DOI: 10.7860/JCDR/2024/72776.20202

Original Article

Surgery Section

Assessment of Risk Factors for Postoperative Mortality Following Pancreaticoduodenectomy Performed for Malignancy: A Cross-sectional Study

SALIH DEMIRELLI[1], MESUT TEZ[2], YUNUS NADI YÜKSEK[3]

ABSTRACT

Introduction: Pancreaticoduodenectomy (PD) has been the primary curative-intent surgical option for resectable periampullary tumours. Despite advancements in relevant surgical techniques, PD-related morbidity and mortality rates continue to remain high. Therefore, the preoperative identification of high-risk patients is vital for tailoring PD approaches to the individual patient.

Aim: To assess early postoperative morbidity and mortality following PD in a tertiary centre in Turkey and identify the associated risk factors.

Materials and Methods: This cross-sectional, single-centre study conducted in the General Surgery Clinics of Ankara Numune Training and Education Hospital in Ankara, Turkey included a population of 64 patients undergoing PD for malignant periampullary tumours between May 2010 and May 2014. Patients' demographic, clinical and intraoperative data were collected. The primary outcome of the study was the 30-day postoperative mortality rate. Pearson's Chi-square, Fisher's-exact and Fisher-Freeman-Halton tests were used to compare differences in categorical variables between the groups.

Results: The study sample consisted of 64 patients with a mean age of 60.1±12.4 years. The 30-day postoperative mortality rate in the sample was 18.75%. Non survivors were significantly older (age >70 years) (p=0.006), had significantly higher American Society of Anaesthesiologists (ASA) physical status classes (>III) (p=0.008), had significantly lower Neutrophil-to-lymphocyte Ratios (NLR) (<2.5) (p<0.001) and had significantly lower serum albumin levels (<3.5 g/dL) (p=0.038) compared to survivors. The rate of patients experiencing intraoperative blood loss exceeding 1000 mL and consequently the median number of blood units transfused, was significantly higher in non survivors than in survivors (p<0.009 and p<0.001, respectively). Similarly, overall and major complications were significantly more common in non survivors than in survivors (p=0.002 and p=0.012, respectively).

Conclusion: The findings of the study indicated that a higher ASA class, older age, lower NLR, hypoalbuminemia, higher intraoperative blood loss, the need for blood transfusion and postoperative complications were associated with increased 30-day mortality after PD.

Keywords: In-hospital mortality, Morbidity, Postoperative complications

INTRODUCTION

Pancreaticoduodenectomy (PD) has been the only treatment aimed at achieving a cure for resectable periampullary tumours [1-3]. Despite significant advancements in relevant surgical techniques and postoperative care over the years, the procedure continues to be associated with high morbidity and mortality rates [3-5]. Complications inherent to PD, such as haemorrhage, pancreatic fistula, bile leak, intra-abdominal abscess, delayed gastric emptying and surgical site infection, negatively affect overall survival outcomes [3]. Hence, the preoperative identification of patients at high risk for overall and PD-related morbidity and mortality is vital for tailoring PD approaches to individual patients [1,5].

Several studies have identified various patient- and PD-related risk factors that contribute to morbidity and mortality after PD [6,7]. Although multiple scoring systems have been developed to predict PD-related mortality, there is widespread agreement that PD-related complications and mortality are neither consistently predictable nor entirely preventable due to the complex interplay of clinical factors that contribute to adverse events [2,8].

Accurate identification of perioperative risk factors may guide physicians in selecting appropriate candidates for PD [9]. The timely identification and management of postoperative morbidities, particularly PD-related complications, are critical in averting undesirable outcomes [10].

Despite numerous studies identifying various risk factors for morbidity and mortality following PD, a significant gap remains in the comprehensive assessment of these factors across different populations and settings [1,2,4,6,8]. Many existing studies have focused on Western populations and more data from tertiary centers in developing countries, such as Turkey, should be collected [11-14]. Additionally, these settings have not fully elucidated the interplay of specific preoperative, intraoperative and postoperative variables in predicting outcomes. Therefore, the present study aimed to fill this gap by providing a detailed analysis of early postoperative morbidity and mortality following PD in a tertiary center in Turkey, identifying associated risk factors and offering insights that can be utilised to improve patient outcomes.

MATERIALS AND METHODS

The present study was designed as a cross-sectional, single-centre study conducted in the General Surgery Clinics of Ankara Numune Training and Education Hospital in Ankara, Turkey, between May 2010 and May 2014. The Institutional Ethics Committee approved the study protocol prior to its commencement (Scientific Research Evaluation Committee of Ankara Numune Training and Research

Hospital, Number: 20796219-E.Kurul-869/2014). The study was conducted in accordance with the ethical considerations outlined in the Declaration of Helsinki. Written informed consent could not be obtained from the patients due to the study's retrospective design and the anonymity of the data. Data regarding patients who underwent PD were collected throughout 2014, with the last patient included in the study undergoing surgery in the last quarter of 2014. To account for the postoperative 30-day mortality period, data collection began in the first quarter of 2015. Following the completion of data collection in early 2015, data analysis and interpretation were conducted, ensuring that all relevant outcomes were thoroughly evaluated. This timeline allowed the authors to capture comprehensive postoperative outcomes and perform a detailed analysis to accurately interpret the data.

Inclusion and Exclusion criteria: All consecutive adult patients aged 18 years and above who underwent elective PD for resectable malignant periampullary tumours were included. Patients with incomplete medical records, benign final postoperative histopathology, those who underwent PD along with other procedures and those who received PD after neoadjuvant chemotherapy were excluded from the study. In the end, the study sample consisted of 64 patients.

Study Procedure

Patients' preoperative demographic (age, gender), clinical (co-morbidities, ASA class) and haematological and biochemical characteristics were collected and recorded in a prospectively maintained database for hepatobiliary surgical patients. Patients' imaging findings and interventions were noted, including Percutaneous Transhepatic Cholangiography (PTC), Endoscopic Retrograde Cholangiography (ERCP) and biliary stenting. Patients' periampullary tumours were classified according to their location: pancreatic head, distal common bile duct, ampulla of Vater and the second part of the duodenum.

The same surgical team performed PD on all patients using a standard technique [2]. Intraoperative data, including the PD subtype (i.e., pylorus-preserving or classical), duration of surgery, anastomotic details, blood loss and need for transfusion, as well as postoperative morbidity and mortality data, were recorded in a prospectively maintained database. Complications occurring within 30 days after PD were categorised as major or minor [15]. Major complications included anastomotic leakage, intra-abdominal abscess, pulmonary embolism and significant cardiovascular and respiratory adverse events, such as myocardial infarction. Minor complications encompassed morbidities such as surgical site infections, evisceration, atelectasis and delayed gastric emptying.

The PD-specific complications, including pancreatic fistula, the grade of pancreatic fistula, delayed gastric emptying, haemorrhage and bile leakage, were diagnosed based on the International Study Group of Pancreatic Surgery Guidelines [16-18]. Postoperative mortality, defined as death within 30 days of PD due to a medical or surgical cause, was the primary outcome of the study. The impact of sociodemographic, clinical and intraoperative characteristics on mortality was considered the secondary outcome.

STATISTICAL ANALYSIS

The descriptive statistics from the collected data were tabulated using either mean±standard deviation or median with minimum and maximum values for continuous (numerical) variables, depending on whether they conformed to a normal distribution. For categorical variables, numbers and percentage values were used. The normal distribution characteristics of the numerical variables were analysed using the Shapiro-Wilk, Kolmogorov-Smirnov and Anderson-Darling tests. Pearson's Chi-square, Fisher's-exact and Fisher-Freeman-Halton tests were employed to compare the differences in categorical variables between the groups in 2×2 tables with five or more expected cells, 2×2 tables with expected cells fewer than five and R×C tables with expected cells fewer than five, respectively. The independent samples t-test and the Mann-Whitney U test were used to compare differences in numerical variables that conformed or did not conform to a normal distribution between the groups. Statistical analyses were performed using Jamovi Project 2.3.28 (Jamovi, version 2.3.28, 2023, retrieved from https://www.jamovi.org) and JASP 0.17.3 (Jeffreys' Amasing Statistics Program, version 0.17.3, 2023, retrieved from https://jasp-stats.org) software packages. A probability (p) value of ≤0.05 was deemed to indicate statistical significance.

RESULTS

The study sample consisted of 64 patients with a mean age of 60.1±12.4 years. Approximately three-fifths 39 (60.9%) of the patients were male. In terms of anatomic locations, the most common site was the pancreatic head 31 (48.44%), followed by the ampulla of Vater 19 (29.69%), the distal common bile duct 10 (15.63%) and the second part of the duodenum 4 (6.25%). The other clinical characteristics of the patients are provided in [Table/Fig-1]. A total of 12 (18.75%) patients died within 30 days of PD. Non survivors were significantly older (p=0.006) and had significantly higher ASA classes (3 and 4) (p=0.008). There was no significant difference in other demographic and clinical characteristics between the groups (p>0.05) [Table/Fig-1].

Parameters		Overall (n=64)	Survivors (n=52)	Non survivors (n=12)	p-value
Age (year)†		60.1±12.4	58.7±13.1	66.1±6.0	0.006*, α
Sex‡	Female	25 (39.1)	22 (42.3)	3 (25.0)	0.338αα
	Male	39 (60.9)	30 (57.7)	9 (75.0)	
Co-morbidity‡		36 (56.2)	26 (50.0)	10 (83.3)	0.076αα
Number of co-morbidities‡	Single	13 (36.1)	11 (42.3)	2 (20.0)	0.270αα
	≥2	23 (63.9)	15 (57.7)	8 (80.0)	
ASA grade‡	2	31 (48.4)	29 (55.8)	2 (16.7)	0.008*, αα
	3	29 (45.3)	22 (42.3)	7 (58.3)	
	4	4 (6.2)	1 (1.9)	3 (25.0)	

[Table/Fig-1]: Demographic and clinical characteristics of patients by mortality status. *: statistical significance; The † symbol denotes that age is presented as mean±standard deviation. Sex, co-morbidity presence and co-morbidity groups, along with ASA (American Society of Anesthesiologists) grade, are represented as count (percentage). Statistical analyses involve the use of the independent samples t-test for age comparisons and the Pearson Chi-square/Fisher's-exact test/Fisher Freeman Halton test for categorical variables, to evaluate the statistical significance between survivors and non survivors. Symbols are utilised to indicate the statistical tests: α denotes the application of the independent samples t-test; and αα signifies the use of Pearson's Chi-square/Fisher's-exact test/Fisher Freeman Halton test for categorical data comparison

The preoperative laboratory data of the survivors and non survivors are presented in [Table/Fig-2]. Accordingly, non survivors had significantly lower Neutrophil-to-lymphocyte Ratios (NLR) (p<0.001) and serum albumin levels (p=0.038) than survivors. There was no significant difference in Carbohydrate Antigen (CA) 19-9 and carcinoembryonic antigen levels between the groups (p>0.05) [Table/Fig-2].

Of the 64 patients, 34 (53.1%) underwent Endoscopic Retrograde Cholangiopancreatography (ERCP), three (4.7%) underwent Percutaneous Transhepatic Cholangiography (PTC) and 27 (42.2%) underwent biliary stenting preoperatively. Classical PD 51 (79.7%) and duct-to-mucosa anastomosis 47 (73.4%) were performed more frequently than pylorus-preserving PD 13 (20.3%) and dunking anastomosis 17 (26.6%), respectively. The rate of patients experiencing blood loss exceeding 1000 mL intraoperatively was significantly higher in non survivors compared to survivors (41.67% vs. 7.69%, p<0.009) and therefore the median number of blood units transfused was significantly greater in non survivors than in survivors (p<0.001) [Table/Fig-3].

All non survivors experienced at least one complication. Both general complications and major complications were significantly more common in non survivors than in survivors (p=0.002 and p=0.012, respectively). However, there was no significant difference

Parameters	Survivors (n=52)	Non survivors (n=12)	p-value
Haemoglobin (g/dL)†	12.3±1.6	11.5±2.1	0.243$^{\alpha}$
White blood cell count (x109/L)†	8.0±3.3	8.8±3.0	0.402$^{\alpha}$
Platelet count (x109/L)†	289.4±96.4	286.7±104.8	0.936$^{\alpha}$
Platelet/lymphocyte ratio§	143.5 (26.9-461.6)	204.2 (99.5-638.6)	0.123$^{\alpha\alpha}$
Neutrophil/ lymphocyte ratio§	0.4 (0.1-6.9)	0.2 (0.1-0.4)	<0.001$^{*,\ \alpha\alpha}$
Glucose (mg/dL)§	101.0 (72.0-285.0)	157.0 (66.0-292.0)	0.151$^{\alpha\alpha}$
Creatinine (mg/dL)§	0.8 (0.4-1.1)	0.8 (0.3-2.4)	0.966$^{\alpha\alpha}$
Albumin (mg/dL)†	34.9±6.6	27.5±10.6	0.038$^{*,\ \alpha}$
ALT (U/L)§	102.0 (5.0-521.0)	56.5 (9.0-550.0)	0.692$^{\alpha\alpha}$
AST (U/L)§	90.5 (8.0-307.0)	111.0 (10.0-791.0)	0.582$^{\alpha\alpha}$
ALP (U/L)§	367.5 (40.0-1259.0)	243.0 (69.0-1312.0)	0.959$^{\alpha\alpha}$
GGT (U/L)§	347.0 (11.0-1299.0)	246.0 (14.0-1757.0)	0.911$^{\alpha\alpha}$
Total bilirubin (mg/dL)§	5.6 (0.2-28.3)	9.7 (0.3-19.5)	0.444$^{\alpha\alpha}$
Direct bilirubin (mg/ dL)§	3.5 (0.1-84.0)	7.0 (0.2-10.8)	0.340$^{\alpha\alpha}$
CA 19-9, >100 IU/L	25 (48.1)	6 (50.0)	0.999$^{\alpha\alpha\alpha}$
CEA (U/L)§	2.7 (0.2-439.0)	3.1 (0.7-40.9)	0.348$^{\alpha\alpha}$

[Table/Fig-2]: Preoperative laboratory values of the survived and non-survived patients.
*: statistical significance; The † symbol signifies that the data for haemoglobin, white blood cell count, platelet count and albumin are provided as mean±standard deviation, reflecting the average and variability around the average. The § symbol indicates that values for platelet/lymphocyte ratio, neutrophil/lymphocyte ratio, glucose, creatinine, albumin, ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; GGT: Gamma-glutamyl transferase; total bilirubin, direct bilirubin and CEA: Carcinoembryonic antigen; are shown as median (minimum-maximum), highlighting the middle value and the range within which the data falls. The presence of CA 19-9 >100 IU/L is represented as count (percentage), indicating the proportion of patients with elevated levels. Statistical significance is assessed using the independent samples t-test for mean values, the Mann-Whitney U test for median values and the Pearson Chi-square test for categorical data, with symbols α for the t-test, $\alpha\alpha$ for the Mann-Whitney U test and $\alpha\alpha\alpha$ for the Chi-square test, denoting the methods used to compare the laboratory values between the two groups

in the incidence of anastomotic leakage and pancreatic fistula between the groups (p=0.351 and p=0.999, respectively) [Table/Fig-4].

DISCUSSION

The study findings revealed that PD performed for malignant periampullary tumours was associated with a high 30-day postoperative mortality rate, which varies according to the patients' clinical characteristics and intraoperative findings. Significant risk factors for 30-day mortality after PD included older age, higher ASA classes, intraoperative blood loss, perioperative blood transfusion and postoperative complications.

Postoperative complications, overall morbidity and mortality rates reported in the literature vary significantly depending on various factors, including patient-related, tumour-related and surgeon-related parameters [2-4,8,11,19]. In a study conducted with 1,348 patients who underwent PD for malignancy, Russell TB et al., reported overall morbidity and mortality rates of 53% and 4%, respectively [1]. Other studies reported mortality rates of less than 5% [4,7-9,20,21]. Nevertheless, several studies have reported relatively high mortality rates following PD [3,11,12,22]. In the study by Agrawal S et al., from Nepal, the in-hospital mortality rate was 12.9% [22]. The present study included 62 patients who underwent PD for benign and malignant conditions between 2015 and 2019. The authors found that morbidity and mortality rates decreased as the number of PDs performed increased over the study period. Another study from Turkey reported a mortality rate of 9.5% among geriatric patients who underwent PD for malignancy [12]. The authors suggested that this high mortality rate could be attributed to the advanced age and underlying malignancy of the patients. In the current study, the mortality rate was 18.75%. The concurrent

Parameters		Overall (n=64)	Survivors (n=52)	Non survivors (n=12)	p-value
Preoperative interventions‡	ERCP	34 (53.1)	27 (51.9)$^{\#}$	7 (58.3)$^{\#\#}$	0.936$^{\alpha}$
	PTC	3 (4.7)	2 (3.8)$^{\#}$	1 (8.3)$^{\#\#}$	0.470$^{\alpha}$
	Biliary stenting	27 (42.2)	20 (38.5)$^{\#}$	7 (58.3)$^{\#\#}$	0.351$^{\alpha}$
Type of PD‡	Pylorus preserving	13 (20.3)	11 (21.2)	2 (16.7)	0.999$^{\alpha\alpha}$
	Classical	51 (79.7)	41 (78.8)	10 (83.3)	
Pancreatic anastomosis‡	Dunking	17 (26.6)	14 (26.9)	3 (25.0)	0.961$^{\alpha}$
	Duct-to-mucosa	47 (73.4)	38 (73.08)	9 (75)	
Intrapancreatic stent‡		7 (10.9)	5 (9.6)	2 (16.7)	0.610$^{\alpha}$
Intraoperative blood loss, >1000 mL‡		9 (14.1)	4 (7.7)	5 (41.7)	0.009$^{*,\ \alpha}$
Need for intraoperative blood loss‡		10 (15.6)	4 (7.7)	6 (50.0)	0.001$^{*,\ \alpha}$
Perioperative blood transfusion (units)§		0.0 (0.0, 6.0)	0.0 (0.0, 6.0)	0.5 (0.0, 6.0)	<0.001$^{*,\ \alpha\alpha}$
Operative time‡	<3 hr.	6 (9.4)	6 (11.5)	0 (0.0)	0.362$^{\alpha}$
	3-4 hr.	24 (37.5)	19 (36.5)	5 (41.7)	
	4-5 hr.	21 (32.8)	18 (34.6)	3 (25.0)	
	5-6 hr.	6 (9.4)	5 (9.6)	1 (8.3)	
	>6 hr.	7 (10.9)	4 (7.7)	3 (25.0)	

[Table/Fig-3]: Perioperative details of the patients grouped by mortality status.
*: statistical significance; The ‡ symbol indicates that data for preoperative interventions (ERCP, PTC, biliary stenting), type of Pancreaticoduodenectomy (PD), pancreatic anastomosis (dunking, duct-to-mucosa) and intrapancreatic stent placement are presented as count (percentage), illustrating the frequency and proportion of occurrences within each group. The § symbol signifies that the perioperative blood transfusion data are shown as median (minimum-maximum), indicating the middle value of the distribution and the range of observed values. ERCP: Endoscopic retrograde cholangiopancreatography; PTC: Percutaneous transhepatic cholangiography; PD: Pancreaticoduodenectomy, specifying the types of preoperative interventions and surgical procedures undertaken. Statistical significance between groups is assessed using Pearson Chi-square/Fisher's-exact test/Fisher Freeman Halton test for categorical data and the Mann-Whitney U test for continuous or ordinal data, as denoted by symbols α for the Chi-square/ Fisher's tests and $\alpha\alpha$ for the Mann-Whitney U test. #: some patients did not have a pre-operative procedure; ##: Some patients had multiple procedures

Parameters		Overall (n=64)	Survivors (n=52)	Non survivors (n=12)	p-value
Complication‡		36 (56.3)	24 (46.2)	12 (100.0)	0.002$^{*,\ \alpha}$
Complication groups‡	Minor	15 (44.1)	14 (58.3)	1 (8.3)	0.012$^{*,\ \alpha}$
	Major	21 (55.9)	10 (41.7)	11 (91.7)	
Type of complication‡	Anastomotic leakage	9 (14.1)	6 (11.5)	3 (25.0)	0.351$^{\alpha}$
	Pancreatic fistula	9 (14.1)	8 (15.4)	1 (8.3)	0.999$^{\alpha}$

[Table/Fig-4]: Postoperative outcomes of the patients.
*: statistical significance; The ‡ symbol signifies that values are presented as a number (n) with its corresponding percentage (%). The statistical test used for comparison between groups is indicated as follows: α denotes the Pearson Chi-square or Fisher's-exact test, employed for assessing the significance of differences in categorical data between two groups. Complications are further divided into "Minor" and "Major" based on their severity, with specific types of complications such as Anastomotic leakage and Pancreatic fistula also reported

presence of multiple independent risk factors within a patient cohort may result in a relatively higher mortality rate [11]. Similarly, poor postoperative outcomes can be attributed to increased patient load, inadequate resources, a lack of a multidisciplinary approach and insufficient critical care management tools, which could lead to poor postoperative outcomes [3]. However, a causality analysis due to the study's retrospective design could not be conducted. Additionally, a year-wise trend analysis of postoperative morbidity and mortality was not performed due to the small number of mortalities each year.

Therefore, large-scale prospective studies are needed to clarify the factors contributing to the relatively higher mortality rate after PD.

Several studies have investigated the potential relationship between various aspects of PD, such as postoperative complications and mortality and the demographic and clinical characteristics of patients who underwent PD for malignancy [1,6]. In one of these studies, Russell TB et al., reported that obesity, ASA class ≥2 and performing PD using the classic Whipple approach were risk factors for overall morbidity after PD [1]. However, they found no significant relationship between 90-day mortality and various demographic and clinical parameters. Zhao Z et al., found that age and albumin levels were significantly associated with major morbidities after PD [6]. On the other hand, several studies did not find a significant relationship between age and mortality after PD [5,8,20]. Parasyris S et al., reported that morbidity and mortality rates after PD were similar in patients under 80 and those over 80 years old [5]. Similar findings have been observed in other studies [13,14]. In comparison, older age, higher ASA classes and lower albumin levels were significantly associated with 30-day mortality after PD, suggesting that selecting appropriate candidates for PD based on perioperative risk factors is critical.

Some studies have suggested that major complications after PD are essential risk factors for 90-day mortality [4,10,19]. The causes of mortality after PD also vary depending on the frequency of PD performed at the centre [19,22,23]. Accordingly, sepsis, multiple system organ failure secondary to aspiration and bleeding, followed by cardiac arrest and pulmonary embolism, were the leading causes of death in centres where PD was frequently performed. In contrast, septic shock, massive bleeding and thromboembolism were the leading causes of death in centres where PD was performed less frequently. In the current study, postoperative morbidity or complications were significantly associated with the development of mortality following PD. Kapoor D et al.'s study also identified clinically relevant pancreatic fistula and post-pancreatectomy haemorrhage as significant predictors of mortality [8]. Although the type of PD-associated complications, such as anastomotic leakage or pancreatic fistula, was not directly related to mortality in this patient group, anastomotic leakage was more frequently observed among non survivors. However, other complications were not analysed separately, which limited the ability to establish causality. Therefore, large-scale studies are needed to clarify the impact of perioperative clinical factors on the development of mortality following PD.

The negative effect of higher ASA classes on the outcomes of PD has been well documented [1,8,24]. Similarly, it has been reported that patients with morbidity are more likely to experience mortality after PD [1,3]. In contrast, Russell TB et al., found that higher ASA classes were significantly correlated with overall morbidity and major morbidity but not with 90-day mortality [20]. In comparison, a significant relationship was observed between higher ASA classes and 30-day mortality after PD. Therefore, patients with co-morbidities that lead to higher ASA classes should be informed about the potentially adverse outcomes of PD in advance.

The surgical approach used in PD and technical modifications have been investigated in the literature for their impact on PD-specific morbidity and mortality [1]. Some studies have reported that conventional PD is a risk factor for more complications [1,25]. However, there was no significant relationship found between the type of PD and pancreatic anastomosis and mortality.

Although the mechanism is not fully understood, high Neutrophil-to-lymphocyte Ratio (NLR) values have been associated with poor short- and long-term outcomes after PD [26]. Russell TB et al., reported a higher risk of major morbidity in patients with higher NLR values [20]. However, they did not find a significant relationship between NLR and the 90-day mortality rate. On the other hand, a significant relationship between lower NLR values and increased 30-day mortality rate after PD was detected, which contradicts the findings of other studies [11,27,28]. Prospective large-scale studies are needed to elucidate the relationship between NLR and mortality in PD patients.

Limitation(s)

The study's primary limitations were its retrospective design, small sample size and the absence of intraoperative data regarding the main pancreatic duct diameter and parenchymal texture of the pancreas. Additionally, the lack of a causal analysis of the factors impacting the mortality rate was another limitation of the study.

CONCLUSION(S)

In conclusion, the present study highlights that older age, a higher ASA class, a lower NLR, hypoalbuminemia, increased intraoperative blood loss, the necessity for blood transfusion and postoperative complications were significant risk factors for 30-day mortality following PD for malignant periampullary tumours. The findings emphasise the importance of preoperative risk assessment and optimisation in improving postoperative outcomes. Tailoring surgical approaches to individual patient risk profiles and ensuring meticulous perioperative care can help reduce mortality rates. Future prospective studies with larger sample sizes must validate these risk factors and develop comprehensive risk stratification models. Ultimately, the goal is to enhance patient selection and perioperative management, thereby improving survival rates and the overall quality of care for patients undergoing PD.

REFERENCES

[1] Russell TB, Labib PL, Denson J, Streeter A, Ausania F, Pando E, et al. Postoperative complications after pancreatoduodenectomy for malignancy: Results from the Recurrence After Whipple's (RAW) study. BJS Open. 2023;7(6):zrad106. Doi: 10.1093/bjsopen/zrad106.

[2] Lalisang ANL, Nugroho A, Putranto AS, Mazni Y, Lalisang TJM. Keep it or leave it? comparison of preoperative scoring as mortality predictor post-pancreaticoduodenectomy. Asian Pac J Cancer Prev. 2023;24(8):2885-93. Doi: 10.31557/APJCP.2023.24.8.2885.

[3] Zubair AB, Khan Sherwani IAR, Ahmad M, Tahir MA, Khalil MI, Bukhari MM, et al. The spectrum of postoperative complications and outcomes after pancreaticoduodenectomy: A retrospective outlook from a developing country. Cureus. 2022;14(2):e22218. Doi: 10.7759/cureus.22218.

[4] Khan MA, Muhammad S, Mehdi H, Parveen A, Soomro U, Ali JF, et al. Surgeon's experience may circumvent operative volume in improving early outcomes after pancreaticoduodenectomy. Cureus. 2023;15(8):e42927. Doi: 10.7759/cureus.42927.

[5] Parasyris S, Hatzaras I, Ntella V, Sidiropoulos T, Margaris I, Pantazis N, et al. Pancreaticoduodenectomy as a feasible choice for periampullary malignancy in octogenarians. Mol Clin Oncol. 2022;17(4):148. Doi: 10.3892/mco.2022.2581.

[6] Zhao Z, Zhou S, Tang Y, Zhou L, Ji H, Tang Z, et al. Impact of age on short-term outcomes after pancreaticoduodenectomy: A retrospective case-control study of 260 patients. Front Surg. 2023;10:1031409. Doi: 10.3389/fsurg.2023.1031409.

[7] Giuliani T, Marchegiani G, Di Gioia A, Amadori B, Perri G, Salvia R, et al. Patterns of mortality after pancreatoduodenectomy: A root cause, day-to-day analysis. Surgery. 2022;172(1):329-35. Doi: 10.1016/j.surg.2022.01.005.

[8] Kapoor D, Perwaiz A, Singh A, Kumar AN, Chaudhary A. Factors predicting 30-day mortality after pancreaticoduodenectomy-the impact of elevated aspartate aminotransferase. Langenbecks Arch Surg. 2023;408(1):130. Doi: 10.1007/s00423-023-02865-w.

[9] de Bakker JK, Suurmeijer JA, Toennaer JGJ, Bonsing BA, Busch OR, van Eijck CH, et al. Surgical outcome after pancreatoduodenectomy for duodenal adenocarcinoma compared with other periampullary cancers: A nationwide audit study. Ann Surg Oncol. 2023;30(4):2448-55. Doi: 10.1245/s10434-022-12701-y.

[10] Li V, Serrano PE. Prediction of postoperative mortality in patients with organ failure following pancreaticoduodenectomy. Am Surg. 2023;89(5):1519-26. Doi: 10.1177/00031348211065104.

[11] Kama NA, Coskun T, Yuksek YN, Yazgan A. Factors affecting postoperative mortality in malignant biliary tract obstruction. Hepatogastroenterology. 1999;46(25):103-07.

[12] Ceylan C, Kocaaslan H, Baran NT, Kulus M, Saglam K, Aydin C. Predictive factors of postoperative pancreatic fistula in geriatric patients undergoing pancreatoduodenectomy for periampullary malignancy. J Coll Physicians Surg Pak. 2023;33(12):1439-44. Doi: 10.29271/jcpsp.2023.12.1439.

[13] Ergenç M, Uprak TK, Özocak AB, Karpuz Ş, Coşkun M, Yeğen C, et al. Pancreaticoduodenectomy in patients<75 years versus≥75 years old: A comparative study. Aging Clin Exp Res. 2024;36(1):141. Doi: 10.1007/s40520-024-02804-9.

[14] Aziret M, Aşıkuzunoğlu F, Altıntoprak F, Tozlu M, Demirci A, Ercan M, et al. Early and long-term morbidity and mortality following pancreaticoduodenectomy for periampullary tumours in elderly patients. Ann Ital Chir. 2024;95(2):235-45. Doi: 10.62713/aic.3380.

[15] Papageorge MV, de Geus SWL, Woods AP, Ng SC, McAneny D, Tseng JF, et al. The effect of hospital versus surgeon volume on short-term patient outcomes after pancreaticoduodenectomy: A SEER-medicare analysis. Ann Surg Oncol. 2022;29(4):2444-51. Doi: 10.1245/s10434-021-11196-3.
[16] Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, et al. Postoperative pancreatic fistula: An international study group (ISGPF) definition. Surgery. 2005;138(1):08-13. Doi: 10.1016/j.surg.2005.05.001.
[17] Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, et al. Delayed gastric emptying (DGE) after pancreatic surgery: A suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery. 2007;142(5):761-68. Doi: 10.1016/j.surg.2007.05.005.
[18] Wente MN, Veit JA, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, et al. Postpancreatectomy hemorrhage (PPH): An International Study Group of Pancreatic Surgery (ISGPS) definition. Surgery. 2007;142(1):20-25. Doi: 10.1016/j.surg.2007.02.001.
[19] Saraee A, Vahedian-Ardakani J, Saraee E, Pakzad R, Wadji MB. Whipple procedure: A review of a 7-year clinical experience in a referral center for hepatobiliary and pancreas diseases. World J Surg Oncol. 2015;13:98. Doi: 10.1186/s12957-015-0523-8.
[20] Russell TB, Labib PLZ, Aroori S. Five-year follow-up after pancreatoduodenectomy performed for malignancy: A single-centre study. Ann Hepatobiliary Pancreat Surg. 2023;27(1):76-86. Doi: 10.14701/ahbps.22-039.
[21] Chen JS, Liu G, Li TR, Chen JY, Xu QM, Guo YZ, et al. Pancreatic fistula after pancreaticoduodenectomy: Risk factors and preventive strategies. J Cancer Res Ther. 2019;15(4):857-63. Doi: 10.4103/jcrt.JCRT_364_18.
[22] Agrawal S, Khanal B, Das U, Sah SP, Gupta RK. Pancreaticoduodenectomy: Impact of volume on outcomes at a tertiary care center-our experience in single institute of Nepal. J Gastrointest Cancer. 2022;53(3):692-99. Doi: 10.1007/s12029-021-00705-y.
[23] Narayanan S, Martin AN, Turrentine FE, Bauer TW, Adams RB, Zaydfudim VM. Mortality after pancreaticoduodenectomy: Assessing early and late causes of patient death. J Surg Res. 2018;231:304-08. Doi: 10.1016/j.jss.2018.05.075.
[24] Wiltberger G, Muhl B, Benzing C, Atanasov G, Hau HM, Horn M, et al. Preoperative risk stratification for major complications following pancreaticoduodenectomy: Identification of high-risk patients. Int J Surg. 2016;31:33-39. Doi: 10.1016/j.ijsu.2016.04.034.
[25] Hüttner FJ, Fitzmaurice C, Schwarzer G, Seiler CM, Antes G, Büchler MW, et al. Pylorus-preserving pancreaticoduodenectomy (pp Whipple) versus pancreaticoduodenectomy (classic Whipple) for surgical treatment of periampullary and pancreatic carcinoma. Cochrane Database Syst Rev. 2016;2(2):CD006053. Doi: 10.1002/14651858.CD006053.pub6.
[26] Mowbray NG, Griffith D, Hammoda M, Shingler G, Kambal A, Al-Sarireh B. A meta-analysis of the utility of the neutrophil-to-lymphocyte ratio in predicting survival after pancreatic cancer resection. HPB (Oxford). 2018;20(5):379-84. Doi: 10.1016/j.hpb.2017.12.009.
[27] Ida M, Tachiiri Y, Sato M, Kawaguchi M. Neutrophil-to-lymphocyte ratio as indicator to severe complication after pancreaticoduodenectomy or distal pancreatectomy. Acta Anaesthesiol Scand. 2019;63(6):739-44. Doi: 10.1111/aas.13341.
[28] Huang H, Wang C, Ji F, Han Z, Xu H, Cao M. Nomogram based on albumin and neutrophil-to-lymphocyte ratio for predicting postoperative complications after pancreaticoduodenectomy. Gland Surg. 2021;10(3):877-91. Doi: 10.21037/gs-20-789.

PARTICULARS OF CONTRIBUTORS:
1. Doctor, Department of General Surgery, University of Health Sciences, Ankara, Turkey.
2. Doctor, Department of General Surgery, University of Health Sciences, Ankara, Turkey.
3. Doctor, Department of General Surgery, University of Health Sciences, Ankara, Turkey.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Salih Demirelli,
Doctor, Department of General Surgery, University of Health Sciences, Ankara, Turkey.
E-mail: dr.salihdemirelli@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: May 23, 2024
- Manual Googling: Jun 29, 2024
- iThenticate Software: Aug 28, 2024 (12%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **May 20, 2024**
Date of Peer Review: **Jun 27, 2024**
Date of Acceptance: **Aug 29, 2024**
Date of Publishing: **Oct 01, 2024**