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***Retrospective Study***

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

Zavrtanik H *et al*. ALBI score for short-term postoperative outcome prediction

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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

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**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 = [log10 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/m2 (IQR: 22.5-28.4 kg/m2). 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).

***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; 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, 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 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 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.

**REFERENCES**

1 **Cameron JL**, He J. Two thousand consecutive pancreaticoduodenectomies. *J Am Coll Surg* 2015; **220**: 530-536 [PMID: 25724606 DOI: 10.1016/j.jamcollsurg.2014.12.031]

2 **Smits FJ**, Verweij ME, Daamen LA, van Werkhoven CH, Goense L, Besselink MG, Bonsing BA, Busch OR, van Dam RM, van Eijck CHJ, Festen S, Koerkamp BG, van der Harst E, de Hingh IH, Kazemier G, Klaase JM, van der Kolk M, Liem M, Luyer MDP, Meerdink M, Mieog JSD, Nieuwenhuijs VB, Roos D, Schreinemakers JM, Stommel MW, Wit F, Zonderhuis BM, de Meijer VE, van Santvoort HC, Molenaar IQ; Dutch Pancreatic Cancer Group. Impact of Complications After Pancreatoduodenectomy on Mortality, Organ Failure, Hospital Stay, and Readmission: Analysis of a Nationwide Audit. *Ann Surg* 2022; **275**: e222-e228 [PMID: 32502075 DOI: 10.1097/SLA.0000000000003835]

3 **Pedrazzoli S**. Pancreatoduodenectomy (PD) and postoperative pancreatic fistula (POPF): A systematic review and analysis of the POPF-related mortality rate in 60,739 patients retrieved from the English literature published between 1990 and 2015. *Medicine (Baltimore)* 2017; **96**: e6858 [PMID: 28489778 DOI: 10.1097/MD.0000000000006858]

4 **Shrikhande SV**, Sivasanker M, Vollmer CM, Friess H, Besselink MG, Fingerhut A, Yeo CJ, Fernandez-delCastillo C, Dervenis C, Halloran C, Gouma DJ, Radenkovic D, Asbun HJ, Neoptolemos JP, Izbicki JR, Lillemoe KD, Conlon KC, Fernandez-Cruz L, Montorsi M, Bockhorn M, Adham M, Charnley R, Carter R, Hackert T, Hartwig W, Miao Y, Sarr M, Bassi C, Büchler MW; International Study Group of Pancreatic Surgery (ISGPS). Pancreatic anastomosis after pancreatoduodenectomy: A position statement by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery* 2017; **161**: 1221-1234 [PMID: 28027816 DOI: 10.1016/j.surg.2016.11.021]

5 **Bassi C**, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M, Allen P, Andersson R, Asbun HJ, Besselink MG, Conlon K, Del Chiaro M, Falconi M, Fernandez-Cruz L, Fernandez-Del Castillo C, Fingerhut A, Friess H, Gouma DJ, Hackert T, Izbicki J, Lillemoe KD, Neoptolemos JP, Olah A, Schulick R, Shrikhande SV, Takada T, Takaori K, Traverso W, Vollmer CR, Wolfgang CL, Yeo CJ, Salvia R, Buchler M; International Study Group on Pancreatic Surgery (ISGPS). The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. *Surgery* 2017; **161**: 584-591 [PMID: 28040257 DOI: 10.1016/j.surg.2016.11.014]

6 **Johnson PJ**, Berhane S, Kagebayashi C, Satomura S, Teng M, Reeves HL, O'Beirne J, Fox R, Skowronska A, Palmer D, Yeo W, Mo F, Lai P, Iñarrairaegui M, Chan SL, Sangro B, Miksad R, Tada T, Kumada T, Toyoda H. Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach-the ALBI grade. *J Clin Oncol* 2015; **33**: 550-558 [PMID: 25512453 DOI: 10.1200/JCO.2014.57.9151]

7 **Johnson PJ**, Pinato DJ, Kalyuzhnyy A, Toyoda H. Breaking the Child-Pugh Dogma in Hepatocellular Carcinoma. *J Clin Oncol* 2022; **40**: 2078-2082 [PMID: 35344390 DOI: 10.1200/JCO.21.02373]

8 **Kloek JJ**, Heger M, van der Gaag NA, Beuers U, van Gulik TM, Gouma DJ, Levi M. Effect of preoperative biliary drainage on coagulation and fibrinolysis in severe obstructive cholestasis. *J Clin Gastroenterol* 2010; **44**: 646-652 [PMID: 20142756 DOI: 10.1097/MCG.0b013e3181ce5b36]

9 **Padillo FJ**, Andicoberry B, Pera-Madrazo C, Sitges-Serra A. Anorexia and malnutrition in patients with obstructive jaundice. *Nutrition* 2002; **18**: 987-990 [PMID: 12431722 DOI: 10.1016/s0899-9007(02)00982-6]

10 **Shen Z**, Zhang J, Zhao S, Zhou Y, Wang W, Shen B. Preoperative biliary drainage of severely obstructive jaundiced patients decreases overall postoperative complications after pancreaticoduodenectomy: A retrospective and propensity score-matched analysis. *Pancreatology* 2020; **20**: 529-536 [PMID: 32107192 DOI: 10.1016/j.pan.2020.02.002]

11 **Sandini M**, Honselmann KC, Birnbaum DJ, Gavazzi F, Chirica M, Wellner U, Guilbaud T, Bolm L, Angrisani M, Moutardier V, Cereda M, Girard É, Montorsi M, Keck T, Zerbi A, Gianotti L. Preoperative Biliary Stenting and Major Morbidity After Pancreatoduodenectomy: Does Elapsed Time Matter?: The FRAGERITA Study Group. *Ann Surg* 2018; **268**: 808-814 [PMID: 30303874 DOI: 10.1097/SLA.0000000000002838]

12 **Roeyen G**, Berrevoet F, Borbath I, Geboes K, Peeters M, Topal B, Van Cutsem E, Van Laethem JL. Expert opinion on management of pancreatic exocrine insufficiency in pancreatic cancer. *ESMO Open* 2022; **7**: 100386 [PMID: 35124465 DOI: 10.1016/j.esmoop.2022.100386]

13 **Gilliland TM**, Villafane-Ferriol N, Shah KP, Shah RM, Tran Cao HS, Massarweh NN, Silberfein EJ, Choi EA, Hsu C, McElhany AL, Barakat O, Fisher W, Van Buren G. Nutritional and Metabolic Derangements in Pancreatic Cancer and Pancreatic Resection. *Nutrients* 2017; **9** [PMID: 28272344 DOI: 10.3390/nu9030243]

14 **Garth AK**, Newsome CM, Simmance N, Crowe TC. Nutritional status, nutrition practices and post-operative complications in patients with gastrointestinal cancer. *J Hum Nutr Diet* 2010; **23**: 393-401 [PMID: 20337847 DOI: 10.1111/j.1365-277X.2010.01058.x]

15 **Gao X**, Liu Y, Zhang L, Zhou D, Tian F, Gao T, Tian H, Hu H, Gong F, Guo D, Zhou J, Gu Y, Lian B, Xue Z, Jia Z, Chen Z, Wang Y, Jin G, Wang K, Zhou Y, Chi Q, Yang H, Li M, Yu J, Qin H, Tang Y, Wu X, Li G, Li N, Li J, Pichard C, Wang X. Effect of Early vs Late Supplemental Parenteral Nutrition in Patients Undergoing Abdominal Surgery: A Randomized Clinical Trial. *JAMA Surg* 2022; **157**: 384-393 [PMID: 35293973 DOI: 10.1001/jamasurg.2022.0269]

16 **Clavien PA**, Barkun J, de Oliveira ML, Vauthey JN, Dindo D, Schulick RD, de Santibañes E, Pekolj J, Slankamenac K, Bassi C, Graf R, Vonlanthen R, Padbury R, Cameron JL, Makuuchi M. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg* 2009; **250**: 187-196 [PMID: 19638912 DOI: 10.1097/SLA.0b013e3181b13ca2]

17 **Pavlou M**, Ambler G, Seaman S, De Iorio M, Omar RZ. Review and evaluation of penalised regression methods for risk prediction in low-dimensional data with few events. *Stat Med* 2016; **35**: 1159-1177 [PMID: 26514699 DOI: 10.1002/sim.6782]

18 **Oh IS**, Sinn DH, Kang TW, Lee MW, Kang W, Gwak GY, Paik YH, Choi MS, Lee JH, Koh KC, Paik SW. Liver Function Assessment Using Albumin-Bilirubin Grade for Patients with Very Early-Stage Hepatocellular Carcinoma Treated with Radiofrequency Ablation. *Dig Dis Sci* 2017; **62**: 3235-3242 [PMID: 28983724 DOI: 10.1007/s10620-017-4775-8]

19 **Abdel-Rahman O**. Impact of baseline characteristics on outcomes of advanced HCC patients treated with sorafenib: a secondary analysis of a phase III study. *J Cancer Res Clin Oncol* 2018; **144**: 901-908 [PMID: 29455421 DOI: 10.1007/s00432-018-2610-z]

20 **Toyoda H**, Johnson PJ. The ALBI score: From liver function in patients with HCC to a general measure of liver function. *JHEP Rep* 2022; **4**: 100557 [PMID: 36124124 DOI: 10.1016/j.jhepr.2022.100557]

21 **Kanda M**, Tanaka C, Kobayashi D, Uda H, Inaoka K, Tanaka Y, Hayashi M, Iwata N, Yamada S, Fujii T, Sugimoto H, Murotani K, Fujiwara M, Kodera Y. Preoperative Albumin-Bilirubin Grade Predicts Recurrences After Radical Gastrectomy in Patients with pT2-4 Gastric Cancer. *World J Surg* 2018; **42**: 773-781 [PMID: 28920160 DOI: 10.1007/s00268-017-4234-x]

22 **Tsilimigras DI**, Hyer JM, Moris D, Sahara K, Bagante F, Guglielmi A, Aldrighetti L, Alexandrescu S, Marques HP, Shen F, Koerkamp BG, Endo I, Pawlik TM; other members of the International Intrahepatic Cholangiocarcinoma Study Group. Prognostic utility of albumin-bilirubin grade for short- and long-term outcomes following hepatic resection for intrahepatic cholangiocarcinoma: A multi-institutional analysis of 706 patients. *J Surg Oncol* 2019; **120**: 206-213 [PMID: 31025380 DOI: 10.1002/jso.25486]

23 **Wang Y**, Pang Q, Jin H, Zhou L, Hu X, Qian Z, Man Z, Yang S, Liu H. Albumin-Bilirubin Grade as a Novel Predictor of Survival in Advanced Extrahepatic Cholangiocarcinoma. *Gastroenterol Res Pract* 2018; **2018**: 8902146 [PMID: 30622562 DOI: 10.1155/2018/8902146]

24 **Yagyu T**, Saito H, Sakamoto T, Uchinaka EI, Morimoto M, Amisaki M, Watanabe J, Tokuyasu N, Honjo S, Ashida K, Fujiwara Y. Preoperative Albumin-Bilirubin Grade as a Useful Prognostic Indicator in Patients With Pancreatic Cancer. *Anticancer Res* 2019; **39**: 1441-1446 [PMID: 30842180 DOI: 10.21873/anticanres.13260]

25 **Imamura T**, Okamura Y, Sugiura T, Ito T, Yamamoto Y, Ashida R, Ohgi K, Otsuka S, Uesaka K. Clinical Significance of Preoperative Albumin-Bilirubin Grade in Pancreatic Cancer. *Ann Surg Oncol* 2021; **28**: 6223-6235 [PMID: 33486645 DOI: 10.1245/s10434-021-09593-9]

26 **Fernandez-Placencia R**, Berrospi-Espinoza F, Uribe-Rivera K, Medina-Cana J, Chavez-Passiuri I, Sanchez-Bartra N, Paredes-Galvez K, Luque-Vasquez Vasquez C, Celis-Zapata J, Ruiz-Figueroa E. Preoperative Predictors for 90-Day Mortality after Pancreaticoduodenectomy in Patients with Adenocarcinoma of the Ampulla of Vater: A Single-Centre Retrospective Cohort Study. *Surg Res Pract* 2021; **2021**: 6682935 [PMID: 33728373 DOI: 10.1155/2021/6682935]

27 **Pereyra D**, Rumpf B, Ammann M, Perrodin SF, Tamandl D, Haselmann C, Stift J, Brostjan C, Laengle F, Beldi G, Gruenberger T, Starlinger P. The Combination of APRI and ALBI Facilitates Preoperative Risk Stratification for Patients Undergoing Liver Surgery After Neoadjuvant Chemotherapy. *Ann Surg Oncol* 2019; **26**: 791-799 [PMID: 30617869 DOI: 10.1245/s10434-018-07125-6]

28 **Kinoshita F**, Yamashita T, Oku Y, Kosai K, Ono Y, Wakasu S, Haratake N, Toyokawa G, Takenaka T, Tagawa T, Shimokawa M, Nakashima N, Mori M. Prognostic Impact of Albumin-bilirubin (ALBI) Grade on Non-small Lung Cell Carcinoma: A Propensity-score Matched Analysis. *Anticancer Res* 2021; **41**: 1621-1628 [PMID: 33788758 DOI: 10.21873/anticanres.14924]

29 **Matsue Y**, Kagiyama N, Yamaguchi T, Kuroda S, Okumura T, Kida K, Mizuno A, Oishi S, Inuzuka Y, Akiyama E, Matsukawa R, Kato K, Suzuki S, Naruke T, Yoshioka K, Miyoshi T, Baba Y, Yamamoto M, Mizutani K, Yoshida K, Kitai T. Clinical and Prognostic Values of ALBI Score in Patients With Acute Heart Failure. *Heart Lung Circ* 2020; **29**: 1328-1337 [PMID: 32165085 DOI: 10.1016/j.hlc.2019.12.003]

30 **Luo Y**, Li Z, Liu J, Chong Y, Wu B. Prognostic value of the albumin-bilirubin score in critically ill patients with heart failure. *Ann Palliat Med* 2021; **10**: 12727-12741 [PMID: 35016474 DOI: 10.21037/apm-21-3424]

31 **Shi L**, Zhang D, Zhang J. Albumin-bilirubin score is associated with in-hospital mortality in critically ill patients with acute pancreatitis. *Eur J Gastroenterol Hepatol* 2020; **32**: 963-970 [PMID: 32433423 DOI: 10.1097/MEG.0000000000001753]

32 **Andreatos N**, Amini N, Gani F, Margonis GA, Sasaki K, Thompson VM, Bentrem DJ, Hall BL, Pitt HA, Wilson A, Pawlik TM. Albumin-Bilirubin Score: Predicting Short-Term Outcomes Including Bile Leak and Post-hepatectomy Liver Failure Following Hepatic Resection. *J Gastrointest Surg* 2017; **21**: 238-248 [PMID: 27619809 DOI: 10.1007/s11605-016-3246-4]

33 **Fagenson AM**, Gleeson EM, Pitt HA, Lau KN. Albumin-Bilirubin Score vs Model for End-Stage Liver Disease in Predicting Post-Hepatectomy Outcomes. *J Am Coll Surg* 2020; **230**: 637-645 [PMID: 31954813 DOI: 10.1016/j.jamcollsurg.2019.12.007]

34 **Zhu C**, Wang X, Chen S, Yang X, Sun J, Pan B, Zhang W, Chen X, Huang Y. Efficacy of the Preoperative Albumin-Bilirubin Grade for Predicting Survival and Outcomes of Postoperative Chemotherapy for Advanced Gastric Cancer. *Cancer Manag Res* 2020; **12**: 11921-11932 [PMID: 33244269 DOI: 10.2147/CMAR.S279782]

35 **Callery MP**, Pratt WB, Kent TS, Chaikof EL, Vollmer CM Jr. A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatoduodenectomy. *J Am Coll Surg* 2013; **216**: 1-14 [PMID: 23122535 DOI: 10.1016/j.jamcollsurg.2012.09.002]

36 **Harrell KN**, Jajja MR, Postlewait LM, Memis B, Maithel SK, Sarmiento JM, Adsay NV, Kooby DA. Influence of margin histology on development of pancreatic fistula following pancreatoduodenectomy. *J Surg Res* 2020; **246**: 315-324 [PMID: 29754962 DOI: 10.1016/j.jss.2018.02.052]

37 **Roh YH**, Kang BK, Song SY, Lee CM, Jung YK, Kim M. Preoperative CT anthropometric measurements and pancreatic pathology increase risk for postoperative pancreatic fistula in patients following pancreaticoduodenectomy. *PLoS One* 2020; **15**: e0243515 [PMID: 33270774 DOI: 10.1371/journal.pone.0243515]

38 **Mungroop TH**, van Rijssen LB, van Klaveren D, Smits FJ, van Woerden V, Linnemann RJ, de Pastena M, Klompmaker S, Marchegiani G, Ecker BL, van Dieren S, Bonsing B, Busch OR, van Dam RM, Erdmann J, van Eijck CH, Gerhards MF, van Goor H, van der Harst E, de Hingh IH, de Jong KP, Kazemier G, Luyer M, Shamali A, Barbaro S, Armstrong T, Takhar A, Hamady Z, Klaase J, Lips DJ, Molenaar IQ, Nieuwenhuijs VB, Rupert C, van Santvoort HC, Scheepers JJ, van der Schelling GP, Bassi C, Vollmer CM, Steyerberg EW, Abu Hilal M, Groot Koerkamp B, Besselink MG; Dutch Pancreatic Cancer Group. Alternative Fistula Risk Score for Pancreatoduodenectomy (a-FRS): Design and International External Validation. *Ann Surg* 2019; **269**: 937-943 [PMID: 29240007 DOI: 10.1097/SLA.0000000000002620]

39 **Ryu Y**, Shin SH, Park DJ, Kim N, Heo JS, Choi DW, Han IW. Validation of original and alternative fistula risk scores in postoperative pancreatic fistula. *J Hepatobiliary Pancreat Sci* 2019; **26**: 354-359 [PMID: 31125494 DOI: 10.1002/jhbp.638]

**Footnotes**

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**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--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 |  |  |  | 0.0191 |
| 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--2.1) | -2.6 (-3.0--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 |

1Likelihood 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.

**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--2.0) | -2.6 (-3.0--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.

**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--2.0) | -2.6 (-3.0--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.

**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--2.0) | -2.7 (-3.0--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.

**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 |  |  |  | 0.5201 |
| 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--2.0) | -2.8 (-3.1--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 |

1Likelihood 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.

**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.