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The Surgical Choice of Incidental Periampullary Carcinoma Management in Emergency Laparotomy

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Background: Laparotomy patients are occasionally diagnosed as having incidental periampullary cancers, making emergency pancreaticoduodenectomy (PD) inevitable. In this situation is difficult to decide whether to perform an emergency PD or a two-stage PD.

Material/Methods: A total of 27 patients who underwent emergency abdominal laparotomy were diagnosed with periampullary or pancreatic cancer during the operation without enough preoperative preparation. Ten patients underwent emergency one-stage PD and 17 patients underwent two-stage PD. Data of 137 patients with elective PD were selected as the control group. The preoperative, operative, and postoperative parameters, including hospital stay, medical cost, blood loss, and postoperative complications between elective PD and emergency PD (one-stage and two-stage) and between one-stage PD and two-stage PD were analyzed by chi-square test, Fisher test, or *t* test.

Results: Patients undergoing emergency two-stage PD had less blood loss (P=0.014), while patients with one-stage PD had shorter hospital stay (P=0.004), shorter operation time (P=0.047), and lower treatment costs (P=0.003). Additionally, the complications rates between one-stage and two-stage PD had no significant difference (P=0.365). Elective PD was the optimal method due to shorter hospital stay (P<0.001), less hemorrhage (P<0.001), shorter operative time (P<0.001), and lower cost (P<0.001) compared with emergency PD.

Conclusions: Based on our experience, one-stage PD had advantages of shorter hospital stay, shorter operation time, and lower treatment costs, while two-stage PD had less blood loss. The emergency two-stage PD may be more suitable for patients with unstable vital signs if emergency PD is inevitable in an emergency laparotomy.

MeSH Keywords: Emergency Treatment • General Surgery • Laparotomy • Pancreaticoduodenectomy

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Background

Pancreaticoduodenectomy (PD) is one of the most challenging operations in abdominal surgeries since it was first reported by Walther Kausch in 1912. Thanks to decades of surgical modifications and improved perioperative techniques, the mortality rate of PD has decreased to less than 5% [1–4]. However, the postoperative complications of PD are still frequent and severe, including delayed gastric emptying, pancreatic fistula, bile leakage, and wound infection [5–7]. It was reported that the rates of postoperative complications range from 30% to 60% [3,8]. PD is usually performed with indications of pancreatic tumor, periampullary tumor, and, occasionally, chronic pancreatitis. In principle, PD should be performed electively for adequate preoperative preparation, controllable intraoperative condition, and fewer postoperative complications because of its long operative time and severe complications.

However, emergency PD is sometimes inevitable to save lives of patients. Emergency PD is regularly carried out in exceptional cases such as irreparable pancreatic or duodenal trauma as a lifesaving procedure [9]. Use of emergency PD should be generally minimized because insufficient preoperative preparation can immensely affect surgery outcome. However, periampullary tumors may be incidentally found in abdominal laparotomy and common bile duct (CBD) exploration in clinical practice. Typical causes include acute abdomen, especially cholangitis caused by biliary obstruction. In these cases of incidental periampullary tumor in an emergency surgery, patients usually had severe overall condition, and surgeons have to decide to perform either an immediate PD or a two-stage PD, with the first step of alleviating jaundice or other procedures to improve patient health status. The reported mortality rates of emergency PD range from 40% to 54% [10,11], but studies reflecting current experience and relevant data on emergency PD are urgently needed because the surgical techniques and equipment have dramatically improved. However, due to the rarity of this kind of case, there have been few such studies.

In the present study, we report on our experience with 27 patients who were diagnosed with periampullary or pancreatic cancer during emergency abdominal laparotomy: 10 patients underwent emergency one-stage PD and 17 underwent two-stage PD. Moreover, to compare the advantages and disadvantages among different kinds of PDs, we for the first time retrospectively analyzed the operation-related data of these 10 emergency one-stage PDs and 17 emergency two-stage PDs, with 137 elective PD patients as a control group.

Material and Methods

Patient information

From May 2004 to May 2015, a total of 265 patients underwent elective PD and 27 patients underwent non-traumatic emergency PD in Qilu Hospital and Shanxian Central Hospital, constituting our primary cohort. A total of 137 elective PD patients and 27 emergency PD patients (10 patients underwent emergency one-stage PD and 17 patients underwent emergency two-stage PD) were enrolled into the validation cohort with complete hospital records, including preoperative blood tests and operative hemorrhage volume. Non-traumatic emergency PD was defined as emergency PD with non-traumatic causes during intraoperative exploration without sufficient preoperative preparation. Clinical data, including operative time, blood loss, length of hospital stay, and complications, were obtained from hospital and medical records with prior consent of patients and approval of the Ethics Committee of Qilu Hospital of Shandong University and Shanxian Central Hospital.

Postoperative complication

According to the international consensus criteria, pancreatic fistula was defined as amylase level in drainage fluid being 3 times greater than the serum amylase activity after the third postoperative day [12]. Bile leakage was defined as bilirubin concentration in the drain fluid being at least 3 times the serum bilirubin level on or after the third postoperative day [13]. Delayed gastric emptying (DGE) was defined as the inability to return to a regular diet by the end of the first postoperative week, and it included prolonged nasogastric intubation of the patient [14].

Surgical procedure of pancreaticoduodenectomy

The emergency PD was performed using the Child procedure without pylorus-preservation, as reported before [15]. Briefly, pancreaticojejunostomy, choledochojejunostomy, and gastrojejunostomy were carried out by Roux-en-Y anastomosis, in that sequence. The pancreatojejunostomy was performed with duct-to-mucosa anastomosis method. A stent tube was placed in the main pancreatic duct and another tube was placed in the CBD. Both tubes led outside the abdominal wall from the jejunum. Braun's anastomosis was performed 5 cm away from the gastrojejunal anastomosis site. Two drainage tubes were routinely set in the lesser sac and near the pancreaticojejunostomy site.

Two-stage PD procedure and perioperative management

Biliary drainage and depression were the first step to the patients with two-stage PD. In the first step of two-stage PD, 3

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patients underwent cholangioenterostomy and 14 patients underwent T-tube drainage of the CBD, with the choice of method depending on the severity of the CBD inflammation. Patients with severe CBD inflammation seemed to be more suitable for T-tube drainage because of the shorter operative time and higher operative safety. Moreover, severe CBD inflammation can increase the risk of hemorrhage and make dissection of the CBD very difficult. Longer operation time increases the intraoperative risk because most patients with emergency PD were in a life-threatening condition. If the CBD inflammation was not so severe and the CBD could be dissected out easily, cholangiojejunostomy with a Roux-en-Y method was recommended for a more simplified second-stage PD.

Time for the second-stage PD

The interval of time to performance of the second-stage PD was an average 23 of (range, 13–96) days in our study, which was based on the recovery of patients from the first-stage operation. In the second-stage, to reduce unnecessary hemorrhage, excessive exploration of the pancreatic region was not recommended. Parenteral alimentation was used until bowel sounds returned. Somatostatin or octreotide was administered to all of the patients postoperatively. Amylase levels of drainage fluid and blood routine examination were measured on the first, third, fifth, and seventh postoperative days. The stent tubes of pancreatic and bile ducts were removed 12 days after the operation if there was no pancreatic fistula or bile leakage.

Statistical analysis

We used SPSS 17.0 software for statistical analysis (SPSS version 17, Chicago, USA). The significance of continuous variables was analyzed by *t* test, including serum bilirubin, white blood cell, serum amylase, operative time (minutes), blood loss (ml), and hospital stay. The chi-square test was used to determine significance of differences between discontinuous data, such as margin status and complications. Significance was defined as a *P* value of less than 0.05.

Results

Demographics and preoperative variables

From 2004 to 2015, 27 patients underwent emergency surgeries including laparotomy or CBD exploration due to non-traumatic causes such as acute obstructive suppurative cholangitis (AOSC) or acute cholecystitis. During the abdominal laparotomy, filling gallbladder and dilated CBD were observed in all patients in our cohort. Choledochoscopy exploration was carried out for every suspicious patient and eventually led to the unexpected diagnosis as periampullary carcinoma (24/27, 88.9%) or pancreatic cancer (3/27, 11.1%) (Table 1). The age of these patients ranged from 43 to 78 years old. The average ages for one-stage and two-stage PD were 53.7 or 64.2 years, respectively. In our study, AOSC was the most common reason for laparotomy (14/27, 51.9%) and bile duct carcinoma was the most common reason in emergency PD (16/27, 37.0%). The percentage of patients with a history of HBV infection, chronic cholecystitis, and cholelithiasis were 7.4% (2/27), 25.9% (7/27), and 29.6% (8/27), respectively. In our study, 10 patients underwent emergency PD during the first surgery while 17 patients received biliary depression first. All the patients received standard PD with Child procedure and duct-mucosa pancreas-jejunal anastomosis as described in detail in the Material and Methods section.

Comparison of elective PD and emergency PD

The operation-related factors of elective PD and emergency PD were analyzed by chi-square test, Fisher test, or *t* test (Table 2). Patients with elective PD obviously had more satisfactory preoperative conditions. The levels of serum bilirubin and amylase and white blood cell count of patients with elective PD were significantly lower than in those with emergency PD ($P<0.001$, $P<0.001$, and $P<0.001$, respectively). There was no remarkable difference in the operative margin status, lymphadenectomy, or TNM stage between elective PD and emergency PD. However, compared with elective PD, the operation time was much longer, and the blood loss was much higher for emergency PD ($P<0.001$ and $P<0.001$, respectively). In addition, the hospital stay was much shorter ($P<0.001$) and the cost was notably lower ($P<0.001$) for elective PD than for emergency PD. Moreover, emergency PD had significantly more frequent postoperation complications than elective PD ($P=0.019$). These results suggest that elective PD is definitely superior to emergency PD in every aspect and the emergency PD should be avoided as much as possible.

Comparison of emergency one-stage PD and two-stage PD

In our study, 27 patients who underwent emergency PD were divided into one-stage and two-stage PD groups according to the surgical method. The preoperative factors of the 2 groups, including preoperative serum bilirubin and amylase levels, shock index, and white blood cell count, had no significant difference between groups, and routine pathology demonstrated that the TNM stages in the 2 groups were not significantly different (Table 3). Among the 17 patients with two-stage PD, 14 received T-tube drainage cholecystectomy first for biliary depression, and 3 patients underwent cholangiojejunostomy + cholecystectomy first because of the severity of CBD inflammation. Interestingly, the operation time of one-stage PD was shorter ($P=0.047$) but the blood loss of one-stage PD was much greater ($P=0.014$) compared with two-stage PD. Based on

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Table 1. Patients demographics.

Parameters	Elective PD	Emergency PD	
		One-stage	Two-stage
Number	137	10	17
Age (year)	57.5 (16–81)	53.7 (43–71)	64.2 (45–78)
Gender			
Male	82 (59.9%)	7 (70.0%)	10 (58.8%)
Female	55 (40.1%)	3 (70.0%)	7 (41.2%)
Emergency surgery reason			
AOSC		4 (40.0%)	10 (58.8%)
Acute cholecystitis		4 (40.0%)	4 (23.5%)
Gallbladder perforation		1 (10.0%)	1 (5.9%)
Intestinal obstruction		0	1 (5.9%)
Unexplained acute abdomen		1 (10.0%)	1 (5.9%)
Disease			
Pancreatic cancer	74 (54.0%)	1 (10.0%)	2 (11.8%)
Bile duct carcinoma	25 (18.2%)	6 (60.0%)	10 (58.8%)
Ampullary carcinoma	17 (12.4%)	3 (30.0%)	5 (29.4%)
Carcinoma of duodenum	3 (2.2%)	0	0
Endocrine tumor	3 (2.2%)	0	0
Other reasons	15 (10.9%)	0	0
Tumor size			
>1cm	64 (46.7%)	2 (20.0%)	8 (47.1%)
≤1cm	73 (53.3%)	8 (80.0%)	9 (52.9%)
Peritoneal irritation			
Significant		7 (70.0%)	11 (64.7%)
Not significant		3 (30.0%)	6 (35.3%)
Shock stage			
No		2 (20.0%)	1 (5.9%)
Compensation		5 (50.0%)	15 (88.2%)
Decompensation		0	1 (5.9%)
Laparotomy reasons			
AOSC		2 (20.0%)	12 (70.6%)
Acute cholecystitis		2 (20.0%)	3 (17.6%)
Cholelithiasis		5 (50.0%)	2 (11.8%)
Gallbladder perforation		1 (10.0%)	0

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Table 1 continued. Patients demographics.

Parameters	Elective PD	Emergency PD	
		One-stage	Two-stage
Bilirubin			
>200 umol/l	29 (21.2%)	2 (20.0%)	6 (35.3%)
≤200 umol/l	108 (78.8%)	8 (80.0%)	11 (64.7%)
White cell			
>20×10^9/l	2 (1.5%)	1 (10.0%)	7 (41.2%)
≤20×10^9/l	135 (98.5%)	9 (90.0%)	10 (58.8%)
HBV infection			
Yes	18 (10.2%)	1 (10.0%)	1 (5.9%)
No	119 (86.9%)	9 (90.0%)	16 (94.1%)
Chronic cholecystitis			
Yes	40 (29.2%)	2 (20.0%)	5 (29.4%)
No	97 (70.8%)	8 (80.0%)	12 (70.6%)
Cholelithiasis			
Yes	26 (19.0%)	3 (30.0%)	5 (29.4%)
No	111 (81.0%)	7 (70.0%)	12 (70.6%)

our experience, we found the greater blood loss in one-stage PD should be attributed to the severe inflammation and edema. However, the adhesion after the first surgery was more severe in the second-stage PD, increasing difficulty of dissection and prolonging the operative time. Additionally, compared with two-stage PD, the hospital stay of one-stage PD patients was significantly shorter and the treatment cost of one-stage PD was much lower (P=0.004 and 0.003, respectively). No other parameters were significantly different between one-stage and two-stage PD, including postoperation complications such as pancreatic fistula and bile leakage.

Discussion

Firstly, we have to declare that the emergency PD caused by non-trauma reasons should generally be avoided because of the frequent complications and higher mortality. The frequency of emergency PD is indeed decreasing because of the improvement of imaging examination methods and instruments. Many patients with biliary obstruction could avoid emergency surgery by undergoing percutaneous trans-hepatic cholangial drainage/percutaneous trans-hepatic gallbladder drainage (PTCD/PTGBD) first. Progress in diagnosis and treatment has decreased the need for emergency PD but it will always be needed in some patients. Incidental periampullary tumors still may occur in patients during abdominal laparotomy, making emergency PD inevitable. This situation occurs more frequently in some developing countries and areas where definite preoperative diagnoses such as CBD tumor are difficult and PTCD/PTGBD is not available. To perform an emergency PD or two-stage PD would be a dilemma faced by every surgeon in that situation and this is why we performed the present study.

Since the two-stage PD was first reported by Hoerr in 1966 [16], there have only been sporadic studies on it. All of the previously reported two-stage PDs were performed by performing pancreaticoduodenectomy first, followed by the second-stage pancreaticojejunostomy [17–19]. However, the clinical significance of this kind of two-stage PD is unclear because of insufficient clinical data and follow-up, and whether the two-stage PD is useful is still controversial. This kind of two-stage PD is very different from our procedures. Our emergency two-stage PD was performed only in special situations. Our first step is T-tube drainage or cholangioenterostomy because the priority is to relieve biliary pressure and reduce intraoperative risk. To the best of our knowledge, this is the first report on the analysis of non-trauma emergency PD. However, the rarity of emergency PD made the cohort number limited, so we were unable to define definite criteria on how to judge

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Table 2. Comparison of one-stage PD and two-stage PD.

Status	Factors	Elective		Emergency		P*
Preoperative	Serum bilirubin (μmol/L)##	73	(31–135)#	141	(52–367)	<0.001**
	White blood cell (×10^9)	7.6	(4.6–15.8)	16.2	(8.4–27.4)	<0.001**
	Serum amylase (IU/L)	110	(32–360)	365	(34–1547)	<0.001**
Operative	Margin status					
	R0	126	(92.0%)	26	(96.3%)	0.509
	R1	11	(8.0%)	1	(3.7%)	
	R2	0		0		
	Lymph node positivity					
	Yes	38	(27.7%)	4	(14.8%)	0.140
	No	99	(72.3%)	23	(85.2%)	
	Operation time (minutes)#	377	(275–645)	497	(310–785)	<0.001
	Blood loss(ml)	385	(200–1600)	617	(250–1300)	<0.001
Postoperative	Hospital stay (d)#	15	(6–33)	31.6	(17–55)	<0.001**
	Pancreatic fistula	23	(16.8%)	6	(22.2%)	0.338
	Bile leakage	13	(9.5%)	3	(11.1%)	0.798
	Would infection	14	(10.2%)	3	(11.1%)	1
	Intra-abdominal abscess	15	(10.9%)	2	(7.4%)	0.741
	Hemorrhage	12	(8.8%)	1	(3.7%)	0.696
	Delayed gastric emptying	15	(10.9%)	2	(7.4%)	0.741
	Death	3	(2.2%)	1	(3.7%)	0.517
TNM stage	I+II	97	(70.8%)	19	(70.4%)	0.964
	III+IV	40	(29.2%)	8	(29.6%)	
Clavien-Dindo classification	I+II	125	(91.2%)	20	(74.1%)	0.019
	III+IV	12	(8.8%)	7	(25.9%)	

PD indicates pancreaticoduodenectomy. * Means calculated by Chi-square test or Fisher test without special instruction; ** means calculated by Student t test; # means the operation time/hospital stay of the second-stage PD; ## means the serum bilirubin before 1st surgery.

suitable patients for one-stage or two-stage PD prospectively. The decision relied on the overall condition of the patient and intraoperative situation, but the following facts must be considered: (1) In abdominal laparotomy, choledochoscopy exploration is always required if there exists unexplained dialiation of CBD; (2) Patients with stable vital signs have the possibility for one-stage emergency PD; (3) One-stage PD is not recommended if biliary or pancreatic inflammation is too severe to dissect clearly; (4) the operation time should be shortened as much as possible once the biliary obstruction is relieved in patients with unstable blood pressure during the operation; and (5) The opportunity to perform the second-stage is dependent on the recovery and the entire situation of the patient, such as body temperature ≤38°C, white blood cell count ≤10×10^9/L, serum bilirubin ≤85 μmol/L, no organ dysfunction, and normal water and electrolyte homeostasis.

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Table 3. Comparison of one-stage PD and two-stage PD.

Status	Factors	One-stage		Two-stage		P*
Preoperative	Serum bilirubin (μmol/L)##	113	(43–261)	157	(52–367)	0.792&
	White blood cell (×10^9)	13.8	(10.6–20.8)	17.6	(8.4–27.4)	0.115&
	Serum amylase (IU/L)	308	(44–1121)	407	(34–1547)	0.499&
	Interval time between surgeries	–		23	(13–96)	
	Shock index	1.34	(1.02–1.76)	1.53	(1.22–2.14)	0.254
1st step	T-tube drainge + Cholecystectomy	–		14	(82.4%)	
	Cholangiojejunostomy + Cholecystectomy	–		3	(17.6%)	
Operative	Margin status					
	R0	9	(90.0%)	17	(100%)	1
	R1	1	(10.0%)	0		
	R2	0		0		
	Lymph node positivity					
	Yes	1	(10.0%)	3	(17.6%)	1
	No	9	(90.0%)	14	(82.4%)	
	Operation time (minutes)*	422	(310–752)	542	(350–823)	0.047
	Blood loss (ml)	780	(360–1300)	522	(250–930)	0.014
Postoperative	Hospital stay (d)#	24.5	(12–43)	36	(23–55)	0.004**
	Pancreatic fistula	2	(20.0%)	4	(23.5%)	1
	Bile leakage	2	(20.0%)	1	(5.9%)	0.535
	Would infection	1	(10.0%)	2	(11.8%)	1
	Intra-abdominal abscess	1	(10.0%)	1	(5.9%)	1
	Hemorrhage	1	(10.0%)	0		0.370
	Delayed gastric emptying	1	(10.0%)	1	(5.9%)	1
	Death	1	(10.0%)	0		0.370
TNM stage	I+II	7	(70.0%)	10	(58.8%)	0.692
	III+IV	3	(30.0%)	7	(41.2%)	
Clavien-Dindo classification	I+II	6	(60.0%)	14	(82.4%)	0.365
	III+IV	4	(40.0%)	3	(17.6%)	

PD indicates pancreaticoduodenectomy. * Means calculated by Chi-square test or Fisher test without special instruction; ** means calculated by Student t test; # means the operation time/hospital stay of the second-stage PD; ## means the serum bilirubin before 1st surgery.

Conclusions

In conclusion, elective PD is optimal and emergency non-trauma PD should be avoided whenever possible. When emergency PD is inevitable, the decision of one- or two- stage PD relies on the judgment of the overall condition of the patient. In our experience, emergency two-stage PD is more suitable for patients with unstable vital signs. In two-stage PD, our first step

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is T-tube drainage or cholangioenterostomy because the priority of this emergency two-stage PD is to relieve biliary pressure and reduce intraoperative risk. To perform the T-tube drainage as the first step may be more suitable for patients with severe inflammation for clear dissection of the CBD. One-stage PD patients had shorter hospital stay, shorter operation time, and lower treatment costs, while two-stage PD patients had less blood loss.

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Conflicts of interest

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