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ABOUT COVER

Peer Reviewer of *World Journal of Gastrointestinal Surgery*, Adrienn Biró, MD, PhD, Assistant Professor, Surgeon, Department of Surgery, Somogy County Kaposi Mor Teaching Hospital, Kaposvár 7400, Hungary. b.adrienn5@gmail.com

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ORIGINAL ARTICLE

Retrospective Study

Retrospective analysis of delta hemoglobin and bleeding-related risk factors in pancreaticoduodenectomy

Yi-Min Lin, Chao Yu, Guo-Zhe Xian

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Yi-Min Lin, Guo-Zhe Xian, Department of Hepatobiliary Surgery, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan 250021, Shandong Province, China

Chao Yu, Department of Emergency Surgery, Affiliated Hospital of Shandong University of Traditional Chinese Medicine, Jinan 250011, Shandong Province, China

Co-first authors: Yi-Min Lin and Chao Yu.

Corresponding author: Guo-Zhe Xian, MD, PhD, Professor, Department of Hepatobiliary Surgery, Shandong Provincial Hospital Affiliated to Shandong First Medical University, No. 324 Jingwu Weiqi Road, Huaiyin District, Jinan 250021, Shandong Province, China. xianguozhe@sdfmu.edu.cn

Abstract

BACKGROUND

Objective and accurate assessment of blood loss during pancreaticoduodenectomy (PD) is crucial for ensuring the safety and efficacy of the procedure. While the visual method remains the most common clinical metric, many scholars argue that it significantly differs from actual blood loss and is inherently subjective.

AIM

To assess blood loss in PD *via* delta hemoglobin (ΔHb) and compare it with the visual method to predict bleeding-related risk factors.

METHODS

In this retrospective analysis, 1722 patients who underwent PD from 2017 to 2022 at Shandong Provincial Hospital were divided into three groups: Open PD (OPD), laparoscopic PD (LPD), and conversion to OPD (CTOPD). Intraoperative ΔHb (IΔHb) was calculated *via* preoperative and 72-hour-postoperative hemoglobin concentrations, and its association with visually obtained estimated blood loss (EBL) was analyzed. Perioperative ΔHb (PΔHb) was calculated *via* preoperative and predischarge hemoglobin concentrations. We compared the differences in IΔHb and PΔHb among the three groups, and performed univariate and multivariate regression analyses of IΔHb and PΔHb.

RESULTS

The preoperative general information of patients showed no statistically significant difference among the three groups ($P > 0.05$). The IΔHb in the OPD, LPD, and CTOPD groups were 22.00 (12.00, 36.00), 21.00 (10.00, 33.00), and 33.00 (18.12, 52.24) g/L, respectively; And the PΔHb in the OPD, LPD, and CTOPD groups were 25.87 (13.51, 42.00), 25.00 (14.00, 45.00), and 37.48 (21.64, 59.65) g/L, respectively, values significantly differed (P < 0.05). IΔHb and EBL were significantly correlated (r = 0.337, P < 0.001). The results of univariate and multivariate regression analyses indicated that American Society of Anesthesiologists (ASA) classification IV [95% confidence interval (CI): 2.330-37.811, P = 0.049] and preoperative total bilirubin > 200 μmol/L (95%CI: 2.805-8.673, P < 0.001) were independent risk factors for IΔHb (P < 0.05), and ASA classification IV (95%CI: 45.934-105.485, P < 0.001), body mass index > 24 kg/m^2 (95%CI: 1.285-9.890, P = 0.011), and preoperative total bilirubin > 200 μmol/L (95%CI: 6.948-16.797, P < 0.001) were independent risk factors for PΔHb (P < 0.05).

CONCLUSION

There is a correlation between IΔHb and EBL in PD, so we can assess the patients' intraoperative blood loss by the ΔHb method. ASA classification IV, body mass index > 24 kg/m^2, and preoperative total bilirubin > 200 μmol/L increased perioperative bleeding risk.

Key Words: Pancreaticoduodenectomy; Delta hemoglobin; Estimated blood loss; Postpancreatectomy hemorrhage; Risk factor

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Core Tip: We collected the medical records of patients who underwent pancreaticoduodenectomy in Shandong Provincial Hospital from 2017 to 2022. We used the difference in hemoglobin concentration (delta hemoglobin) before and after surgery to assess the amount of perioperative bleeding in patients, compared with the estimated blood loss obtained by the visual method, and analyzed the correlation between the two. Moreover, univariate and multivariate regression analyses were performed on the patients' delta hemoglobin to predict risk factors related to bleeding.

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INTRODUCTION

Pancreaticoduodenectomy (PD) is a standard surgical procedure used to treat benign and malignant tumors, including pancreatic head cancer, duodenal cancer, and bile duct cancer. However, PD is regarded as one of the most complex and challenging surgeries in general surgery because of its extensive resection range, intricate gastrointestinal tract reconstruction, and high rate of postoperative complications[1]. With the development of laparoscopic technology, Gagner and Pomp[2] successfully performed the world's first laparoscopic PD (LPD) in 1994, after which LPD was gradually introduced into clinical practice and widely adopted. Compared with open PD (OPD), LPD is more technically challenging, and its safety and clinical outcomes remain uncertain[3]. The amount of intraoperative blood loss in PD patients is a crucial factor related to surgical safety and patient prognosis. Therefore, an accurate assessment of intraoperative blood loss is essential for smooth operation and postoperative recovery. There are various clinical methods for estimating blood loss[4,5], including visual estimation and calculation methods, but both are often unreliable and inaccurate. Despite its limitations, the visual estimation method remains the most commonly used approach in clinical practice. In this method, surgeons and anesthesiologists estimate blood loss on the basis of the amount collected in suction canisters, observe intraoperative bleeding, and determine the amount of blood absorbed by surgical gauze[5-8]. While this method is simple, quick, and easy to apply, it is highly subjective and susceptible to individual bias, making it difficult to accurately reflect actual intraoperative blood loss[9]. We used the difference between preoperative and postoperative hemoglobin (Hb) concentrations, accounting for intraoperative and postoperative transfusions, and introduced the concept of a modified delta Hb (ΔHb) to reflect bleeding in patients undergoing PD. The intraoperative bleeding analyzed included blood loss from before the start of the operation to 72 hours after the operation. Perioperative bleeding was defined as blood loss from before the start of the operation to discharge from the hospital.

In this study, we retrospectively analyzed the clinical data of 1722 patients who underwent PD from January 2017 to December 2022 at Shandong Provincial Hospital, assessed the amount of intraoperative bleeding and analyzed the risk factors associated with bleeding to provide new insights into comparing the clinical efficacy of different surgical procedures and reducing the risk of surgical bleeding.

MATERIALS AND METHODS

General information

In this study, we collected the clinical data of 1873 patients who successfully underwent PD at Shandong Provincial Hospital Affiliated to Shandong First Medical University from January 2017 to December 2022. After excluding 27 patients due to age, 111 patients who underwent combined resection of other organs, and 13 patients with missing test results, 1722 patients were ultimately included. The inclusion criteria were as follows: (1) Preoperative patients who underwent computed tomography, magnetic resonance imaging, ultrasound endoscopy, and other examinations for preliminary diagnosis; (2) Surgical indications for PD with no contraindications for surgery; (3) No invasion of the portal vein, mesenteric artery, inferior vena cava, *etc*, and no distant metastasis to organs such as the liver or abdominal cavity; (4) No insufficiency of vital organs, including the heart, lungs, brain, or kidneys; (5) Aged between 18 years and 80 years; and (6) Patient and family members signed the informed consent form for surgery. The exclusion criteria were as follows: (1) Cardiac, pulmonary, cerebral, or other functional insufficiencies; (2) Incomplete case data; and (3) Multiple-organ resections, such as combined hepatic, colonic, or superior mesenteric vessel resections. The patients were divided into three groups on the basis of the surgical method used: The OPD group (n = 511), the LPD group (n = 982), and the CTOPD group (n = 229). This study was approved by the Ethics Committee of Shandong Provincial Hospital, approval No. 2024-403.

Surgical methods

In patients who underwent LPD, the entire surgical procedure was performed laparoscopically. The main steps included the following: (1) Explore the abdominal cavity to identify any metastasis to the peritoneum or abdominal organs; (2) Isolate and resect the tumor and performing lymph node dissection; and (3) Reconstruct the digestive tract[10]. The surgical approach for OPD primarily involves classical PD. The methods for exploration, isolation, resection, and reconstruction of the digestive tract are essentially the same as those used in LPD. If intraoperative bleeding, severe adhesions, or a close relationship between the tumor and major blood vessels occurred during LPD, the laparoscopic operation was difficult, and conversion to open surgery was performed.

Definitions of relevant indicators

Intraoperative ΔHb (IΔHb) was defined as the difference between the preoperative Hb concentration and the Hb concentration within 72 hours after surgery plus the increase in the Hb concentration due to transfusion. Typically, patients' blood volume nearly returns to normal 72 hours after surgery, and the Hb concentration remains relatively stable[11]. Perioperative ΔHb (PΔHb) was defined as the difference between the preoperative Hb concentration and the predischarge Hb concentration plus the increase in the transfusion-induced Hb concentration. Intraoperative bleeding obtained *via* the visual method was termed estimated blood loss (EBL). The postpancreatectomy hemorrhage (PPH)-related grading criteria were based on the International Study Group of Pancreatic Surgery definitions[12].

Observation and analysis of indicators

Preoperative general data, including sex, age, body mass index (BMI), diabetes history, previous abdominal surgeries, preoperative alkaline phosphatase, preoperative glutamyl transpeptidase, preoperative Hb, American Society of Anesthesiologists (ASA) classification, and preoperative total bilirubin, were compared among the OPD, LPD, and CTOPD groups. The differences in IΔHb and PΔHb among these groups were also examined. The correlation between patients' IΔHb and EBL was analyzed. Univariate and multivariate regression analyses were conducted for IΔHb and PΔHb.

Formula

$\Delta Hb = Hb_{preop} - Hb_{postop}$ + infused Hb[13]; infused Hb = number of units transfused × 28/(BV/1000)[14]; Hb_{preop} (g/L): Patient's preoperative Hb concentration; Hb_{postop} (g/L): Hb concentration measured within 72 hours post-surgery or before discharge; if multiple test results were available within the first 72 hours postoperatively, the last result was selected for calculation; BV (mL): Patients' estimated blood volume calculated *via* the International Council for Standardization in Haematology formula[11].

Statistical analysis

SPSS statistical software (IBM SPSS Statistics, version 26.0; IBM Corporation, Armonk, NY, United States) was used to analyze and process the data in this study. Normally distributed data are expressed as the means ± SDs, and one-way analysis of variance was used to compare the three groups. Measurement data not conforming to a normal distribution are expressed as the medians (interquartile ranges), and the rank sum test was used for comparisons among the three groups. Count data are expressed as n (%), and comparisons among groups were made *via* the χ^2 test or Fisher's exact test. Univariate and multivariate analyses of ΔHb were conducted *via* linear regression. $P < 0.05$ was considered to indicate statistical significance.

RESULTS

Comparison of preoperative general information

In this study, we analyzed and studied the case data of 1722 patients in the Department of Hepatobiliary Surgery at Shandong Provincial Hospital Affiliated to Shandong First Medical University. The cohort included 1083 males and 639 females aged 61.0 (53.0, 67.0) years. Patients were divided into three groups based on the surgical method: The OPD group (n = 511), the LPD group (n = 982), and the CTOPD group (n = 229). The preoperative general characteristics of the patients in the three groups, including age, sex, BMI, comorbid conditions, preoperative alkaline phosphatase, preoperative glutamyl transpeptidase, preoperative Hb concentration, ASA classification, and preoperative total bilirubin, were not significantly different (P > 0.05), as shown in Table 1.

Comparison of mortality rates

The perioperative mortality rates of the three groups are shown in Table 2, and the total mortality rate of the 1722 patients in this study was 1.1%, with no statistically significant difference among the three groups (P > 0.05).

Comparison of EBL and ΔHb among the three groups

There was a statistically significant difference in EBL among the three groups (P < 0.05), with the LPD group having a median EBL of 50.0 (50.0, 200.0) mL, which was lower than that of the other two groups. For IΔHb, the results of 22.00 (12.00, 36.00) g/L in the OPD group and 21.00 (10.00, 33.00) g/L in the LPD group were similar, and both were lower than 33.00 (18.12, 52.24) g/L in the CTOPD group. Statistically significant differences were observed among the three groups (P < 0.05). Similarly, when the PΔHb values of the three groups were compared, the results of 25.87 (13.51, 42.00) g/L in the OPD group were similar to those of 25.00 (14.00, 45.00) g/L in the LPD group, and both were lower than those of 37.48 (21.64, 59.65) g/L in the CTOPD group. Statistically significant differences were also observed among the three groups (P < 0.05), as detailed in Table 3.

Analysis of the relationship between IΔHb and EBL

There was a correlation between IΔHb and EBL in this study (r = 0.337, P < 0.001), as shown in Table 4; thus, IΔHb can be used to assess intraoperative blood loss.

Comparison of IΔHb and PΔHb in patients

A comparison of IΔHb and PΔHb in patients who underwent PD revealed that PΔHb 27.00 (14.00, 45.49) g/L was slightly greater than IΔHb 22.00 (11.00, 36.00) g/L, and the difference between the two was statistically significant (P < 0.05), as shown in Table 5.

Analysis of risk factors affecting patient IΔHb

Univariate regression analysis of IΔHb: Twelve variables were included for univariate regression analysis of IΔHb. The results revealed that ASA classification IV, BMI > 24 kg/m^2, and preoperative total bilirubin > 200 μmol/L were identified as risk factors for IΔHb (P < 0.05), as detailed in Table 6.

Multivariate regression analysis of IΔHb: The statistically significant results were further analyzed *via* multifactorial linear regression analysis. This analysis revealed that ASA classification IV and preoperative total bilirubin > 200 μmol/L were independent risk factors for IΔHb (P < 0.05). These findings suggest that ASA classification IV and elevated preoperative total bilirubin levels (> 200 μmol/L) are associated with a higher risk of intraoperative hemorrhage, as detailed in Table 7.

Analysis of risk factors affecting patient PΔHb

Univariate regression analysis of PΔHb: For the study of PΔHb, we also included 12 variables for univariate regression analysis. The results revealed that ASA classification IV, BMI > 24 kg/m^2, and preoperative total bilirubin > 200 μmol/L were also risk factors for PΔHb (P < 0.05), as shown in Table 8.

Multivariate regression analysis of PΔHb: The above statistically significant results were then analyzed *via* multifactorial linear regression analysis, which revealed that ASA classification IV, BMI > 24 kg/m^2, and preoperative total bilirubin > 200 μmol/L were independent risk factors for PΔHb (P < 0.05), implying that they are associated with increased perioperative bleeding risk, as detailed in Table 9.

DISCUSSION

PD involves a large resection area, requiring the removal of part of the stomach, the entire duodenum, the upper part of the jejunum, part of the pancreas, the gallbladder, and the common bile duct. Additionally, the procedures include pancreaticoenteric anastomosis, bilioenteric anastomosis, and gastrointestinal anastomosis. These factors make PD surgery particularly challenging, leading to numerous unpredictable complications both during and after the operation. Since Gagner and Pomp[2] successfully completed the world's first LPD in 1994, it has gradually gained acceptance in clinical practice and is now widely performed. However, its clinical efficacy remains uncertain. A multicenter clinical trial

Table 1 Comparison of the general patient characteristics among the three groups, *n* (%)

Characteristic	OPD (*n* = 511)	LPD (*n* = 982)	CTOPD (*n* = 229)	*P* value
Sex				
Male	312 (61.1)	616 (62.7)	155 (67.7)	0.223
Female	199 (38.9)	366 (37.3)	74 (32.3)	-
Age (years), interquartile range	61 (54.0-67.0)	61 (53.0-67.0)	61 (52.0-69.0)	0.992
BMI (kg/m^2), interquartile range	23.83 (21.48-26.03)	23.69 (21.77-25.95)	23.68 (21.62-26.22)	0.997
History of abdominal surgery				
Yes	83 (16.2)	135 (13.7)	33 (14.4)	0.430
No	428 (83.8)	847 (86.3)	296 (85.6)	-
History of diabetes				
Yes	98 (19.2)	166 (16.9)	38 (16.6)	0.506
No	413 (80.8)	816 (83.1)	191 (83.4)	-
Preoperative alkaline phosphatase (U/L), interquartile range	301.0 (126.0-516.0)	283.5 (119.75-510.25)	246.0 (97.0-459.5)	0.079
Preoperative glutamyl transpeptidase (U/L), interquartile range	336.0 (84.0-801.0)	372.0 (78.5-806.5)	267.0 (45.0-716.0)	0.132
Preoperative Hb (g/L), interquartile range	127.0 (115.0-138.0)	126.0 (114.0-136.0)	125.0 (114.0-139.0)	0.696
Preoperative albumin (g/L), interquartile range	38.7 (35.4-41.7)	38.5 (35.5-41,4)	38.2 (34.8-41.2)	0.482
ASA classification				
I	2 (0.4)	3 (0.3)	0 (0)	0.905
II	358 (70.1)	701 (71.4)	160 (69.9)	-
III	147 (28.8)	274 (27.9)	68 (29.7)	-
IV	4 (0.8)	4 (0.4)	1 (0.4)	-
Preoperative total bilirubin (μmol/L), interquartile range	82.57 (17.65-197.68)	73.25 (17.97-204.36)	60.07 (14.91-204.55)	0.441

OPD: Open pancreaticoduodenectomy; LPD: Laparoscopic pancreaticoduodenectomy; CTOPD: Conversion to open pancreaticoduodenectomy; BMI: Body mass index; Hb: Hemoglobin; ASA: American Society of Anesthesiologists.

Table 2 Comparison of mortality rates among the three groups, *n* (%)

Characteristic	OPD (*n* = 511)	LPD (*n* = 982)	CTOPD (*n* = 229)	*P* value
Perioperative death				
Yes	4 (0.8)	13 (1.3)	2 (0.9)	0.598
No	507 (99.2)	969 (98.7)	227 (99.1)	-

OPD: Open pancreaticoduodenectomy; LPD: Laparoscopic pancreaticoduodenectomy; CTOPD: Conversion to open pancreaticoduodenectomy.

in the Netherlands aimed to assess the feasibility of LPD by comparing its clinical outcomes with those of OPD. Unfortunately, the trial was prematurely terminated because of the high mortality rate associated with LPD-related complications and safety concerns[15]. Currently, even in experienced high-volume pancreatic centers, the overall complication rate after PD remains 30%-50%[1]. The major complications of PD include bleeding, pancreatic fistula, biliary fistula, and abdominal infection[16]. However, the primary complication that poses the greatest threat to a patient's life is bleeding [17]. The volume of intraoperative blood loss is a vital factor for surgical safety and patient outcomes, making accurate assessment of blood loss and prediction of risk factors essential for surgeons' preoperative preparation and timely intervention.

There are several methods for estimating blood loss, which can be broadly categorized into two types: Visual methods and calculation methods[4]. The visual method is still widely used in clinical practice[6]. However, this method is based on the estimation of blood loss by the surgeon on the basis of personal experience combined with clinical manifestations,

Table 3 Comparison of estimated blood loss and delta hemoglobin among the three groups

Blood loss	OPD (*n* = 511)	LPD (*n* = 982)	CTOPD (*n* = 229)	*P* value
EBL (mL), interquartile range	200.0 (50.0-300.0)	50.0 (50.0-200.0)	200.0 (50.0-400.0)	< 0.001
IΔHb (g/L), interquartile range	22.00 (12.00-6.00)	21.00 (10.00-33.00)	33.00 (18.12-52.24)	< 0.001
PΔHb (g/L), interquartile range	25.87 (13.51-42.00)	25.00 (14.00-45.00)	37.48 (21.64-59.65)	< 0.001

OPD: Open pancreaticoduodenectomy; LPD: Laparoscopic pancreaticoduodenectomy; CTOPD: Conversion to open pancreaticoduodenectomy; EBL: Estimated blood loss; IΔHb: Intraoperative delta hemoglobin; PΔHb: Perioperative delta hemoglobin.

Table 4 Correlation analysis between intraoperative delta hemoglobin and estimated blood loss

Classification	Spearman correlation coefficient	*P* value
IΔHb (g/L)	-	-
EBL (mL)	0.337	< 0.001

EBL: Estimated blood loss; IΔHb: Intraoperative delta hemoglobin.

Table 5 Comparison of intraoperative delta hemoglobin and perioperative delta hemoglobin

Classification	ΔHb (g/L)	*Z* value	*P* value
IΔHb, interquartile range	22.00 (11.00-36.00)	-	-
PΔHb, interquartile range	27.00 (14.00-45.49)	-10.729	< 0.001

ΔHb: Delta hemoglobin; IΔHb: Intraoperative delta hemoglobin; PΔHb: Perioperative delta hemoglobin.

Table 6 Univariate regression analysis of intraoperative delta hemoglobin

Parameter	*B* value	95%CI	*P* value
Age ≥ 65 years	0.236	-2.429-2.901	0.862
History of diabetes	0.724	-2.658-4.107	0.674
History of abdominal surgery	-1.076	-4.721-2.569	0.563
Preoperative biliary drainage	-2.606	-5.948-0.735	0.126
ASA classification IV	19.236	1.420-37.052	0.034
BMI > 24 kg/m^2	2.605	0.031-5.179	0.047
Malignant tumor	-0.717	-4.380-2.946	0.701
Preoperative albumin < 35 g/L	1.834	-1.288-4.955	0.249
Pancreatic tumor	1.737	-0.973-4.447	0.209
Pancreatic carcinoma	2.041	-0.851-4.933	0.166
Ampulla of Vater carcinoma	-0.921	-5.055-3.214	0.662
Preoperative total bilirubin > 200 μmol/L	5.800	2.861-8.738	< 0.001

CI: Confidence interval; ASA: American Society of Anesthesiologists; BMI: Body mass index.

and the results are more subjective[9]. The calculation methods include techniques such as the weighing calculation method and the concentration calculation method. The weighing calculation method estimates blood loss by measuring the weight difference before and after surgery[18]. While it is more accurate than the visual method, it still has significant errors. The method for calculating concentration assesses blood loss by calculating the difference in Hb concentration or hematocrit between the preoperative and postoperative periods[19-21]. This method converts the change in these concen-

Table 7 Multivariate regression analysis of intraoperative delta hemoglobin

Parameter	*B* value	95%CI	*P* value
ASA classification IV	20.071	2.330-37.811	0.049
BMI > 24 kg/m^2	2.576	0.013-5.140	0.078
Preoperative total bilirubin > 200 μmol/L	5.739	2.805-8.673	< 0.001

CI: Confidence interval; ASA: American Society of Anesthesiologists; BMI: Body mass index.

Table 8 Univariate regression analysis of perioperative delta hemoglobin

Parameter	*B* value	95%CI	*P* value
Age ≥ 65 years	-0.293	-4.804-4.219	0.899
History of diabetes	-3.663	-9.385-2.060	0.210
History of abdominal surgery	3.798	-2.369-9.966	0.227
Preoperative biliary drainage	-4.268	-9.924-1.389	0.139
ASA classification IV	73.919	43.926-103.911	< 0.001
BMI > 24 kg/m^2	5.468	1.114-9.822	0.014
Malignant tumor	1.284	-4.916-7.485	0.685
Preoperative albumin < 35 g/L	0.778	-4.507-6.064	0.773
Pancreatic tumor	-0.076	-4.665-4.514	0.974
Pancreatic carcinoma	-0.469	-5.367-4.428	0.851
Ampulla of Vater carcinoma	1.670	-5.327-8.668	0.640
Preoperative total bilirubin > 200 μmol/L	11.975	7.011-16.938	< 0.001

CI: Confidence interval; ASA: American Society of Anesthesiologists; BMI: Body mass index.

Table 9 Multivariate regression analysis of perioperative delta hemoglobin

Parameter	*B* value	95%CI	*P* value
ASA classification IV	75.710	45.934-105.485	< 0.001
BMI > 24 kg/m^2	5.588	1.285-9.890	0.011
Preoperative total bilirubin > 200 μmol/L	11.872	6.948-16.797	< 0.001

CI: Confidence interval; ASA: American Society of Anesthesiologists; BMI: Body mass index.

trations into an estimate of blood loss. However, it overlooks potential variations in blood volume, Hb levels, and hematocrit among patients with different body weights, leading to a certain degree of bias. The concept of ΔHb was introduced by Hogervorst *et al*[22] in their analysis of the impact of Hb concentration reduction during cardiac surgery on postoperative adverse outcomes. Spolverato *et al*[13] introduced ΔHb into general surgery and reported that a postoperative ΔHb ≥ 50% was linked to an increased complication rate. This conclusion was drawn from an analysis of 4669 patients who underwent major abdominal surgeries, including hepatobiliary, pancreatic, and colorectal procedures. However, that study did not account for the impact of blood transfusions on ΔHb. Therefore, we applied this method to PD, incorporating the transfusion factor to derive a modified ΔHb, which provides a more accurate and objective assessment of blood loss during PD. Research indicates that patients require a minimum of 72 hours to mobilize sufficient plasma proteins to normalize intravascular blood volume following acute blood loss and that the Hb concentration stabilizes within 2-4 days after surgery[11,23]. Consequently, we used the Hb concentration at 72 hours postoperatively to calculate IΔHb.

In this study, the analysis of intraoperative blood loss revealed a correlation between IΔHb and EBL, indicating that IΔHb can be used to assess intraoperative blood loss effectively in PD patients. An analysis of the EBL obtained by the visual method in the three groups revealed that the results for the LPD group were lower than those for the other two groups. However, in major abdominal surgeries such as PD, where significant bleeding is common, visual methods often underestimate actual blood loss. This method relies solely on the surgeon's and anesthesiologist's general judgment, making it subjective and potentially inaccurate[24,25]. Especially in laparoscopic surgery, substantial bleeding within the surgical field can hinder the surgeon's visibility and complicate the procedure. If the operation becomes too challenging to continue laparoscopically, it may be converted to open surgery. The inherent visual bias in estimating blood loss during laparoscopic procedures *via* the visual method often leads to an underestimation of the actual amount of bleeding [26]. In our study, the IΔHb values in the LPD, OPD, and CTOPD groups were 22.00 (12.00, 36.00) g/L, 21.00 (10.00, 33.00) g/L, and 33.00 (18.12, 52.24) g/L, respectively, with statistically significant differences among the three groups (P < 0.05). Compared with EBL, the intraoperative blood loss calculated *via* the ΔHb method was significantly greater. This discrepancy can be attributed to two main factors: The inaccuracy of the visual method, which tends to underestimate blood loss, and the use of Hb concentrations measured 72 hours postoperatively. This postoperative period includes not only intraoperative hemorrhage but also additional bleeding from gastrointestinal anastomoses, trauma oozing, stress ulcer bleeding, and other sources within 72 hours after surgery. Intraoperative blood loss was comparable between the OPD and LPD groups, with no statistically significant differences observed. Consistent with the findings of many other studies, LPD did not significantly increase the risk of intraoperative hemorrhage, demonstrating that it is as safe and effective as traditional OPD[27]. Intraoperative blood loss was significantly greater in the CTOPD group than in the other two groups. This can be attributed to the fact that during LPD, patients undergo immediate conversion to open surgery if intraoperative exploration reveals that the tumor is closely related to major blood vessels, making laparoscopic separation difficult, or if intraoperative hemorrhage is difficult to control, thereby compromising the surgical field and procedure. A study by Lof *et al*[28] identified age ≥ 75 years, pancreatic tumors, tumor size > 40 mm, and laparoscopic surgery as risk factors for conversion from LPD to open surgery. Pancreatic tumors, in particular, are more likely to require conversion than periampullary or duodenal tumors are, likely due to their anatomical proximity to major blood vessels[29]. This conversion is associated with an increased incidence of grade B/C PPH, higher 30-day mortality, and other adverse outcomes, which likely explains the greater degree of intraoperative bleeding observed in the CTOPD group. In our study, the conversion rate from LPD to open surgery was 18.9%, which is consistent with the 3.1%-24.6% conversion rates reported in other studies[30-33]. The overall mortality rate among the 1722 patients was 1.1%, which aligns with the 1%-2% mortality rates reported in previous studies[27,34]. There was no significant difference in mortality rates among the three groups, with the CTOPD group having a mortality rate of only 0.9%. This lack of increased mortality in the CTOPD group may be attributed to our proactive approach in converting to open surgery as soon as laparoscopic difficulties were identified, thereby ensuring patient safety.

We conducted univariate and multivariate regression analyses of IΔHb, identifying ASA classification IV and preoperative total bilirubin > 200 μmol/L as independent risk factors for IΔHb. The ASA classification, developed by the ASA, is a preanesthesia assessment tool that categorizes patients on the basis of their physical status and surgical risk, with higher grades indicating greater risk[35]. Studies have demonstrated that the ASA classification is a reliable predictor of postoperative complications, with higher ASA grades being significantly associated with an increased incidence of complications and mortality[36]. Wolters *et al*[37] examined the relationship between the ASA classification and perioperative risk factors in 6301 surgical patients and revealed a significant correlation between the ASA classification and intraoperative bleeding through univariate analysis. Intraoperative bleeding was shown to increase progressively from ASA grade I to grade IV. Consequently, accurate preoperative assessment of a patient's ASA classification is crucial for predicting intraoperative bleeding and enabling timely intervention.

Preoperative total bilirubin > 200 μmol/L was also an independent risk factor for IΔHb. Elevated bilirubin levels due to intrahepatic cholestasis from biliary obstruction lead to hepatic impairment, which in turn affects coagulation. Furthermore, obstructive jaundice is linked to a proinflammatory state caused by systemic endotoxemia, which compromises the body's immune function and inhibits intravascular coagulation[38]. Das *et al*[39] retrospectively analyzed the clinical data of patients who underwent PD between 2007 and 2018 and conducted both univariate and multivariate regression analyses of post-PD bleeding. Their findings indicated that elevated preoperative total bilirubin was an independent risk factor for bleeding in PD patients. Similarly, Wang *et al*[40] demonstrated that in patients with high preoperative bilirubin levels, performing preoperative biliary drainage (PBD) reduced inflammation, alleviated intrahepatic cholestasis, minimized hepatocellular injury, and improved coagulation factor levels and fibrinolytic processes. This intervention ultimately reduced the incidence of overall complications, including grade B/C PPH. Chen *et al*[41] also reported that routine PBD in patients with preoperative total bilirubin > 200 μmol/L could significantly reduce both the complication rate and mortality rate. On the basis of these findings, PBD should be routinely performed in such patients to effectively lower bilirubin levels and mitigate associated risks.

PPH is one of the more severe complications following PD. Although its incidence is lower than that of other complications, PPH remains a leading cause of poor postoperative outcomes. The current incidence of PPH ranges from approximately 3% to 16%, with a mortality rate between 11% and 38%[17,42,43]. PPH is primarily categorized into abdominal bleeding and gastrointestinal bleeding on basis of the bleeding site. However, regardless of the type, current methods only allow for approximate estimation or qualitative assessment rather than precise quantitative analysis. The International Study Group of Pancreatic Surgery classifies PPH into grades A, B, and C on the basis of factors such as the bleeding site, timing, severity, and other clinical considerations[12,44]. Patients with grade A PPH typically exhibit no significant clinical symptoms and have a favorable prognosis, generally not requiring special intervention. In contrast, patients with grade B or C PPH often experience a marked reduction in Hb levels and typically require blood transfusions, interventional embolization for hemostasis, or even additional surgery, which can be life-threatening[45]. The current classification of PPH severity mainly relies on the degree of decrease in the Hb concentration and the volume of blood transfusion during the bleeding episode. However, these criteria are not fully quantitative, leading to potential inaccuracies. Factors such as hemoconcentration at the time of bleeding can result in misleading Hb levels, potentially causing incorrect PPH classification and delays in treatment. For the above reasons, we utilized the ΔHb method and measured the Hb concentration at 72 hours postoperatively and again before discharge. By this time, the patient's blood volume had typically returned to normal, and Hb levels had stabilized, making the calculations more accurate. This approach allows for a more objective and quantitative assessment of postoperative hemorrhage[11].

We also analyzed PΔHb and found that the differences among the three groups paralleled those observed in IΔHb, with significantly higher values in the CTOPD group than in the other two groups. The PΔHb [27.00 (14.00, 45.49) g/L] was slightly greater than the IΔHb [22.00 (12.00, 36.00) g/L] in the patients who underwent PD in this study. This suggests that perioperative hemorrhage primarily occurs during the operation and within the first 72 hours postoperatively, with a comparatively smaller decrease in the Hb concentration after the initial 72-hour period. Univariate and multivariate regression analyses of PΔHb identified ASA classification IV, BMI > 24 kg/m², and preoperative total bilirubin > 200 μmol/L as independent risk factors for PΔHb. Many researchers believe that a high preoperative BMI restricts the surgeon's maneuverability, increases surgical difficulty, and heightens the risk of bleeding. In 2004, Chang *et al*[46] identified high BMI as a predictor of intraoperative bleeding in radical prostatectomy. Similarly, Krane *et al*'s study [47] of 626 patients who underwent laparoscopic colorectal surgery reported a significant increase in intraoperative bleeding in overweight and obese patients. Moreover, Izumo evaluated the incidence and risk factors for PPH among 1169 patients who underwent pancreatectomy and found that a BMI ≥ 25 kg/m² was an independent risk factor for PPH after pancreatectomy, as determined by univariate and multivariate analyses[48]. Their conclusion was that higher BMI levels make surgeries more technically challenging, raising the likelihood of bleeding, which aligns with our findings.

In this research, we used an objective approach to access blood loss and examine bleeding risk factors in patients undergoing PD. However, there are several limitations to our study. Although the results obtained using this method may be influenced by factors such as rehydration, nutritional management, and others, in the vast majority of cases, the patient's blood volume stabilizes within 72 hours post-surgery. Therefore, this method remains an objective and accurate approach for assessing blood loss, especially when compared to the visual method. In addition, as a single-center retrospective analysis, selection bias may have influenced the data collection. Consequently, further multicenter randomized controlled and prospective studies are needed to validate the applicability of this method and to better guide its use in clinical practice.

CONCLUSION

In conclusion, assessing intraoperative blood loss *via* the ΔHb method is more objective and accurate than the visual method, with a demonstrable correlation between the two methods. This approach can be effectively applied to evaluate both intraoperative and perioperative blood loss in patients undergoing PD. Our univariate and multivariate regression analyses revealed that ASA classification IV, BMI > 24 kg/m², and preoperative total bilirubin > 200 μmol/L were significant risk factors for increased bleeding during hospitalization. To improve patient outcomes, surgeons should enhance preoperative preparations to mitigate these risks, thereby benefiting both treatment and prognosis.

FOOTNOTES

Author contributions: Lin YM designed the study, collected and analyzed data, and wrote the manuscript; Yu C participated in the study's conception, data collection, and assisted in writing the manuscript; Lin YM and Yu C they contributed equally to this article, they are the co-first authors of this manuscript; Xian GZ participated in study design and provided guidance; and all authors read and approved the final manuscript.

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Country of origin: China

ORCID number: Yi-Min Lin 0009-0004-5231-7058; Chao Yu 0009-0007-7432-8972; Guo-Zhe Xian 0000-0001-8620-620X.

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