

ผลลัพธ์ระหว่างการผ่าตัด Pancreaticoduodenectomy ในโรงพยาบาล สุราษฎร์ธานี

The Perioperative Outcomes of the Pancreaticoduodenectomy at Suratthani Hospital

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บทคัดย่อ:

วัตถุประสงค์: เพื่อประเมินผลลัพธ์ระหว่างการผ่าตัด pancreaticoduodenectomy ในโรงพยาบาลสุราษฎร์ธานี

วัสดุและวิธีการ: ศึกษาย้อนหลังผู้ป่วย 26 ราย ที่ผ่าตัด pancreaticoduodenectomy ตั้งแต่เดือนมกราคม พ.ศ. 2555 ถึงเดือนมกราคม พ.ศ. 2558 โดยการรวบรวมข้อมูล ก่อนการผ่าตัด ระหว่างการผ่าตัด และการดูแลหลังผ่าตัด

ผลการศึกษา: ผู้ป่วย 26 ราย เป็นเพศชาย 17 ราย เพศหญิง 9 ราย อายุเฉลี่ยเท่ากับ 61.1 ± 11.9 ปี อัตราการเสียชีวิตเท่ากับร้อยละ 11.5 (3 ราย) อัตราการเกิดภาวะแทรกซ้อนหลังผ่าตัดเท่ากับร้อยละ 61.5 (16 ราย) เกิด delayed gastric emptying time เท่ากับร้อยละ 42.3 เกิด pancreaticojejunal anastomotic leakage เท่ากับร้อยละ 30.8 การศึกษานี้ไม่พบความสัมพันธ์กันระหว่างปัจจัยก่อนผ่าตัดและระหว่างผ่าตัด มีผลต่อการเกิดภาวะแทรกซ้อนหลังผ่าตัด

สรุป: pancreaticoduodenectomy มีอัตราการเสียชีวิต และอัตราการเกิดภาวะแทรกซ้อนหลังผ่าตัดสูง จึงจำเป็นต้องพัฒนาการเตรียมผู้ป่วยก่อนผ่าตัด วิธีการผ่าตัด และการดูแลหลังผ่าตัด เพื่อสู่ผลการผ่าตัดในระดับสากล

คำสำคัญ: pancreaticoduodenectomy, อัตราการเกิดภาวะแทรกซ้อน, อัตราการเสียชีวิต

Abstract:

Objective: To evaluate the perioperative outcomes of pancreaticoduodenectomy at Suratthani Hospital.

Material and Method: Retrospective study of data from 26 patients who underwent pancreaticoduodenectomy from January 2012 through January 2015, at Suratthani Hospital. The primary endpoints are the morbidity and mortality rate.

Results: Twenty six patients (17 male and 9 female) with mean age 61.1 ± 11.9 years were analyzed. The overall hospital mortality rate was 11.5% (n=3). The morbidity rate was 61.5% (n=16). Delayed gastric emptying time (42.3%) and pancreaticojejunal anastomotic leakage (30.8%) were the two most common complications. In this study, preoperative and operative factors had no significant effect on morbidity rate.

Conclusion: Pancreaticoduodenectomy still has high morbidity and mortality rate. Further improvement of surgical technique together with the good pre and postoperative care may help to reduce mortality and morbidity rate.

Keywords: morbidity, mortality, pancreaticoduodenectomy

Introduction

Pancreaticoduodenectomy (PD) is one of the most complex surgical procedures and is associated with substantial operative mortality and morbidity rates. The first successful PD was performed by the German surgeon, Kausch¹ in 1912 and the operation was popularized in 1935 by Whipple et al.², who reported three cases of PD. In Whipple's series, the mortality rate was higher than 30%³. Until the 1980s, the operative mortality rate of PD was 20–25%, and at one time some surgeons even proposed that it should be completely abandoned as a treatment option for carcinoma of the head of the pancreas.^{4,5} A comprehensive literature review that included 1859 patients who underwent pancreatic resection for pancreatic cancer between 1980 and 1986 showed a mortality rate of 16%, which was unacceptably high when compared with other types of elective surgery⁶. In the 1990s, several major centers in western countries reported dramatically reduced operative mortality rates as a result of improved surgical management and increased experience.^{7–12}

An association between high procedure volume and better patient outcomes has been identified for numerous surgical procedures. Several studies showed improved operative outcomes of PD in the 1990s. While a post-operative mortality rate of less than 5% had been achieved in high volume centers, mortality rates in low volume hospitals remained in the range of 13–20% in the 1990s.^{7–12} In centers with case volume of more than 40 per year, a mortality rate of less than 2% has been reported^{1,10,13} Despite a reduction in mortality rates, morbidity rates remain 38–52%.^{9,10,14}

The most common indication for PD is carcinoma of the head of pancreas.^{9,10,15} With improved safety of PD, the operation is also considered an appropriate treatment for selected patients with chronic pancreatitis, which constitutes the second most common indication for operation in western series.^{10,13} The aim of this study is to evaluate the perioperative outcomes of patients who underwent PD in Suratthani Hospital, a regional referral center.

Material and Method

From January 2012 to January 2015, 26 patients underwent elective PD at Suratthani Hospital's Department of Surgery. All patients were operated on by general surgeons. A retrospective study was performed by reviewing the records of patients for clinical, laboratory, operative and pathologic data. Any postoperative complications and mortality were documented. Pancreatic leakage and delayed gastric emptying time were defined in accordance with the International Study Group of Pancreatic Surgery (ISGPS).^{15,16} Operative mortality was defined as death within 30 days of surgery.

Statistical analysis

All data were expressed as median, range, mean, standard deviation (S.D.) or percentages as appropriate. Statistical analyses were performed using student's t-test and chi-squared test with Fisher's exact test to evaluate the impact of clinical, preoperative and operative parameters. Statistical analysis was performed using the SPSS statistical software. A p-value<0.05 was considered statistically significant.

Results

Patients included 17 male and 9 female, with mean age of 61.1 years; range 30–85 years; S.D.=11.9 years. There were 15 (57.7%) elderly patients aged 60 years or older. Thirteen patients (50%) had one or more chronic co-morbidity illnesses, mostly diabetes mellitus (30.8%) and hypertension (19.2%) (Table 1). The top 3 most common presenting symptoms were jaundice 18 (69.2%), weight loss 17 (65.4%) and abdominal pain 17 (65.4%). Preoperative serum chemistry values are shown in Table 2. Ten (38.5%) patients had serum albumin level was less than 3.5 mg/dL.

Table 1 Demographic, clinical presentation and co-morbidity for patients with PD

Variable	Number of patients (%)
Age, year, mean (S.D.)	61.1 (11.9)
Sex	
Female n (%)	9 (34.6)
Male n (%)	17 (65.4)
Presenting symptoms	
Jaundice	18 (69.2)
Abdominal pain	17 (65.4)
Weight loss	17 (65.4)
Cholangitis	6 (23.0)
Abdominal mass	2 (7.7)
Bleeding	1 (3.8)
Co-morbidity	
Diabetes mellitus	8 (30.8)
Hypertension	5 (19.2)
Smoking	4 (15.4)
Dyslipidemia	3 (11.5)
Ischemic heart disease	2 (7.7)
Chronic renal failure	2 (7.7)
Alcoholic	2 (7.7)
Cirrhosis	1 (3.8)

Table 2 Preoperative serum chemistry

Variable	Value
Sodium, mEq/L, mean (S.D.)	137.9 (4.2)
BUN, mg/dL, mean (S.D.)	11.3 (6.4)
Creatinine, mg/dL, mean (S.D.)	0.9 (0.3)
Albumin, mg/dL, mean (S.D.)	3.6 (0.8)
Total bilirubin, mg/dL, mean (S.D.)	4.6 (6.0)
SGOT, U/L, mean (S.D.)	79.0 (87.0)
Alkaline phosphatase, U/L, mean (S.D.)	372.8 (375.8)
White blood cell count, $\times 10^3/\text{mm}^3$, mean (S.D.)	10.5 (12.7)
Hematocrit, %, mean (S.D.)	35.4 (4.2)
INR, mean (S.D.)	1.0 (0.1)

BUN=blood urea nitrogen, SGOT=serum glutamic oxaloacetic transaminase, INR=international normalized ratio

The mean body mass index (BMI) of patients was 20.3 kg/m² (S.D.=3.2). Ten patients (38.5%) had BMI<18.5 kg/m². The American Society of Anesthesiologist performance score was class I in 5 patients (19.2%), class II in 12 (46.2%), class III in 9 (43.6%). Preoperative biliary drainage was performed in 14 patients (53.8%), either by endoscopic stenting (n=13) or percutaneous transhepatic biliary drainage (n=1). Nineteen patients (73.1%) underwent the standard PD and seven (26.9%) underwent Pylorus-Preserving PD (PPPD). The mean duration of the procedure was 359.9 minutes (S.D.=101.9). The mean estimated blood loss was 1,107 mL (S.D.=681) (range 300–2,900 mL) (Table 3).

Table 3 Perioperative outcomes of PD

Characteristic	Value
Body mass index, kg/m ² , mean (S.D.)	20.3 (3.2)
ASA score, n (%)	
I	5 (19.2)
II	12 (46.2)
III	9 (43.6)
Operative procedure	
Standard PD, n (%)	19 (73.1)
Pylorus preserving PD, n (%)	7 (26.9)
Preoperative biliary drainage, n (%)	14 (53.8)
Procedure duration, min, mean (S.D.)	359.9 (101.9)
Blood loss, mL, mean (S.D.)	1,107 (681.0)
Blood transfusion, unit, mean (S.D.)	3.3 (2.9)
ICU stay, day, mean (S.D.)	4.4 (6.6)
Respirator support, day, mean (S.D.)	3.6 (6.6)
Length of stay after surgery, day, mean (S.D.)	20.0 (13.1)
Reoperation, n (%)	2 (7.7)
Morbidity, n (%)	16 (61.5)
Mortality, n (%)	3 (11.5)

Malignant pathology was confirmed in 23 specimens (88.5%). The most common one was ampullary carcinoma (57.7%), followed by pancreatic duct carcinoma (7.7%) and pancreatic neuroendocrine tumor (7.7%). Pathological diagnosis of the patients is shown in Table 4.

Table 4 Pathologic data of PD

Final histopathology	Number of patients (%)
Malignant	23 (88.5)
Ampullary adenocarcinoma	15 (57.7)
Pancreatic ductal carcinoma	2 (7.7)
Pancreatic neuroendocrine tumor	2 (7.7)
Carcinoma of 2nd part of duodenum	1 (3.8)
Carcinoma of pylorus	1 (3.8)
Lymphoma	1 (3.8)
Cholangiocarcinoma	1 (3.8)
Benign	3 (11.5)
Microcystic serous cystadenoma of pancreas	2 (7.7)
Chronic pancreatitis	1 (3.8)

Postoperative morbidity rate was 61.5% (16 patients). The two most common complications were delayed gastric emptying time (42.3%) and leakage of pancreaticojejunal anastomosis (30.8%). There was no significant difference between delayed gastric emptying time among the procedures of operation (standard PD, PPPD) (p-value=1.00). Most pancreatic fistulas were managed successfully by conservative treatment except in 2 cases with grade C leakage, which needed reoperation. Both patients were dead from both sepsis and multiple organ failure. Other complications are shown in Table 5.

The mean intensive care unit (ICU) stay was 4.4 days (S.D.=6.6). The mean postoperative respiratory

support was 3.6 days (S.D.=6.6) and the mean hospital stay after surgery was 20.0 days (S.D.=13.1). Overall mortality rate was 11.5% (3 patients). The first patient had massive hemorrhaging during the operation (portal vein tear) and died on the following day. The second and third patients had anastomotic leakage and intra-abdominal collection, requiring reoperation. As mentioned above, both patients expired from sepsis and multiple organ failure. Table 6 shows the results of univariate analysis of risk factors of postoperative morbidity. There was no preoperative and operative factors associated with morbidity.

Table 5 Complication after PD

Complication	Number of patients (%)
Delay gastric emptying time	11 (42.3)
Grade A	2 (7.7)
Grade B	4 (15.4)
Grade C	5 (19.2)
Pancreatic fistula	8 (30.8)
Grade A	1 (3.8)
Grade B	5 (19.2)
Grade C	2 (7.7)
Wound infection	6 (23.1)
Respiratory tract infection	6 (23.1)
Sepsis	5 (19.2)
Cardiac complication	4 (15.4)
Intra-abdominal abscess	3 (11.5)
Renal complication	2 (7.7)
Post-operative hemorrhage	1 (3.8)
Neurological complication	1 (3.8)
Lymphatic leakage	1 (3.8)
Urinary tract infection	1 (3.8)
Ascites	1 (3.8)

Discussion

PD is a complex, high-risk general surgical procedure that has been widely studied during the past decade with respect to its perioperative outcomes. In this study we concentrated on studying which factors result in low operative morbidity and mortality rate for patients undergoing this procedure. Most of the patients were elderly (mean age=61.1 years) and 57.7% were ≥ 60 years old. Thirteen patients (50%) had co-morbid illness.

The most common indication for PD is the presence of malignant or premalignant neoplasm of the pancreas or one of the other periampullary structures (bile duct, ampulla, or duodenum).^{9,10,13} In this study, the most common indication was ampullary carcinoma (57.7%). Carcinoma of the head of pancreas accounted for only 7.7%, which is much less than those report in western countries. This difference may be due to the incidence of the carcinoma of the head of pancreas is lower here than in western countries, and because in Suratthani Hospital we mainly encounter advanced stage disease on which we cannot perform PD owing to lack of skills to conduct the required vascular reconstruction.

In this study there were 14 patients (53.4%) with preoperative biliary drainage to relieve the biliary obstruction in order to lessen the jaundice, coagulopathy and improve the malabsorption status. However, results from randomized trials have not been consistent.¹⁷⁻¹⁹ No significant difference in mortality was found, but overall serious morbidity rate was higher in the pre-operative drainage group.²⁰ So we performed the biliary decompression for selected patients in whom surgery will be delayed for longer than two weeks or in the presence of cholangitis.

Table 6 Morbidity according to preoperative and operative factors

Factor	Number of patients	Number of patients with morbidity (%)	P-value
Age (years)			
<60	11	5 (45.5)	0.23
≥60	15	11 (73.3)	
Sex			
Male	17	12 (70.6)	0.23
Female	9	4 (44.4)	
Co-morbid illness			
Yes	13	7 (53.8)	0.67
No	13	9 (69.2)	
BMI (kg/m ²)			
<18.5	10	6 (60.0)	1.00
≥18.5	16	10 (62.5)	
Albumin (mg/dL)			
<3.5	10	7 (70.0)	0.68
≥3.5	16	9 (56.2)	
Disease			
Benign	3	1 (33.3)	0.54
Malignant	23	15 (65.2)	
Biliary drainage			
Yes	14	11 (78.6)	0.11
No	12	5 (41.7)	
Operation			
Standard PD	19	12 (63.2)	1.00
PPPD	7	4 (57.1)	
Operative blood loss (L)			
<1	16	8 (50.0)	0.22
≥1	10	8 (80.0)	

There were 19 patients (73.1%) who underwent standard PD and 7 (26.9%) who underwent pyloric preserving pancreaticoduodenectomy (PPPD). There was no significant difference between delayed gastric emptying time and type of procedure ($p=1.00$). The mean incidence of delayed gastric emptying was 17%. In a meta-analysis from the Cochrane database²¹, there

were no significant differences in perioperative mortality for pylorus preserving versus conventional Whipple procedure, nor for overall survival. There were also no significant differences in the rates of pancreatic fistula or biliary leakage. There was a non-significant trend toward a higher rate of delayed gastric emptying after a pylorus preserving procedure. The possible risk factors

for delayed gastric emptying include prior abdominal surgery, history of cholangitis, and diabetes mellitus.²²

There were 8 patients (30.8%) with pancreatic fistula. Pancreatic leakage rate of 10–20% after PD have been reported in western centers and have not declined significantly in the past 30 years.²³ Despite intensive effort by pancreatic surgeons to prevent pancreatic anastomotic leakage through modification of surgical techniques or use of prophylactic octreotide, none of the measures has thus far been proved to be effective in reducing the pancreatic leakage rate.²⁴ Pancreatic leakage is a potentially serious complication that can lead to intraabdominal sepsis and haemorrhage, which has been associated with high mortality rates. Placement of a pancreatic stent has the potential to decompress the main pancreatic duct and provide drainage of pancreatic secretions. However, the role of pancreatic stents in preventing pancreatic fistula is unclear. A meta-analysis found a significant reduction in the incidence of postoperative pancreatic fistula (POPF) for those who were stented compared with those who were not (21.7% versus 28.9%).^{25–27} The risk of POPF increased by various factors including high body mass index (BMI), preoperative comorbidities such as jaundice, as well as a soft pancreas and a narrow pancreatic duct. Other factors that have been associated with an increased risk of POPF include drain amylase >4,000 U/L on the first postoperative day, increased intraoperative blood loss, and prolonged operative time.^{28,29} In this study, there were 2 patients with grade C pancreatic fistula and both of them died postoperatively.

In this study, our morbidity and mortality rate were 61% and 11.5% respectively. Although previously associated with high morbidity and mortality rates, recent studies showed that in experienced hands, the conventional Whipple procedure is associated with

a perioperative mortality rate of less than 4%, and the five-year survival rate was 20–30% in patients with completely resected tumor.^{10,14,30} One of the most important reasons for this is the greater experience of the surgeons who perform the procedure regularly in high volume institutions.^{11,31,32} There is a significant association between hospital volume and postoperative mortality. In a study of the results of PD in 39 hospitals in the US, low-, medium-, and high-volume centers for PD were defined as 1–5 cases per year, 6–20 cases per year, and more than 20 cases per year respectively, and the corresponding hospital mortality rates were 19%, 12%, and 2.2%. However, morbidity rates remain high (40–50%).³³ In this study, there was no significant factor associated with postoperative morbidity. This may be due to the low number of patients. Greenblatt DY et al.³⁴ reported that there were significant predictors of morbidity which included older age, male gender, overweight and obesity, dependent functional status, chronic obstructive pulmonary disease (COPD), steroid use, bleeding disorder, leukocytosis, elevated serum creatinine and hypoalbuminemia. Significant predictors of 30-day mortality included COPD, hypertension, neoadjuvant radiation therapy, elevated serum creatinine and hypoalbuminemia.

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Conclusion

Pancreaticoduodenectomy at Suratthani Hospital has still high mortality and morbidity rate. But these values are within the range of those from studies in low volume hospitals in western countries. However, Suratthani Hospital is a tertiary, regional referral center of the Thai healthcare system, so we need to reduce these rates, even though we are a low volume hospital.

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