Risk factors for 30-day unplanned reoperation after pancreateoduodenectomy: A single-center experience

ABSTRACT

Objective: The purpose of this study was to investigate the rate and reasons and also the risk factors for unplanned reoperation after pancreateoduodenectomy (PD) in a single center.

Patients and Methods: This retrospective analysis included patients who underwent PD in the First Affiliated Hospital of Nanchang University between January 2010 and January 2018. The patients were divided into nonreoperation and reoperation groups according to whether they underwent unplanned reoperation following the primary PD. The incidence and reasons were examined. In addition, multivariate logistic regression analysis was performed to identify the risk factors for unplanned reoperation.

Results: Of the 330 patients who underwent PD operations, 22 (6.67%) underwent unplanned reoperation. The main reasons for reoperation were postpancreaticoduodenectomy hemorrhage (PPH) (12/22 [54.5%]) and pancreaticoenteric anastomotic (PEA) leak (5/22 [22.7%]). Multivariate logistic regression analyses identified that diabetes (odds ratio [OR], 3.70; 95% confidence interval [CI], 1.06–12.90; \(P=0.04\)), intraoperative blood loss ≥400 mL (OR, 4.06; 95% CI, 1.29–12.84; \(P=0.02\)), occurrence of postoperative complications in the form of PPH (OR, 30.67; 95% CI, 8.85–106.31; \(P<0.001\)), and PEA leak (OR, 11.53; 95% CI, 3.03–43.98, \(P<0.001\)) were independent risk factors for unplanned reoperation.

Conclusions: Our results suggest that diabetes, intraoperative blood loss ≥400 mL, PPH, and PEA leak were independent risk factors for unplanned reoperation after primary PD.

KEY WORDS: Complications, pancreateoduodenectomy, reoperation, risk factors

INTRODUCTION

Pancreateoduodenectomy (PD) is the routine available curative operation measure for the treatment of malignant or potentially malignant pancreatic and periampullary tumors.[1] In recent years, the PD-related perioperative mortality rate has decreased significantly, but the incidence of postoperative complications remains high (range, 20%–60%).[2] As a result, patients who develop complications after PD can have fatal outcomes and may require unplanned surgical interventions despite the use of radiological and endovascular interventions.

For patients and surgeons, unplanned reoperation after primary surgery is an adverse event that not only increases treatment costs and extends hospital stays, it increases morbidity and mortality rates that are associated with poor results.[3] In multiple organizations, unplanned reoperation was suggested as a useful screening indicator for quality assurance in clinical practice.[4,5] Consequently, full knowledge and understanding of the incidence, reasons for, and risk factors for unplanned reoperation after PD contributes to improving the clinical outcomes of surgical therapy and can effectively avoid it. To our knowledge, no studies to date have reported the reoperation rates of and reasons for PD or the risk factors for unplanned reoperation after PD.

With the above in mind, this retrospective study analyzed the clinical data of 330 patients who underwent PD in our hospital and investigated the incidences of, reasons for, and risk factors for unplanned reoperation after PD.
PATIENTS AND METHODS

Patients
The study protocol received approval from the Human Research Ethics Committee of First Affiliated Hospital of Nanchang University, and the patients and their family members provided informed consent. The related clinical data of the patients who underwent conventional or pylorus-sparing PD between January 2010 and January 2018 were retrospectively reviewed. The primary eligibility criterion was having undergone PD due to periampullary malignant or potentially malignant tumors and some other certain benign diseases. The exclusion criteria were other synchronous diseases requiring surgical intervention and having undergone emergency PD.

Clinical and surgical outcome measures
Unplanned reoperation, the primary outcome, was defined as an unanticipated return to the operating room for relaparotomy involving general anesthesia and tracheal intubation within 30 days after the initial PD. Demographic variables (age, sex, marital status, and body mass index), protopathy, medical history, concomitant diseases (hypertension, diabetes mellitus, cardiovascular and cerebrovascular disease, chronic pulmonary disease), preoperative serologic indexes (bilirubin, albumin, international normalized ratio), intraoperative outcomes (time, estimated blood loss, and procedure characteristics), and postoperative complications after the primary PD surgery were obtained from the database of the First Affiliated Hospital of Nanchang University.

Statistical analyses
The statistical analysis was performed using SPSS Statistics 22.0. (IBM Corp., Armonk, NY). The Chi-square or Fisher’s exact test was used as appropriate to evaluate the potential differences in categorical variables, while Student’s t-test was used to examine continuous variables. Univariate analyses using the Chi-square test were performed to evaluate the risk factors for unplanned reoperation. The factors with \( P \leq 0.1 \) on univariate analyses were included in the multivariate logistic regression analysis. \( P < 0.05 \) was considered statistically significant.

RESULTS

Unplanned reoperation rates
From 2010 to 2018, a total of 330 patients (213 men, 117 women; mean age, 57.0 ± 9.4 years) underwent PD at the First Affiliated Hospital of Nanchang University. Among them, 22 (6.67%) underwent an unplanned reoperation within 30 days after their primary surgery. Of the patients who underwent revision surgery, 18 were diagnosed with malignant disease and 4 were diagnosed with benign disease. The patients’ baseline clinical and operative characteristics are summarized in Table 1.

Reasons for reoperation
Reasons for the unplanned reoperation included postpancreaticoduodenectomy hemorrhage (PPH) (12/22 [54.5%]), pancreaticoenteric anastomotic (PEA) leak (5/22 [22.7%]), hepaticojejunostomy (HJ) leak (2/22 [9.1%]), wound dehiscence due to an incision infection (2/22 [9.1%]), and miscellaneous causes (1/22 [4.5%]). The incidence of PPH was significantly higher than those of other reoperation reasons, and all PPH cases were confirmed by arterial angiography or revision surgery. For the PPH, suture ligation of the bleeding vessels or the cut surface and adequate abdominal drainage

Table 1: The baseline clinical and operative characteristics of the patients

| Variables                        | Reoperation group (n=22) | Nonreoperation group (n=308) | \( \chi^2 \) or \( t \) | \( P \) |
|----------------------------------|-------------------------|-----------------------------|-------------------------|-------|
| Sex (male:female)                | 16:6                    | 197:111                     | 0.69                    | 0.41  |
| Age (years)                      | 57.36±8.15              | 56.97±9.49                  | 0.19                    | 0.27  |
| BMI (kg/m\(^2\))                 | 21.40±2.80              | 21.71±2.91                  | 0.49                    | 0.79  |
| ASA scores (1+2:3+4)             | 5:17                    | 197:111                     | 0.21                    | 0.65  |
| Current smoker (yes:no)          | 10:12                   | 98:210                      | 1.73                    | 0.19  |
| Current drinker (yes:no)         | 6:16                    | 77:231                      | 0.06                    | 0.81  |
| History of abdominal surgery (yes:no) | 5:17                  | 47:261                      | 0.86                    | 0.35  |
| Protopathy (benign:malignant)    | 4:18                    | 261:47                      | 1.94                    | 0.16  |
| Comorbidities                    |                         |                             |                         |       |
| DM (yes:no)                      | 9:13                    | 19:289                      | 31.92                   | <0.001|
| CAD (yes:no)                     | 6:16                    | 51:257                      | 1.65                    | 0.20  |
| COPD (yes:no)                    | 2:20                    | 32:276                      | 0.04                    | 0.85  |
| CKD (yes:no)                     | 3:19                    | 20:288                      | 1.62                    | 0.20  |
| Preoperative total bilirubin (umol/L) | 102.45±141.04          | 117.34±109.32               | 0.61                    | 0.57  |
| Preoperative albumin (g/L)       | 37.58±8.32              | 40.62±29.38                 | 0.48                    | 0.95  |
| Preoperative hemoglobin (g/L)    | 114.50±19.98            | 118.40±18.01                | 0.97                    | 0.27  |
| Operation time (min)             | 404.77±99.98            | 374.59±79.87                | 1.68                    | 0.24  |
| Intraoperative blood loss (ml)   | 654.55±333.06           | 404.09±224.09               | 4.88                    | <0.001|
| INR                              | 1.00±0.74               | 1.01±0.12                   | 0.29                    | 0.36  |
| Blood transfusion (yes:no)       | 10:12                   | 55:2530                     | 9.89                    | 0.02  |
| Vascular reconstruction (yes:no) | 5:17                    | 44:264                      | 1.16                    | 0.28  |
| Stapling apparatus (yes:no)      | 19:3                    | 260:48                      | 0.06                    | 0.81  |
| Somatostatin (yes:no)            | 20:2                    | 286:22                      | 0.12                    | 0.73  |

BMI=Body mass index, ASA=American Society of Anesthesiologist, DM=Diabetes mellitus, CAD=Coronary artery disease, COPD=Chronic obstructive pulmonary disease, CKD=Chronic kidney disease, INR=International Normalized Ratio
were the most common surgical protocols. Of the 12 patients who underwent reoperation for PPH, 10 patients recovered after the first reoperation, while the other two patients presented with rebleeding. Of the two patients, one recovered after transcatheter arterial embolization (TAE) and the other died after a second reoperation. Seven patients underwent relaparotomy for anastomotic leakage with intra-abdominal collection due to percutaneous drainage failure. The detailed surgical indications, treatments, and unplanned reoperation outcomes are presented in Table 2.

Risk factor analysis
In the univariate analysis [Table 3], diabetes, intraoperative blood loss ≥400 mL, and the occurrence of postoperative complications in the form of PPH and PEA leak were identified as risk factors for reoperation. Multivariate logistic regression analysis [Table 4], which included factors with \( P \leq 0.1 \) on univariate analysis, identified that diabetes, intraoperative blood loss ≥400 mL, and the occurrence of postoperative complications in the form of PPH and PEA leak were independent risk factors for unplanned reoperation.

DISCUSSION
Unplanned reoperation was defined as an unanticipated return to the operating room for a relaparotomy involving general anesthesia and tracheal intubation within 30 days after the primary surgery. Unplanned reoperations were usually due to serious postoperative complications after PD, such as PPH, PEA leak, intestinal obstruction, intra-abdominal infection, HJ leak, duodenocjejunostomy leak, and incision infection. However, reoperation not only causes more trauma for patients, but it also increases their economic and psychological burden and requires much more medical resources because of the prolonged hospital stay. Therefore, identifying the potential risk factors of reoperation ahead of time and then intervening with the risk factors and strengthening the perioperative management is very important for patients, their families, surgeons, and society as a whole.

Unfortunately, studies that aimed to investigate the incidences of reoperation after initial PD are rare. A retrospective study examined the reoperation incidence following PD and showed a relaparotomy rate of 18.5% (99/520). Another study by Chen Dong et al. found that patients underwent PD had a reoperation rate of 7.1% (24/339). Lyu et al. recently conducted a study including 9949 patients who underwent PD in 435 hospitals participating in the American College of Surgeons National Surgical Quality Improvement Program demonstrated a reoperation rate of 5.9% (585/9949). In detail, the revision rate of conventional PD was 6.2%, while that of pylorus-preserving PD was 5.4%. In the current study, the reoperation rate was 6.67%, which was consistent with the rates reported in previous studies.

PPH, the most dreaded complication following PD, has associated mortality rates as high as 30% and an overall incidence of 4%–16%. Therefore, 64% of patients require intervention and over 35% require more than one procedure. Indeed, hemorrhage is an important predictor of prognosis and mortality. Although uncommon, PPH is the most common indication for reoperation. In our study, nearly 54.5% (12/22) of our patients underwent reoperation attributable to PPH.

Early PPH is directly related to the surgical procedure, such as incomplete hemostasis, lack of experience with vessel ligature, and unreasonable use of gastrointestinal staple, while delayed PPH is often related to pseudoaneurysm formation, wound

Table 2: Unplanned reoperation after pancreatoduodenectomy (n=22)

| Number | Sex, age | Reason for reoperation | Reoperation | Interval (d) |
|--------|----------|------------------------|-------------|--------------|
| 1      | Male, 53 | Mesocolic artery bleeding | Suture      | 0.5          |
| 2      | Male, 72 | Wound dehiscence        | Relaxation suture | 15          |
| 3      | Female, 58 | PEA leak            | Debridement and drainage | 10          |
| 4      | Male, 57 | GJ bleeding           | Suturing of GJ site bleed | 12          |
| 5      | Male, 64 | PEA bleeding          | Suturing of PEA site bleed | 3           |
| 6      | Female, 43 | HJ leak              | Repair over T-tube | 6           |
| 7      | Male, 54 | HJ bleeding           | Suturing of HJ site bleddr | 4.5         |
| 8      | Female, 53 | HJ leak             | Repair over T-tube | 10          |
| 9      | Male, 76 | Miscellaneous         | Dismantling and resiting of GJ | 18          |
| 10     | Male, 56 | Wound dehiscence      | Relaxation suture | 20          |
| 11     | Male, 45 | GDA bleeding          | Suture      | 1.8          |
| 12     | Male, 66 | Portal vein and splenic vein bleeding | Suture and splenectomy | 2           |
| 13     | Female, 56 | PEA leak            | Debridement and drainage | 8           |
| 14     | Male, 51 | Omentum arterial bleeding | Suture      | 3           |
| 15     | Male, 57 | HJ bleeding           | Suturing of HJ site bleed | 4           |
| 16     | Male, 61 | Hepatic arterial bleeding | Suture      | 0.2          |
| 17     | Female, 64 | PEA bleeding | Suturing of PEA site bleed | 5.5         |
| 18     | Male, 54 | PEA leak             | Debridement and drainage | 11          |
| 19     | Male, 56 | Lesser curvature adipose tissue bleeding | Suture | 6           |
| 20     | Male, 48 | PEA leak             | Debridement and drainage | 15          |
| 21     | Female, 66 | PEA leak           | Debridement and drainage | 17          |
| 22     | Male, 52 | PEA bleeding         | Suturing of PEA site bleed | 2           |

PPA=Pancreaticoenteric anastomosis, GJ=Gastrojejunostomy, HJ=Hepaticojejunostomy, GDA=Gastroduodenal artery
Table 3: Univariate analysis for unplanned reoperation after pancreatoduodenectomy

| Variables                               | Reoperation group (n=22) | Nonreoperation group (n=308) | \( \chi^2 \) | \( P \) |
|-----------------------------------------|-------------------------|-------------------------------|-------------|--------|
| Sex (male:female)                       | 16:6                    | 197:111                       | 0.69        | 0.41   |
| Age (≥65/<65)                           | 4:18                    | 66:242                        | 0.13        | 0.72   |
| Age (≥70/<70)                           | 2:20                    | 17:291                        | 0.92        | 0.34   |
| BMI (≥25/<25)                           | 3:19                    | 38:270                        | 0.03        | 0.86   |
| ASA scores (≥3/<3)                      | 17:5                    | 111:197                       | 0.21        | 0.65   |
| Current smoker (yes/no)                 | 10:12                   | 98:210                        | 1.73        | 0.19   |
| Current drinker (yes/no)               | 6:16                    | 77:231                        | 0.06        | 0.81   |
| History of abdominal surgery (yes/no)   | 5:17                    | 47:261                        | 0.86        | 0.35   |
| Pathology (benign:malignant)            | 4:18                    | 28:280                        | 1.94        | 0.16   |
| Comorbidities                           |                         |                               |             |        |
| DM (yes/no)                             | 7:15                    | 25:283                        | 13.17       | <0.001 |
| CAD yes/no                              | 6:16                    | 51:257                        | 1.65        | 0.20   |
| COPD (yes/no)                           | 2:22                    | 32:276                        | 0.04        | 0.85   |
| CKD (yes/no)                            | 3:19                    | 20:288                        | 3.06        | 0.08   |
| Indications for reoperation             |                         |                               |             |        |
| PPH (yes/no)                            | 14:8                    | 28:280                        | 55          | <0.001 |
| PEA leak (yes/no)                       | 8:14                    | 46:262                        | 6.89        | <0.001 |
| HJ leak (yes/no)                        | 4:18                    | 29:279                        | 1.75        | 0.19   |
| Incision infection (yes:no)             | 2:20                    | 14:298                        | 0.92        | 0.34   |
| Preoperative total bilirubin (≥34.2/<34.2) | 9:13                    | 196:112                       | 4.51        | 0.03   |
| Preoperative total bilirubin (≥171/<171) | 4:18                    | 94:214                        | 1.50        | 0.22   |
| Preoperative albumin (≥35/<35)          | 16:6                    | 236:72                        | 0.17        | 0.68   |
| Preoperative hemoglobin (≥100/<100)     | 16:6                    | 225:83                        | 0         | 0.97   |
| Preoperative hemoglobin (≥120/<120)     | 11:11                   | 146:162                       | 0.06        | 0.82   |
| Operation time (≥300/<300)              | 10:12                   | 109:199                       | 0.90        | 0.34   |
| Intraoperative blood loss (≥400/<400)   | 16:6                    | 96:212                        | 12.93       | <0.001 |
| Blood transfusion (yes/no)              | 10:12                   | 55:253                        | 9.89        | 0.02   |
| Vascular reconstruction (yes/no)        | 5:17                    | 44:264                        | 1.16        | 0.28   |
| Stapling apparatus (yes/no)             | 19:3                    | 260:49                        | 0.96        | 0.31   |
| Somatostatin (yes/no)                   | 20:2                    | 286:22                        | 2.59        | 0.01   |

BMI=Body mass index, ASA=American Society of Anesthesiologist, DM=Diabetes mellitus, CAD=Coronary artery disease, COPD=Chronic obstructive pulmonary disease, CKD=Chronic kidney disease, HJ=Hepaticojejunostomy, PPH=Postpancreatoduodenectomy hemorrhage, PEA=Pancreaticoenteric anastomotic hemorrhage.

Table 4: Multivariate analysis for unplanned reoperation after pancreatoduodenectomy

| Variables                                      | Exp. (B) | 95% CI for Exp. (B) | \( P \) |
|-----------------------------------------------|----------|---------------------|--------|
| Diabetes mellitus                             | 3.70     | 1.06-12.90          | 0.04   |
| Intraoperative blood loss ≥400 ml             | 4.06     | 1.29-12.84          | 0.02   |
| Postpancreatoduodenectomy hemorrhage          | 30.67    | 8.85-106.31         | <0.001 |
| Pancreaticoenteric anastomotic leak           | 11.53    | 3.03-43.98          | <0.001 |

CI=Confidence interval

The second most common reason for unplanned reoperation was PEA leak in our study. A PEA leak may be mild and manifest only as an increase in surgical drainage, or it may be severe and cause intraperitoneal infection and corrosive hemorrhage. The management of PEA leak mainly includes adequate drainage by percutaneously placed drains, intravenous antibiotics and octreotide, reinforcement nutrition support, and other conservative treatments. Nevertheless, in severe cases, doctors recommend a reoperation when percutaneous drainage failure occurs or abdominal bleeding due to the peripancreatic blood vessels is corroded by inflammation. In addition, abdominal abscess formation and upper gastrointestinal hemorrhage caused by the infection were additional reasons for surgery. The reoperation procedures always involve repeated suturing as well as jejunum-to-pancreas anastomosis, pancreatic anastomosis, or even complete pancreatectomy and splenectomy. Regardless of which procedure is performed, the ultimate purpose is to drain all collections and abscesses.

Risk factors are crucial information for surgeons selecting surgical methods and an important basis for reminding
surgeons and patients to pay attention to complications during surgical decision-making. According to Lyu et al., patients with preoperative albumin <3.5 mg/dL and American Society of Anesthesiologists (ASA) Class 3 or 4 were more likely to undergo reoperation after the index conventional PD, and male sex and ASA Class 4 were closely correlated with the incidence of unplanned reoperation after index pylorus-preserving PD. Consistently, in our multivariate analysis, ASA class and preoperative hypoproteinemia independently predicted reoperation after the index PD. We also found that diabetes was a risk factor for reoperation, which might due to diabetics having decreased phagocytic function and poor vascular elasticity. Furthermore, there are more intraoperative blood losses in the unplanned reoperation group. On the one hand, a large amount of intraoperative blood loss indicates that the operation is more difficult, the intraoperative injury to the blood vessels is higher; the intraoperative ligation of the blood vessels is more complex, and the possibility of bleeding caused by shedding of the thread knot is relatively higher. On the other hand, massive intraoperative blood loss may result in serious loss of body nutrients, affecting postoperative wound healing and thus causing bleeding. Knowledge of these predictive factors of reoperation is significant for patients.

The present study had several limitations. First, this retrospective study was performed in a single center and data were limited to 30 days. Second, due to the insufficient sample size, we could not perform a subgroup analysis of the different surgical strategies. Third, the operations were not performed by the same surgical team, which might lead to significant variability.

CONCLUSIONS

Diabetes, intraoperative blood loss ≥400 mL, PPH, and PEA leak were suggested as independent risk factors for unplanned reoperation after primary PD. The findings of our study showed that preoperative optimization, meticulous surgical manipulation, and tailoring of postoperative management are significant factors for improving the safety of PD and reducing the reoperation rate. Further multicenter prospective investigations with long-term follow-up data are needed to verify our findings.

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Conflicts of interest

There are no conflicts of interest.

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