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Retrospective Study

Hemoglobin loss method calculates blood loss during pancreaticoduodenectomy and predicts bleeding-related risk factors

Hemoglobin loss method analyzes blood loss

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

Abstract

BACKGROUND

The common clinical method to evaluate blood loss during pancreaticoduodenectomy (PD) is visual inspection, but most scholars believe that this method is extremely subjective and inaccurate. Currently, there is no accurate, objective method to evaluate the amount of blood loss in PD patients.

AIM

The hemoglobin (Hb) loss method was used to analyze the amount of blood loss during PD , which was compared with the blood loss estimated by traditional visual methods, and the risk factors for bleeding were predicted at the same time.

METHODS

We retrospectively analyzed the clinical data of 341 patients who underwent PD in Shandong Provincial Hospital from March 2017 to February 2019. According to different surgical methods, they were divided into an open pancreaticoduodenectomy (OPD) group and a laparoscopic pancreaticoduodenectomy (LPD) group. The

differences and correlations between the intraoperative estimation of blood loss (IEBL) obtained by visual inspection and the intraoperative calculation of blood loss (ICBL) obtained using the Hb loss method were analyzed. ICBL, IEBL and perioperative calculation of blood loss (PCBL) were compared between the two groups, and single-factor regression analysis was performed.

RESULTS

There was no statistically significant difference in the preoperative general information of the patients between the two groups ($P > 0.05$). PD had an ICBL of 743.2 (393.0, 1173.1) mL and an IEBL of 100.0 (50.0, 300.0) mL ($P < 0.001$). There was also a certain correlation between the two ($r = 0.312$, $P < 0.001$). Single-factor analysis of ICBL showed that a history of diabetes [95% CI (53.82-549.62); $P = 0.017$] was an independent risk factor for ICBL. In addition, the single-factor analysis of PCBL showed that body mass index (BMI) [95% CI (0.62-76.75); $P = 0.046$] and preoperative total bilirubin > 200 μmol/L [95% CI (7.09-644.26); $P = 0.045$] were independent risk factors for PCBL. The ICBLs of the LPD group and OPD group were 767.7 (435.4, 1249.0) mL and 663.8 (347.7, 1138.2) mL, respectively ($P > 0.05$). The IEBL of the LPD group 200.0 (50.0, 200.0) mL was slightly greater than that of the OPD group 100.0 (50.0, 300.0) mL ($P > 0.05$). PCBL was greater in the LPD group than the OPD group [1061.6 (612.3, 1632.3) mL vs. 806.1 (375.9, 1347.6) mL] ($P < 0.05$).

CONCLUSION

The ICBL in the patients who underwent PD was greater than the IEBL, but there is a certain correlation between the two. The Hb loss method can be used to evaluate intraoperative blood loss. A history of diabetes, preoperative bilirubin > 200 μmol/L and high BMI increase the patient's risk of bleeding.

Key Words: Pancreaticoduodenectomy; Hemoglobin loss; Calculated blood loss; Estimated blood loss.

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Core Tip: Visual inspection is commonly used clinically to assess blood loss during pancreaticoduodenectomy (PD), but most scholars believe that this method is extremely subjective and inaccurate. We applied the hemoglobin loss method to calculate the intraoperative and perioperative blood loss in patients with PD, and compared the blood loss of different surgical methods. Univariate regression analysis revealed that a history of diabetes, a preoperative bilirubin concentration >200 µmol/L, and high body mass index (BMI) increased the risk of bleeding.

INTRODUCTION

Pancreaticoduodenectomy (PD) is a classic surgical method for the treatment of benign and malignant tumors such as pancreatic cancer, duodenal cancer, cholangiocarcinoma, and intraductal papillary mucinous tumor of the pancreas. In 1994, the Canadian scholar Gagner *et al*[1] successfully performed the world's first laparoscopic pancreaticoduodenectomy (LPD), pioneering laparoscopic PD. Since then, LPD has been gradually performed more frequently in the clinic. Since the procedure of LPD is extremely complex and difficult, the clinical effect of LPD is not precise when compared with open pancreaticoduodenectomy (OPD)[2, 3]. The indicator that best reflects the clinical efficacy and surgical safety of PD is bleeding because bleeding has the most direct impact on the patient's prognosis and survival. There are many methods for estimating blood loss[4, 5], such as the gravimetric method, formula method, colorimetric method, and visual inspection method. The most commonly used method in clinical practice is visual inspection. However, visual inspection often underestimates the amount of blood loss in patients, and most scholars believe that this approach is extremely subjective and inaccurate[6, 7]. Even surgeons with specific training and

experience have difficulty determining the true amount of blood loss in a patient. In addition, each surgeon has his or her own habits and methods for estimating the amount of bleeding. Even if the estimated amount of bleeding is the same for each patient, there will be large differences in the recorded amounts. Therefore, these methods are even less reliable when comparing blood loss in patients treated with different surgical procedures. To evaluate patient blood loss more accurately and conveniently, we have used the hemoglobin (Hb) mass loss formula[7] to evaluate intraoperative blood loss and perioperative blood loss and introduced the concepts of intraoperative calculation of blood loss (ICBL) and perioperative calculation of blood loss (PCBL). ICBL refers to the amount of blood loss from before the operation to 72 h after the operation, and PCBL refers to the amount of blood loss from before the operation to discharge. This article retrospectively analyzed the amount of blood loss and its risk factors in patients who underwent PD in Shandong Provincial Hospital from 2017.3 to 2019.2 to provide a new method for comparing the amount of blood loss associated with different surgical methods, with the aim of reducing intraoperative and postoperative bleeding.

MATERIALS AND METHODS

General information

In this study, the clinical data of 400 patients who successfully underwent PD in Shandong Provincial Hospital from 2017.3 to 2019.2 were collected, except for 4 patients who did not meet the age requirement, 15 patients who underwent combined resection of other organs, 4 patients with missing test results, and 36 patients who underwent endoscopic conversion to laparotomy. In total, 341 patients were finally included. Based on the surgical method, they were divided into the OPD group (n = 175) and the LPD group (n = 166). Sex, age, body mass index (BMI), preoperative total bilirubin > 200 μmol/L, history of diabetes, history of abdominal surgery, preoperative alkaline phosphatase, preoperative glutamyl transpeptidase, preoperative Hb concentration, and American Society of Anesthesiologists (ASA) classification were not statistically

significant between the two groups ($P > 0.05$). Inclusion criteria: (1) patients who underwent CT, MRI, endoscopic ultrasound or other examinations for preliminary diagnosis before surgery; (2) patients with surgical indications for PD and no surgical contraindications; (3) patients with no invasion of the portal vein, mesenteric arteries and veins, inferior vena cava, *etc.*, and no distant metastasis to other organs such as the liver, abdominal cavity, *etc.*; (4) patients with no heart, lung, brain, kidney and other important organ insufficiency;(5) patients aged 18-80 years old; and (6) patients who signed informed consent for surgery or whose family member signed it. Exclusion criteria: (1) patients with heart, lung, brain or other functional insufficiency; (2) patients with incomplete case information; and (3) patients who underwent combined multiorgan resection such as liver, colon, and superior mesenteric vessel resection.

Surgical method

All LPD surgeries were completed laparoscopically in the following manner: (1) First, we explore the abdominal cavity to determine whether there is metastasis to any of the abdominal organs. (2) Second, resection and lymph node dissection were performed. (3) Finally, the digestive tract was reconstructed. The specific surgical steps are detailed in the expert consensus on LPD[8]. The surgical method of OPD is mainly classic PD. Its process of separation and resection method, lymph node dissection sequence, and digestive tract reconstruction are basically the same as in LPD.

Observe and analyze indicators

The preoperative general information of the two groups of patients treated with OPD and LPD was compared, including sex, age, BMI, history of diabetes, history of abdominal surgery, preoperative alkaline phosphatase, preoperative glutamyl transpeptidase, preoperative Hb concentration, ASA classification, preoperative total bilirubin > 200 μmol/L, and the intraoperative estimation of blood loss (IEBL), ICBL, and PCBL were compared between the two groups. The differences and correlations

between the patients' IEBL and ICBL were analyzed, and univariate regression analysis was performed on ICBL and PCBL.

Formula

Hb mass loss formula:

$mHb_{CBL} = 1000 * (Hb_{preop} - Hb_{postop}) * BV + Infusion\ of\ Hb$

mHb_{CBL} (g): Calculated Hb mass loss

Hb_{preop} (g/L): The patient's preoperative Hb concentration

Hb_{postop} (g/L): Hb concentration within 72 h after surgery or before discharge

BV (mL): Patient estimated blood volume calculated using the ICSH formula[9]

Infusion of Hb (g): Amount of Hb infused by the during surgery or perioperative period

Calculate blood loss (mL):

Male: [mHb_{CBL} (g) / 140 (g/L)] * 1000

Female: [mHb_{CBL} (g) /130 (g/L)] * 1000

Statistical analysis and processing

SPSS 25.0 statistical software was used for analysis and processing. Measurement data that conformed to the normal distribution are expressed as mean ± SD, and they were compared between groups using the *t* test of two independent samples. Measurement data that did obey the normal distribution are represented by median (interquartile range), and these were compared between groups using the rank sum test. Count data are expressed as n (%), and the c^2 test or Fisher's exact test was used for comparison between groups. When $P < 0.05$, the difference was considered statistically significant.

RESULTS

Comparison of general information before surgery

This trial retrospectively analyzed the clinical data of 341 patients who were treated in the Hepatobiliary Surgery Department of Shandong Provincial Hospital, including 201 males and 140 females, aged 60.0 (52.0, 65.0) years old. According to the surgical

method, they were divided into the LPD (*n* = 166) group and the OPD group (*n* = 175). The general preoperative information of the patients such as age, sex, BMI, combined underlying diseases (history of diabetes, abdominal surgery), preoperative total bilirubin > 200 µmol/L, preoperative carcinoembryonic antigen (CEA), preoperative alkaline phosphatase, preoperative Hb concentration, and ASA classification was not significantly different between the two groups (*P* > 0.05) (Table 1).

Compare the blood loss between OPD and LPD and analyze the relationship between IEBL and ICBL

ICBL was 767.7 (435.4, 1249.0) mL in the LPD group, which was slightly greater than the 663.8 (347.7, 1138.2) mL in the OPD group, but it was not significantly difference between the two groups (*P* > 0.05). In addition, the blood loss in the LPD group was 200.0 (50.0, 200.0) mL, which was more than the 100.0 (50.0, 300.0) mL in the OPD group, but not significantly (*P* > 0.05). Compared with the OPD group, the LPD group had greater PCBL, at 1061.6 (612.3, 1632.3) mL vs. 806.1 (375.9, 1347.6) mL (*P* < 0.05) (Table 2).

In this study, PD patients had greater ICBL than IEBL, at 743.2 (393.0,1173.1) mL and 100.0 (50.0,300.0) mL, respectively (*P* < 0.001) (Table 3). There is also a certain correlation between IEBL and ICBL (*r* = 0.312, *P* < 0.001) (Table 4).

ICBL and PCBL single factor regression factor analysis

This study included 8 variables in the single-factor regression analysis of ICBL. The results showed that a history of diabetes was an independent risk factor for ICBL (*P* < 0.05), which meant that a history of diabetes before surgery was expected to increase the amount of intraoperative bleeding. Age, abdominal surgery history, BMI, nature of tumor, preoperative albumin levels, pancreatic tumors, *etc.*, were not related to ICBL by univariate analysis (*P* > 0.05) (Table 5).

For the study of PCBL, we also included 8 variables in a single-factor regression analysis. The results show that BMI and preoperative total bilirubin > 200 μmol/L are independent risk factors for perioperative blood loss ($P < 0.05$), indicating that high BMI and preoperative total bilirubin > 200 μmol/L will increase the risk of perioperative blood loss and the risk of intraoperative bleeding. The results of the PCBL univariate analysis are shown in Table 6.

DISCUSSION

Pancreas-specific complications are a major cause of severe morbidity and mortality[10]. Pancreatic fistula, biliary fistula, delayed gastric emptying, bleeding, *etc.*, are common complications of PD, and they are also important reasons for delayed postoperative recovery of patients[11, 12]. Generally, the most important factor that threatens a patient's life is bleeding[13, 14], including intraoperative bleeding and postoperative bleeding.

We often describe intraoperative bleeding through IEBL and the blood transfusion rate. There are many methods to estimate intraoperative blood loss[4, 5], such as the gravimetric method, formula method, visual inspection method, *etc.* The more commonly used method in clinical practice is visual inspection [15, 16]. The visual inspection method is also called the visual estimation method[17]. During the operation, doctors and anesthesiologists estimate blood loss by visually assessing the color and flow rate of the blood, size of the blood pool, amount of blood soaked into the gauze, amount of blood observed on the doctor's gloves, and volume of blood on clothes, but intraoperative blood loss estimated by this method is considered by most scholars to be extremely subjective and inaccurate[7]. Even surgeons with specific training and experience have difficulty determining the true amount of blood loss in a patient. In addition, each surgeon has different habits and methods for estimating it. Even if the amount of bleeding is estimated for the same patient, there will be large differences. Therefore, the reliability is reduced when comparing the blood loss of different surgical methods. The gravimetric method[18, 19] is relatively accurate. Generally, the amount of blood loss is estimated by weighing the amount of the suction bucket and the gauze and

absorbent materials used before and after the operation, and calculating the weight difference. This method is too cumbersome and requires weighing the gauze and absorbent material before and after the operation, and it also does not account for the blood that not collected by the suction device or gauze during the operation, which may lead to underestimation of intraoperative blood loss. Large amounts of blood loss during surgery can promote systemic inflammatory responses and have a negative impact on the prognosis of postoperative patients. Therefore, surgeons should accurately assess patients' intraoperative blood loss and strive to reduce blood loss and blood transfused during surgery to improve patient prognosis[20, 21]. To more accurately estimate the intraoperative blood loss of patients, Jaramillo *et al*[7] studied 100 patients who underwent laparoscopic urological surgery. Comparing the Hb mass loss formula method, the López-Picado formula method and the empirical volume formula method, they found that the Hb mass loss formula method has advantages over other methods in assessing various parameters of blood loss. Therefore, we can calculate the amount of Hb lost by comparing the changes in the patient's Hb concentration from before to after surgery, and from this calculate the patient's intraoperative blood loss more accurately and objectively.

Although the incidence of post pancreaticoduodenectomy hemorrhage (PPH) is low, it is the main cause of adverse patient outcomes. The current incidence of PPH ranges from 1% to 8%[22], but its mortality rate is as high as 11% to 38%. PPH is mainly divided into abdominal bleeding and gastrointestinal bleeding according to the location of bleeding[23-25]. When a patient suffers from abdominal bleeding after surgery, because there is not only blood in the abdominal drainage bag but also exudate, leakage, *etc.*, the amount of blood loss calculated from the scale on the drainage bag is inaccurate. On the other hand, when gastrointestinal bleeding occurs, the amount of hematemesis, melena, or bleeding fluid drained from the gastric tube cannot be measured directly. Whether it is abdominal bleeding or gastrointestinal bleeding, we can only make qualitative judgments and cannot conduct quantitative analysis. In such cases, the Hb mass loss method can quantitatively calculate the patient's postoperative blood loss. Therefore, in

this study, we calculated the patient's intraoperative blood loss and perioperative blood loss through changes in Hb concentration, and analyzed their risk factors to provide empirical data support for improving PD.

The results of this study showed that the intraoperative blood loss estimated by the surgeon, 100.0 (50.0, 300.0) mL, was significantly less than the ICBL of 743.2 (393.0, 1173.1) mL by the Hb loss method ($P < 0.05$). It shows that there is a difference in the intraoperative blood loss obtained by the two methods. This situation occurs, on the one hand, because visual inspection will underestimate the patient's intraoperative blood loss[6]; on the other hand, it may be related to the fact that we count Hb loss from before surgery to 72 h after surgery. However, there is a certain significant positive correlation between IEBL and ICBL. The intraoperative blood loss estimated by experienced and trained surgeons can reflect the patient's true blood loss to a certain extent. In this study, the IEBL of OPD and LPD was 100.0 (50.0,300.0) mL and 200.0 (50.0, 200.0) mL, respectively ($P > 0.05$). The ICBL of OPD and LPD was 663.8 (347.7, 1138.2) mL and 767.7 (435.4, 1249.0) mL, respectively ($P > 0.05$). Whether IEBL or ICBL, the blood loss of the LPD group was greater than that of the OPD group, which may be mainly related to the shorter development time of LPD in our center. We also analyzed the risk factors related to ICBL and found that a history of diabetes [95% *CI* (53.82-549.62): $P = 0.017$] is an independent risk factor for ICBL, which means that a history of diabetes before surgery will increase the patient's risk of intraoperative bleeding. Diabetes can cause coagulation defects by causing changes in coagulation protein concentration and changes in metal ion homeostasis, thereby affecting physiological changes and functions of hemostasis[26, 27]. Diabetes is an independent risk factor for atherosclerosis[28]. Diabetes will cause atherosclerosis of small arteries, weakening the endothelial cells of small arteries, making blood vessels more likely to rupture and atherosclerosis easily leads to thrombus formation, leading to tissue hypoxia, accumulation of lactic acid, and increased permeability of blood vessel walls. Some scholars believe that normal platelet function is essential for surgical hemostasis. Diabetes can cause changes in glycoprotein molecules on the surface of patients'

platelets, thereby affecting hemostatic function[29]. When Zheng *et al*[30] studied the relationship between blood sugar and incidence of cerebral hemorrhage, they found that high blood sugar level was significantly related to the poor prognosis of patients with cerebral hemorrhage, indicated by an increased short-term and long-term mortality risk. In addition, research by Zhang *et al*[31] also shows that elevated blood sugar can damage the integrity of microvessels and easily cause bleeding. Therefore, controlling the patient's perioperative blood sugar level and maintaining a stable internal environment are extremely important for surgical safety[32].

We also performed a quantitative analysis of PCBL, which is intraoperative plus postoperative blood loss. PCBL can not only reveal the patient's overall surgical effect during hospitalization but also indirectly reflect the patient's postoperative blood loss. According to the definition of the International Study Group on Pancreatic Surgery (ISGPS)[23], PPH can be divided into grade A, grade B and grade C. In this study, 17 patients had grade C bleeding, accounting for 4.5% of all cases of postoperative bleeding. Among them, 6 had gastrointestinal bleeding and 11 had abdominal bleeding, indicating that severe postoperative bleeding was mainly caused by abdominal bleeding. At present, there are relatively few studies using perioperative blood loss on the overall surgical effect during and after PD. Therefore, we analyzed it from the perspective of PCBL to provide a basis for the development of PD. The PCBL of the OPD and LPD groups was 806.1 (375.9,1347.6) mL and 1061.6 (612.3,1632.3) mL, respectively ($P < 0.05$). This shows that the overall blood loss of LPD is greater than that of OPD. This is mainly because the pancreatic-intestinal and gastrointestinal anastomoses are reinforced and sutured during OPD, which decrease the loss of postoperative Hb and reduce the patient's risk of postoperative bleeding. We found that the PCBL of patients undergoing PD in our center was 886.4 (487.3, 1466.2) mL, and performed a univariate analysis on the risk factors for PCBL. It was found that preoperative total bilirubin level > 200 μmol/L [95% *CI* (7.09-644.26); $P = 0.045$] and BMI [95% *CI* (0.62-76.75); $P = 0.046$] were independent risk factors for PCBL, indicating that preoperative total bilirubin > 200 μmol/L and high BMI increase the risk of

perioperative bleeding. Preoperative total bilirubin > 200 μmol/L can impair liver function and weaken coagulation function, while also causing endotoxemia, impairing the body's immune function, and inhibiting intravascular coagulation of blood cells[33]. Wang et al[34] analyzed the clinical data of patients who underwent PD from 2009 to 2014. Their single- and multi factor analyses on post-PD bleeding, showed that higher total bilirubin concentration was an independent risk factor for PD bleeding. Shen et al[35] conducted a retrospective cohort study of patients who underwent percutaneous bile duct drainage (PBD) and found that PBD reduced the incidences of overall complications and grades B and C bleeding after PD. They pointed out that for patients with total bilirubin > 250 μmol/L, PBD should be routinely performed before surgery. Studies have shown that a high BMI will limit the surgeon's surgical options, make the operation more difficult, and increase the patient's risk of bleeding. In an observational study[36], 155,332 patients at risk for atherogenesis participated in a clinical trial of clopidogrel. Compared with patients with a high BMI, patients with a low BMI had a lower risk of bleeding, in line with the idea that patients with a high BMI have an increased risk of bleeding and consistent with the results of our study. Farvacque et al[37] analyzed risk factors for post pancreatectomy bleeding in 307 patients and found that higher BMI was associated with bleeding. They concluded that higher BMI will increase the technical difficulties during various operations, leading to an increased risk of bleeding and an increase in bleeding volume.

In this study, we provide an objective method for assessing blood loss during PD and analyze risk factors for bleeding. However, this study also has certain limitations. First, this is a retrospective study, which may be affected by selection bias during data collection. Secondly, this is a single-center study. In the future, multi-center studies with well-designed and larger sample sizes are needed for verification.

CONCLUSION

In summary, we found that there are some differences between intraoperative blood loss estimated using visual inspection and intraoperative blood loss calculated using the Hb loss method, but there is also a correlation between the two. The Hb loss method can be used to calculate the intraoperative and perioperative blood loss of PD patients, and to compare the blood loss of different surgical methods. Univariate regression analysis showed that a history of diabetes, preoperative bilirubin >200 μmol/L, and high BMI increase the PD patient's bleeding risk.

ARTICLE HIGHLIGHTS

Research background

The most common way to evaluate blood loss during pancreaticoduodenectomy (PD) is visual inspection, but this method is inaccurate. The hemoglobin (Hb) loss method provides a new way to evaluate blood loss during PD.

Research motivation

There was no accurate and objective way to assess blood loss in PD and thus to identify the risk factors for blood loss.

Research objectives

The Hb loss method was used to analyze blood loss during PD and predict risk factors for bleeding.

Research methods

We retrospectively collected the clinical data of 341 patients who underwent PD in Shandong Provincial Hospital from March 2017 to February 2019. The differences and correlations between the intraoperative estimation of blood loss (IEBL) obtained by visual inspection and the intraoperative calculation of blood loss (ICBL) obtained using the Hb loss method were analyzed. Univariate regression analysis was performed on ICBL, IEBL, and perioperative calculation of blood loss (PCBL).

Research results

PD had an ICBL of 743.2 (393.0, 1173.1) mL and an IEBL of 100.0 (50.0, 300.0) mL ($P < 0.001$), but the two were also correlated ($r = 0.312$, $P < 0.001$). Single-factor analysis of ICBL showed that a history of diabetes [95% CI (53.82-549.62); $P = 0.017$] was an independent risk factor for ICBL. In addition, the single-factor analysis of PCBL showed that body mass index (BMI) [95% CI (0.62-76.75); $P = 0.046$] and preoperative total bilirubin > 200 µmol/L [95% CI (7.09-644.26); $P = 0.045$] were independent risk factors for PCBL.

Research conclusions

The Hb loss method can be used to evaluate intraoperative blood loss. A history of diabetes, preoperative bilirubin > 200 µmol/L and high BMI increase the patient's risk of bleeding.

Research perspectives

This study provides an objective measure to evaluate blood loss during PD and thoroughly explores the risk factors for bleeding.

Footnotes

Institutional review board statement: The study was reviewed and approved by the Ethics Committee of the Shandong Provincial Hospital Affiliated to Shandong First Medical University (Shandong Provincial Hospital) [Approval No. 2023-462].

Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

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