carcinoma[6,18,19]. Its application was later extended to the prediction of survival in patients with non-malignant liver diseases, including chronic hepatitis B and C, primary biliary cholangitis, and autoimmune hepatitis[20]. Apart from liver diseases, several studies demonstrated the prognostic significance of ALBI score in certain cancers other than hepatocellular carcinoma (*e.g.*, gastric cancer[21], intra-[22] and extrahepatic[23] cholangiocarcinoma, pancreatic cancer[24,25], ampullary cancer[26], colon cancer[27], and lung cancer[28]) and non-malignant diseases (heart failure[29,30] and acute pancreatitis[31]).

With respect to its increasing application, the ability of ALBI grading system to identify postoperative morbidity has also been evaluated. Hence, the ALBI grade has been found to be a predictor of postoperative outcome in patients undergoing liver surgery[27,32,33]. In their study including 3064 patients, Andreatos *et al*[32] found higher model for end-stage liver disease (MELD) score and ALBI grade to be independently associated with an increased risk of postoperative complications, major complications, need for perioperative blood transfusion, prolonged length of stay, and 30-d mortality. Additionally, higher ALBI grade but not MELD score was associated with a greater risk of developing postoperative liver failure, its severity, and the development of a bile leak[32]. Another study assessed the potential of preoperative aspartate aminotransferase-to platelet ratio index (APRI) and ALBI score to predict postoperative morbidity,

Table 5 Factors associated with reoperation (univariate logistic regression), *n* **(%)**

	No reoperation (*n* = 273)	Reoperation (*n* = 74)	OR (95%CI)	*P* value
Male gender	143 (52.4)	50 (67.6)	1.89 (1.10-3.26)	0.021
Age (yr), median (IQR)	68 (61-75)	70.5 (63-76)	1.02 (0.99-1.04)	0.192
BMI, median (IQR)	24.9 (22.4-27.9)	26.1 (22.8-30.1)	1.07 (1.01-1.14)	0.018
ASA score				
1	9 (3.3)	1 (1.4)	1	
2	108 (39.6)	28 (37.8)	2.33 (0.28-19.2)	0.431
3	155 (56.8)	42 (56.8)	2.44 (0.30-19.79)	0.404
4	1 (0.4)	3 (4.1)	27 (1.26-578.35)	0.035
ALBI score	-2.6 (-3.0 to -2.0)	-2.7 (-3.0 to -1.7)	1.27 (0.87-1.85)	0.211
Operation type				
PPPD	144 (52.7)	31 (41.9)	1	
Whipple	129 (47.3)	43 (58.1)	1.55 (0.92-2.60)	0.099
Somatostatin use	142 (52)	43 (58.1)	1.28 (0.76-2.15)	0.352
Soft pancreatic texture	114 (47.5)	50 (74.6)	3.25 (1.77-5.96)	< 0.001
Blood loss (mL), median (IQR)	400 (250-500)	400 (300-800)	1.07 (1.02-1.13)	0.007
Pathology				
Pancreatic carcinoma	144 (52.7)	26 (35.1)	0.49 (0.28-0.83)	0.008
Bile duct carcinoma	28 (10.3)	8 (10.8)	1.06 (0.46-2.44)	0.890
Duodenal carcinoma	3 (1.1)	6 (8.1)	7.94 (1.94-32.57)	0.004
Ampullary carcinoma	36 (13.2)	10 (13.5)	1.03 (0.48-2.18)	0.941
NET	20 (7.3)	7 (9.5)	1.32 (0.54-3.26)	0.544
IPMN	11 (4.0)	5 (6.8)	1.73 (0.58-5.13)	0.326

OR: Odds ratio; IQR: Interquartile range; BMI: Body mass index; ALBI: Albumin-bilirubin; ASA score: American Society of Anesthesiologists score; PPPD: Pylorus-preserving pancreatoduodenectomy; NET: Neuroendocrine tumour; IPMN: Intraductal papillary mucinous neoplasm.

liver dysfunction, and mortality in patients with colorectal cancer liver metastases undergoing liver resection after completion of neoadjuvant chemotherapy[27]. Patients with postoperative morbidity had higher preoperative levels of ALBI score but not APRI. Higher preoperative values of both were observed in patients who experienced postoperative liver dysfunction and patients who died. Combined score of APRI and ALBI was found to improve the predictive potential compared with both scores assessed individually and was found to identify patients at risk for prolonged hospital stay, prolonged intensive care unit stay, morbidity, liver dysfunction, and mortality[27]. Similarly, preoperative ALBI grade proved to be associated with postoperative complication and severe (Clavien-Dindo grade ≥ III) complication rates in patients with advanced gastric cancer who underwent radical resection[34]. This was evident especially in case of surgical complications as the difference in medical complication rates between the two groups did not reach statistical significance. Patients in high ALBI grade group also had significantly longer postoperative hospital stay and increased hospitalization costs. Importantly, in this study, the optimal cut-off value to determine ALBI high and ALBI low grade groups was set at -2.34 to provide an effective preoperative assessment tool for clinicians[34].

In contrast, ALBI grade was unable to predict postoperative complications in a retrospective analysis of patients undergoing pancreatic resection due to pancreatic cancer[25]. In this study, high ALBI grade correlated with a lower frequency of morbidity. High ALBI grade was also associated with high CA 19-9 levels, venous resection, lymph node metastasis, and involvement of paraaortic lymph nodes, indicating tumour progression. The authors explained these contradictory results by the fact that hardening of the pancreatic texture induced by tumour progression is inversely correlated to the occurrence of POPF, and that both pancreatoduodenectomies as well as distal pancreatectomies were included in the analysis with their different rates of invasiveness and associated morbidity. Moreover, in a recent retrospective cohort study conducted by Fernandez-Placencia *et al*[26] to determine preoperative factors related to 90-d severe morbidity and mortality after pancreatoduodenectomy in patients with adenocarcinoma of the ampulla of Vater, ALBI grade 3 was an independent predictor of 90-d mortality but not of severe morbidity.

In line with these findings, the ALBI score did not prove to be associated with postoperative morbidity or mortality in the current study. This might be due to low number of patients with severe hyperbilirubinemia or decreased albumin

Table 6 Factors associated with postoperative mortality (univariate logistic regression), *n* (%)

	Survived (*n* = 329)	Died (*n* = 18)	OR (95%CI)	*P* value
Male gender	182 (55.3)	11 (61.1)	1.27 (0.48-3.36)	0.631
Age (yr), median (IQR)	68 (61-75)	75.5 (69-82)	1.07 (1.01-1.14)	0.015
BMI, median (IQR)	25 (22.5-28.4)	27.7 (24.9-29.7)	1.07 (0.96-1.19)	0.223
ASA score				0.520[1]
1	10 (3)	0 (0)		
2	129 (39.2)	7 (38.9)		
3	188 (57.1)	9 (50.0)		
4	2 (0.6)	2 (11.1)		
ALBI score	-2.6 (-3.0 to -2.0)	-2.8 (-3.1 to -1.8)	1.18 (0.59-2.34)	0.639
Operation type				
PPPD	168 (51.1)	7 (38.9)	1	
Whipple	161 (48.9)	11 (61.1)	1.64 (0.62-4.33)	0.319
Somatostatin use	178 (54.1)	7 (38.9)	0.54 (0.20-1.43)	0.214
Soft pancreatic texture	152 (52.2)	12 (75.0)	2.74 (0.86-8.71)	0.087
Blood loss (mL), median (IQR)	400 (250-500)	600 (400-1000)	1.07 (1.02-1.13)	0.007
Pathology				
Pancreatic carcinoma	164 (49.8)	6 (33.3)	0.50 (0.18-1.37)	0.180
Bile duct carcinoma	32 (9.7)	4 (22.2)	2.65 (0.82-8.54)	0.102
Duodenal carcinoma	9 (2.7)	0 (0)		0.324*
Ampullary carcinoma	42 (12.8)	4 (22.2)	1.95 (0.61-6.21)	0.257
NET	26 (7.9)	1 (5.6)	0.69 (0.09-5.36)	0.719
IPMN	15 (4.6)	1 (5.6)	1.23 (0.15-9.88)	0.845

[1]Likelihood ratio test.

OR: Odds ratio; IQR: Interquartile range; BMI: Body mass index; ALBI: Albumin-bilirubin; ASA score: American Society of Anesthesiologists score; PPPD: Pylorus-preserving pancreatoduodenectomy; NET: Neuroendocrine tumour; IPMN: Intraductal papillary mucinous neoplasm.

levels. Blood samples were obtained one day prior to the operation as a part of routine testing and most patients had their bilirubin and albumin levels within reference values (median levels of bilirubin and albumin were 21 μmol/L and 41 g/L, respectively). Therefore, only 7.3% of patients corresponded to ALBI grade 3. Also, only ALBI score was included in our analysis since the ALBI score cut-off values to determine different grades have originally been validated for chronic liver disease and do not necessarily represent the optimal cut-off values in the setting of pancreatoduodenectomy. On the other hand, although weak, there seems to be an association of ALBI score with the length of hospital stay observing an increase of 13% for each ALBI score.

Overall incidence of adverse short-term postoperative outcomes in our study were 52.7%, 22.2%, 23.9%, 21.3%, and 5.2% for postoperative complications, major postoperative complications, POPF, reoperation, and death, respectively. Not surprisingly, several factors were associated with the risk, including patient-specific factors such as male sex, BMI, and ASA classification, as well as intraoperative factors such as soft pancreatic texture, resection due to duodenal or pancreatic carcinoma, and blood loss. Pancreatic carcinoma was a protective factor for the development of adverse events as it was associated with a reduced risk of postoperative and major postoperative complications, POPF, and reoperation. On the other hand, duodenal carcinoma posed a significant risk for major postoperative complications, POPF, and reoperation, even showing independent association with the latter on multiple logistic regression analysis. This is in line with previous studies as histopathological diagnosis other than pancreatic adenocarcinoma or chronic pancreatitis is generally associated with less fibrosis and softer pancreatic texture which is a relevant predictor of POPF and associated complications[35-37].

In patients undergoing pancreatoduodenectomy, POPF represents a major source of morbidity and mortality[2,5]. Consequently, there has been a considerable interest in identifying factors associated with a high risk of POPF among patients undergoing pancreatoduodenectomy[35,38,39]. In the current study, we identified a number of variables associated with POPF which were consistent with findings from previous reports[3,35,38]. An increased risk of POPF was observed in patients who were obese, had soft pancreatic texture, or were operated due to bile duct or duodenal

Table 7 Association between risk factors and logarithmized length of hospitalization (multiple linear regression)

	Regression coefficient (SE)	*P* value
(Constant)	2.54 (0.44)	< 0.001
Male gender	0.12 (0.08)	0.129
Age	0 (0)	0.337
BMI	0.02 (0.01)	0.026
ASA 3 *vs* ASA 1 or 2	-0.03 (0.08)	0.755
ASA 4 *vs* ASA 1 or 2	-0.26 (0.55)	0.633
ALBI score	0.12 (0.06)	0.050
PPPD *vs* Whipple	0.12 (0.08)	0.127
Somatostatin use	-0.09 (0.08)	0.228
Soft pancreatic texture	0.08 (0.09)	0.342
Blood loss	0 (0)	0.144
Pathology		
Pancreatic carcinoma	-0.44 (0.12)	< 0.001
Bile duct carcinoma	-0.17 (0.16)	0.280
Duodenal carcinoma	0.69 (0.25)	0.006
Ampullary carcinoma	-0.41 (0.14)	0.004
NET	0.09 (0.18)	0.620
IPMN	-0.54 (0.21)	0.012

SE: Standard error; BMI: Body mass index; ALBI: Albumin-bilirubin; ASA score: American Society of Anesthesiologists score; PPPD: Pylorus-preserving pancreatoduodenectomy; NET: Neuroendocrine tumour; IPMN: Intraductal papillary mucinous neoplasm.

Table 8 Association between risk factors and short-term postoperative outcomes (multiple logistic regression)

	Postoperative complications		Major postoperative complications		POPF		Reoperation	
	OR (95%CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Male gender	1.63 (0.97-2.75)	0.066	2.12 (1.15-3.93)	0.016	1.75 (0.92-3.33)	0.090	1.97 (1.01-3.83)	0.046
Age (yr)	1.01 (0.98-1.04)	0.435	1.01 (0.98-1.04)	0.621	1.02 (0.99-1.06)	0.177	1.02 (0.99-1.05)	0.265
BMI	1.04 (0.98-1.11)	0.161	1.06 (0.98-1.13)	0.124	1.07 (0.99-1.15)	0.090	1.06 (0.98-1.14)	0.160
ASA 3 or 4	0.91 (0.53-1.57)	0.740	0.69 (0.38-1.28)	0.240	0.60 (0.31-1.17)	0.135	0.73 (0.38-1.41)	0.351
ALBI score	1.22 (0.82-1.82)	0.323	1.30 (0.83-2.04)	0.245	1.23 (0.76-1.99)	0.390	1.38 (0.85-2.22)	0.190
Soft pancreatic texture	2.09 (1.19-3.67)	0.011	3.06 (1.56-5.97)	0.001	5.11 (2.38-10.95)	< 0.001	2.95 (1.42-6.11)	0.004
Blood loss	1.03 (0.97-1.09)	0.283	1.07 (1-1.14)	0.045	1.00 (0.96-1.05)	0.908	1.08 (1.01-1.16)	0.022
Pathology								
Pancreatic carcinoma	0.68 (0.38-1.21)	0.187	0.76 (0.39-1.48)	0.417	0.77 (0.37-1.59)	0.477	0.70 (0.34-1.46)	0.345
Duodenal carcinoma	3.32 (0.39-28.63)	0.274	5.06 (0.93-27.66)	0.061	2.99 (0.64-13.95)	0.164	6.58 (1.2-36.15)	0.030

POPF: Postoperative pancreatic fistula; OR: Odds ratio; BMI: Body mass index; ALBI: Albumin-bilirubin; ASA score: American Society of Anesthesiologists score.

carcinoma. Specifically, patients with a soft pancreatic texture demonstrated a five times greater odds of developing POPF. The recognition of these factors is important as in case of their presence, the operating surgeon may opt for other possible management options, including a variety of anastomotic techniques with insertion of a prophylactic pancreatic duct stent or total pancreatectomy as an alternative strategy to avoid the occurrence of POPF.

Our study has certain limitations starting with the retrospective nature being subject to selection bias and confounders. Second, the optimal cut-off values for assessment of ALBI grades in the setting of pancreatoduodenectomy were not determined and remain to be investigated prospectively in a wider patient population to ensure optimal sensitivity and specificity.

CONCLUSION

Pancreatic resection, especially pancreatoduodenectomy, remains a challenging procedure with substantial potential for morbidity and mortality. Identification of preoperative risk factors might help clinicians to select patients fit for resection and tailor the treatment accordingly. Due to its objectivity and simplicity being based on routine laboratory parameters, the ALBI score can readily be implicated in clinical routine. However, it failed to predict short-term postoperative outcomes in our study. Determination of optimal cut-off values to calculate ALBI grade which could be employed in the setting of pancreatoduodenectomy, prospectively validated in a large cohort of patients, might aid in better risk stratification to anticipate adverse events and improve patient care.

ARTICLE HIGHLIGHTS

Research background

Pancreatoduodenectomy remains associated with high rates of severe morbidity, even in high-volume centres.

Research motivation

Understanding and recognition of possible complications is essential when providing adequate care for patients after pancreatoduodenectomy. Prognostic tools, including preoperatively obtained patient-related factors, could help identify patients at high risk for postoperative complications, tailor their perioperative management accordingly, and ultimately improve treatment outcomes. The predictive and prognostic value of albumin-bilirubin (ALBI) score has been evaluated in several patient cohorts, but not in patients after pancreatoduodenectomy.

Research objectives

Clinical significance of the preoperative ALBI score and other risk factors in relation to short-term postoperative outcomes in patients after pancreatoduodenectomy was evaluated.

Research methods

Electronic data of 347 patients who underwent a pancreatoduodenectomy in a five-year period were retrospectively reviewed. Multiple logistic regression models were built to identify risk factors associated with short-term postoperative outcomes.

Research results

Upon conducting univariate analysis, no statistically significant association was found between the ALBI score and any of the short-term postoperative outcomes. However, when considering other predictor variables in a logistic regression model, certain risk factors exhibited statistically significant association.

Research conclusions

The ALBI score failed to predict short-term postoperative outcomes in our study. Nonetheless, other risk factors, including male sex, soft pancreatic texture, blood loss, and resection due to duodenal carcinoma seem to exert an influence. In case of their recognition, the operating surgeon may consider alternative management options to avoid unfavourable treatment outcomes.

Research perspectives

Only ALBI score was evaluated in our study as current cut-off values to determine ALBI grades have originally been validated for chronic liver disease. The optimal cut-off values in the setting of pancreatoduodenectomy remain to be investigated prospectively in a larger patient cohort to ensure optimal sensitivity and specificity.

FOOTNOTES

Badovinac D, Hadžialjević B, Horvat G, Plevel D, Bogoni S, and Tarchi P contributed to the acquisition, analysis, and interpretation of the data; all authors participated in drafting the manuscript; Tomažič A and de Manzini N critically revised the manuscript for important intellectual content.

Institutional review board statement: Based on local policies, retrospective reviews of existing medical records recorded by the investigator in an anonymous manner are exempt from Institutional Review Board review and do not require its approval.

Informed consent statement: All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

Conflict-of-interest statement: The authors declare no conflicts of interest for this article.

Data sharing statement: No additional data are available.

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