Risk factors and managements of hemorrhage associated with pancreatic fistula after pancreaticoduodenectomy

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BACKGROUND: Post-pancreaticoduodenectomy pancreatic fistula associated hemorrhage (PPFH) is one of the leading lethal complications. Our study was to analyze the risk factors and managements of hemorrhage associated with pancreatic fistula after pancreaticoduodenectomy, and to evaluate treatment options.

METHOD: We analyzed 445 patients who underwent pancreaticoduodenectomy or pylorus-preserving pancreaticoduodenectomy and evaluated the relevance between clinical data and PPFH.

RESULTS: The incidence of postoperative pancreatic fistula (POPF) was 27.42% (122/445), and the incidence of PPFH was 4.49% (20/445). Among the 20 patients with PPFH, 7 died and 13 were cured. Interventional angiographic therapy was performed for 10 patients and 5 were successfully treated. Relaparotomy was performed for 5 patients and 2 were successfully cured. Univariate logistic regression analysis indicated that several risk factors were related to PPFH: the nature of tumor (carcinoid/low-grade or high-grade malignancy), preoperative day 1 serum prealbumin, preoperative day 1 total bilirubin (TBIL), operative time, blood loss in the operation, operative method (vascular resection and revascularization), postoperative day 3 TBIL, biliary fistula, and the grade of POPF. The multivariate stepwise logistic regression analysis demonstrated that the nature of tumor and the grade of POPF were independently risk factors of PPFH. Receiver operating characteristic curve indicated that preoperative day 1 serum prealbumin level <173 mg/L and postoperative day 3 TBIL level ≥168 μmol/L were the risk factors of PPFH.

CONCLUSIONS: The risk of PPFH was found to be increased with high potential malignancy and high grade of POPF. Angiography-embolization is one of the major and effective therapies for PPFH. Extraluminal-intraluminal PPFH is more serious and needs more aggressive treatments.

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KEY WORDS: pancreatic neoplasms;
pancreaticoduodenectomy;
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risk factors

Introduction

Pancreaticoduodenectomy and pylorus-preserving pancreaticoduodenectomy are main curative treatments of periampullary neoplasms such as pancreatic head, lower bile duct, and periampullary region of the duodenum.[1] However, incidence rate of postoperative complications still remains high. Especially postoperative pancreatic fistula (POPF) and postoperative hemorrhage are the most severe ones, which contribute to high morbidity rates. It is reported that, POPF has a high incidence of 3%-30%.[2, 3] Due to unapparent symptoms and insufficient drainage, the actual incidence rate could be even higher. The incidence of postoperative hemorrhage is 5%-10%.[4-7] Although postoperative hemorrhage can involve multiple causes, POPF is confirmed as a leading cause of delayed postoperative hem-

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orrhage.[8-12] The mortality rate of POPF is 7.1%-23.3%, and this rate can be as high as 18%-82% if pancreatic fistula associated hemorrhage occurs.[12-14] Due to the lack of effective methods to manage the high incidence of POPF, it is important to pay more attention to the occurrence of post-pancreaticoduodenectomy pancreatic fistula associated hemorrhage (PPFH). The purpose of this study is to explore the potential risk factors of PPFH, and to summarize the experience of therapies in order to improve treatment efficacy and to decrease the incidence and mortality of PPFH.

Methods

Patients' characteristics and operating procedures

A total of 445 patients operated from January 1 to December 31 of 2013 in pancreatic surgery department of Changhai Hospital, Shanghai, were included. Among them, 209 underwent pancreaticoduodenectomies and 236 underwent pylorus-preserving pancreaticoduodenectomies. All patients received D2 lymph node dissection. Partial superior mesenteric and portal veins were resected and reconstructed if invaded. Pancreas was transected by scalpel. Pancreaticojejunostomies were all end-to-side and duct-mucosa, and a pancreatic duct stent was placed routinely. No external pancreatic or biliary drainage was performed. Polypropylene sutures (4-0) were used for the pancreaticojejunostomy, and 5-0 monofilament synthetic absorbable sutures were used for the hepaticojejunostomy. Hepaticojejunostomy was performed about 10 cm distally to pancreaticojejunostomy. End-to-side mucosa-to-mucosa double-layer gastrojejunostomy or duodenojejunostomy was performed 50 cm distally to hepaticojejunostomy. Conventional procedure was to place two peritoneal drainage tubes: one was posterior to the pancreaticojejunostomy and extended to hepaticojejunostomy, the other was placed near the pancreaticojejunostomy and extended to splenorenal area.

Perioperative management and data collection

If a patient had severe obstructive jaundice, preoperative biliary drainage would be performed by percutaneous transhepatic cholangial drainage. All patients received prophylactic antibiotics and proton pump inhibitors or H2 blockers for the first 3 postoperative days and then were treated according to the symptoms. Octreotide was not used routinely after operation. Drain fluid amylase and serum amylase were assayed 1 and 3 days after surgeries. If patients were considered to develop pancreatic fistulas or biliary fistulas, peritoneal drainage tubes would be changed to abdominal double cannulas, so that continuous lavage and low negative pressure drainage would be performed. Laboratory parameters were evaluated in preoperative day 1 and postoperative day 3, respectively.

Definition of complications

POPF and postpancreatectomy hemorrhage were diagnosed, graded, and treated in accordance with guideline and recommendations of the International Study Group on Pancreatic Fistula (ISGPF).[15, 16] POPF was defined as the amylase level of drainage fluid three times greater than the upper limit of normal serum value after postoperative day 3. The severity of POPF was graded as follows. Grade A: The fistula is transient with no clinical effect and may need a little change in management. Grade B: a change in management or adjustment of treatment is required (e.g. drain replacement because of infectious fluid or prolonged drain insertion, prolonged drain insertion because of high amylase level of drainage fluid more than 7 days even without infection, interventional drainage, antibiotics, partial or total parenteral nutrition). Grade C: the fistula is severe, life-threatening, and need special treatment or surgery.

According to the criteria of ISGPS,[16] postpancreatectomy hemorrhage was categorized as early (≤24 hours after the operation) or late (>24 hours after the operation), intraluminal or extraluminal, mild (hemoglobin decreases less than 3 g/dL without clinical symptoms and surgical or nonsurgical interventions are not necessary) or severe (hemoglobin decreases more than 3 g/dL with clinical symptoms, and relaparotomy or interventional angiographic therapy is needed). Based on the three criteria above, postpancreatectomy hemorrhage is graded from A to C (grade A: early mild postpancreatectomy hemorrhage; grade B: early severe postpancreatectomy hemorrhage or late mild postpancreatectomy hemorrhage; grade C: late severe postpancreatectomy hemorrhage).

In this study, PPFH was defined as postpancreatectomy hemorrhage which occurred secondary to POPF and excluded other causes (e.g. surgical relative factors, coagulation disorders). The primary mechanism of PPFH is the erosion of arteries near pancreaticojejunostomies by pancreatic enzymes and infection, or rupture of pancreatic anastomosis. And only extraluminal postpancreatectomy hemorrhage is associated with POPF, with or without intraluminal bleeding.[12, 17] The grade of PPFH was consistent with the grade of postpancreatectomy hemorrhage in the following. Grade B: postpancreatectomy hemorrhage occurred mildly after 24 hours and might not be immediately life-threatening during the most