Seven Years Experience of Pancreaticoduodenectomy at Sawanpracharak Hospital

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Background: *Pancreaticoduodenectomy is a major procedure with significant mortality and morbidity. Pancreaticoduodenectomy is a safe procedure for a variety of periampullary conditions at Sawanpracharak Hospital.*

Objective: *To evaluate complications, morbidity, and mortality. The effects of clinical and variables related to patient mortality.*

Material and Method: *Retrospective medical records review of 52 patients who underwent pancreaticoduodenectomy at Sawanpracharak Hospital between February 2000 and November 2006 was conducted. Of these, 12 patients who died after pancreaticoduodenectomy were studied.*

Results: *Of 52 cases, 29 males and 23 females, the median age was 64 years (age range, 32-82 years). Median operative time was 3.70 hours (range, 2.0-9.5 hours). Pathological examination demonstrated 38.46% ampullary cancer, 26.92% pancreatic cancer, 1.92% duodenal cancer, 11.54% periampullary cancer, 3.85% gastric cancer, 1.92% gastrointestinal stromal tumor, 5.77% chronic pancreatitis, 1.92% cystadenoma of pancreas, 1.92 chronic gastric ulcer, 1.92% leiomyoma of duodenum, and 3.85% no pathologic report. Fifty percent of patients underwent pylorus preservation pancreaticoduodenectomy. Postoperative complications occurred in 40.38% of patients, including intraabdominal abscess (19.05%), pancreatic fistula (14.29%), bowel fistula(9.52%), internal bleeding(9.52%), sepsis (9.52%), superior mesenteric occlusion (4.76%), bile fistula(4.76%), cholangitis (4.76%),acute renal failure (14.29%), pneumonia(4.76%), acute myocardial infarction(4.76%), and additional surgery was required in 13.46% of patients. Overall perioperative mortality was 23.08% with only one patient with benign disease (chronic pancreatitis) died postoperatively. Underlying medical disease conditions did not influence postoperative morbidity or mortality. Natures of surgical complications were indicated as causes of significant higher mortality. The median follow-up for patients was 3.37 months (range, 0.5-65.7 months, mean 8.71 $\pm$ 13.66 months).*

Conclusion: *Pancreaticoduodenectomy still causes considerable morbidity and mortality. With careful patient selection, preoperative assessment of respectability, surgical technique, critical care anesthesia, and postoperative care, pancreaticoduodenectomy can be performed safely and improve the results to an acceptable level.*

Keywords: *Pancreaticoduodenectomy*

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Pancreaticoduodenectomy has its origins in the late 1800s. William Halsted performed the first transduodenal local excision of a tumor of the ampulla of Vater in 1898. Alessandro Codivilla, in that same year, was the first to perform a pancreaticoduodenectomy, in Italy. In 1909 in Berlin, Walter Kausch performed the first successful 2-stage pancreaticoduodenectomy. Allen Whipple et al reported the first series of pancreaticoduodenectomy in 1935[1], and since that time, the operation has been known as the "Whipple" operation. Operative mortality from the original report of Whipple to 1970s was in excess of 25%[2-4].

While earlier studies reported operative mortality rates of 15% to 23%, and morbidity rates of 40% to 60%[5-9]. Since then, operative mortality has

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been significantly reduced to about 5% in specialized centers[10,11]. Recent reports describe operative mortalities of less than 5% and morbidity rates of 30% to 50%[12-14]. High operative morbidity and mortality rates led to technical modifications of the operation which, combined with improvements in anesthesia and critical care, have resulted in current perioperative mortality rates of 2 percent or less[15]. More recently, however, several series have reported large numbers of consecutive Whipple procedures without mortality[16-18].With the standardization of perioperative care, advances in surgical technique, and interventional radiology and intensive care support, the procedure has become considerably safer. Pancreaticoduodenectomy has become an increasingly common and safe operation for selected patients with benign and malignant periampullary disorders.

The aim of the present study was to assess the safety of pancreaticoduodenectomy in Sawanpracharak Hospital, and to identify risk factors influences morbidity and mortality in such a demanding procedure.

Material and Method

This is a retrospective review collected from medical records of 52 patients who underwent pancreaticoduodenectomy for various indications at Sawanpracharak Hospital between February 2000, and November 2006. Patients underwent pancreaticoduodenectomy due to trauma were excluded.

The review included basic demographic characteristics (age and sex), surgical data (type of resection, duration of surgery), pathological diagnosis (pancreatic adenocarcinoma, ampullary tumor, bile duct tumor, duodenal tumor, chronic pancreatitis, benign and malignant cystic tumor, and others), and reoperation before discharge from the hospital. The postoperative hospital stay was calculated and morbidity and mortality were assessed. Follow-up data were obtained through medical record review, and direct patient contact.

Statistical analyses were calculated using SPSS statistical software. Data were presented as number (%), standard deviation mean $\pm$ SD, median and range. Differences in the continuous variables were conducted with the use of an independent sample t-test and a Chisquare X^2 test for categorical data. A 2-sided P values of less than 0.05 were considered to indicate statistical significance.

Result

During the study period from February 2000 to November 2006, 52 patients underwent pancreaticoduodenectomy by six surgeons at Sawanpracharak Hospital. There were 23 women and 29 men, with a median age of 64 years (range, 32-82 years; mean $\pm$ SD, 61.15 $\pm$ 10.86 years).

All were performed for a variety of diagnoses. Two patients of resection had no pathological reports. Demographic and perioperative data are summarized in Table 1.

Of the 52 patients' preoperative symptoms, physical signs, and associated conditions recorded, 42 patients had jaundice (80.8%), 18 abdominal pain (34.62%), and 4 abdominal mass (7.69%). In addition, the record showed 39 preoperative serum chemistry values, and 2 serum tumor marker values (CA 19-9). All are presented in Table 2.

Preoperative evaluation with ultrasound in 38 patients (73.08%) and CT scan in 19 patients (36.54%). Twenty-four patients (46.15%) underwent endoscopic retrograde cholangiopancreatography as part of their preoperative work up, with two of these patients receiving a biliary stent during this procedure.

Medical comorbidity was presented in 13 patients (25%): diabetes (n = 5), diabetes and hypertension (n = 2), diabetes and old CVA (n = 1), pulmonary tuberculosis (n = 4), and Hb E Trait (n = 1).

Twenty-six patients (50%) underwent a pylorus-preserving pancreaticoduodenectomy and 26 (50%) underwent a classic pancreaticoduodenectomy.

Table 1. Demographic and pathologic data for 52 patients

Variables	Patients No. (%)
Age, mean (range) (year)	61.15, (32-82)
Males	29 (55.8)
Diagnosis	
Malignant (n = 44)	
Ampullary	20 (38.46)
Pancreatic	14 (26.92)
Periampullary*	6 (11.54)
Stomach	2 (3.85)
Gastrointestinal stromal Tumor of stomach	1 (1.92)
Duodenum	1 (1.92)
Benign (n = 6)	
Chronic pancreatitis	3 (5.77)
Microcystic cystadenoma of pancreas	1 (1.92)
Leiomyoma of duodenum	1 (1.92)
Chronic gastric ulcer	1 (1.92)
Unknown	2 (3.85)

* Failed to accuracy confirmation of organ origin

Almost all were routinely performed using an end-to-side pancreaticojejunostomy with a double-layer suture. Only two patients had an end-to-end invagination pancreaticojejunostomy performed. No pancreaticogastrostomies were performed in this series. A pancreaticoduodenectomy en bloc in conjunction with subtotal gastrectomy and with hemicolectomy were performed in two and one patient respectively. Right salphingo-oopholectomy was also performed in one patient. Prophylactic octreotide was not routinely used. Some surgeons used it if there was a pancreatic fistula. The median operative time was 3.7 hours (range 2.0-9.5 hours), and mean duration of operation was 4.07 $\pm$ 1.29 hours.

Of 43 patients with adenocarcinomas, thirty-four patients (79.07%) had well-differentiated tumors, five patients (11.63%) had moderately, and two patients had poorly differentiated histology. Eight patients (18.60%) had tumor metastasis to one or more lymph nodes. Thirteen patients (30.23%) had tumor invaded surrounding structures.

Postoperative complications occurred in 21 of the 52 patients in the present study, for an overall postoperative morbidity rate of 40.38%. The complication rate was highest in patients aged 60-69 years (n = 11; 52.38%), followed by those aged 50-59 years (n = 7; 33.33%), and aged $\geq$ 70 years (n = 3; 14.29%) respectively. There was no complication in patients' aged < 50 years.

Sixteen patients (76.2%) had surgical complications and five patients (23.8%) had postoperative medical complications. There were 12 patients (23.08%) with more than one complication. Seven patients (13.46%) required early reoperation due to leakage (n = 4), intra-abdominal abscess (n = 2), and bleeding (n = 1). Specific postoperative complication data are presented in Table 3.

Median postoperative hospital stay was 14 days, and mean postoperative hospital stay was 16.11 $\pm$ 11.79 days (range, 0-60 days).

There were12 postoperative deaths (23.08%). There were no intra-operative deaths. Eight (66.67%) deaths occurred in the group with postoperative surgical complication (sepsis with multi-organ failure in six patients, internal hemorrhage in one patient, mesenteric ischemia in one patient) and four patients (33.33%) died in the group with postoperative medical complications (acute renal failure in two patients, cardiopulmonary complications in two patients). Three died after reoperation. The mortality associated with pancreatic fistula was 8.3%. Cause of death is presented in Table 4.

The comparison of postoperative outcome (age, gender, previous preoperative surgery, preoperative comorbidity, postoperative complication, operative time) is presented in Table 5.

Total number of postoperative death, complication, and mean operative time in each calendar year is presented in Table 6. For forty patients alive at the time of present study, the median follow-up in this group was 3.37 months (range, 0.5-65.7 months, mean 8.71 $\pm$ 13.66 months). Ten patients were greater after 1-year follow-up (19.23%), and five were greater after 2-year follow-up (9.12%). One patient had adjuvant chemo-radiation. Four patients were lost to follow-up. During the follow-up, six patients had recurrence. Three patients had liver metastasis (6.5months, 6.7 months, 2 yrs 5.8 months post-operative), one metastasis to left supraclavicular lymph node(1 yrs 4.1 months), and one had carcinomatosis peritoneii (2 yrs 7.9 months). One patient died 7.7month postoperatively from lung metastasis, and another died 6.7 months postoperatively from unknown cause.

Table 2. Preoperative serum chemistry and tumor marker

Variable	Patients (No.)	Value		
		Mean	Median	Range
Total bilirubin, mg/dL	39	12.80	11.40 $\pm$ 11.14	0.30-43.30
Alkaline phosphatase, U/L	38	695.45	490.00 $\pm$ 636.50	47.00-2450.00
AST (SGOT), U/L	38	111.05	81.50 $\pm$ 103.45	11.00-470.00
ALT (SGPT), U/L	38	102.61	75.00 $\pm$ 106.76	4.00-484.00
Total protein, g/dL	33	8.92	7.20 $\pm$ 10.27	5.00-8.80
Albumin, U/L	33	3.58	3.70 $\pm$ 0.73	2.30-5.60
Amylase, U/L	3	45.67	44.00 $\pm$ 15.58	33.00-60.00
CA 19-9	2	394.16	394.16 $\pm$ 149.69	288.31-500.00

Table 3. Postoperative complication, re-operation and outcome in 21 patients

	Benign (n = 1)		Malignant (n = 20)		Re-operation (n = 7)	
	Survived	Death	Survived	Death	Survived	Death
Surgical complication (n = 16)						
Intraabdominal sepsis	-	1	3	2	2	-
Pancreatic fistula	-	-	2	1	1	1
Bile fistula	-	-	1	1	-	1
Bowel fistula	-	-	-	1	-	1
Cholangitis	-	-	1	-	-	-
Internal hemorrhage	-	-	1	1	1	-
SMA occlusion	-	-	-	1	-	-
Medical complication (n = 5)						
Acute renal failure	-	-	1	2	-	-
Pneumonia	-	-	-	1	-	-
Myocardial infarction	-	-	-	1	-	-
Total	-	1	9	11	4	3

Table 4. Cause of death

Age (yr)	Co-morbid	Cause of death	Days after operation
52, female	-	Sepsis, MOF	23
60, male	-	Sepsis, MOF	10
78, female	HbE trait	Sepsis, MOF	3
61, male*	TB	Pancreatic fistula, Sepsis, MOF	50
62, female*	-	Bile fistula, Sepsis, MOF	36
53,female*	-	Bowel fistula, Sepsis, MOF	60
57, male	-	Internal hemorrhage	1
55, female	-	SMA occlusion	4
66, male	-	ARF	2
67, male	-	ARF	16
64, female	-	MI	0
74, male	DM	Pneumonia	23

* Re-operation
MOF = multi-organ failure

Table 5. Compare postoperative outcome between the survived group and the death group

	Survived	Death	p-value
Age, year			
Mean	60.78 $\pm$ 11.63	62.42 $\pm$ 7.99	0.60
Median	64	61.50	
Range	32-82	52-78	
Gender			
Male	23	6	0.65
Female	17	6	
Previous preoperative surgery	6	1	0.62
Preoperative comorbidity	10	3	1.00
Complication	9	12	0.64
Operative time, hour			
Mean	4.06 $\pm$ 13.31	4.09 $\pm$ 1.26	0.95
Median	3.75	3.66	
Range	2-9.5	2.58-7	

Table 6. Total number of pancreaticoduodenectomy and outcome in each calendar year

Year	Patients (No.)	Death (No.) (%)	Complication (No.) (%)	Mean Op. time
2000	9	0 (0)	3 (33.3)	6.00 ± 3.19
2001	6	3 (50)	4 (66.7)	3.72 ± 0.88
2002	4	0 (0)	2 (50)	3.80 ± 0.64
2003	13	2 (15.4)	3 (23.1)	3.86 ± 0.64
2004	7	3 (42.9)	3 (42.9)	3.40 ± 1.29
2005	4	2 (50)	2 (50)	3.89 ± 1.12
2006	9	2 (22)	4 (44.4)	4.12 ± 1.34

Discussion

In the present study, most of these patients were elderly (median age was 64 years and 59.62% were aged more than 60 years old). The male-female ratio was 29:26. All except two were confirmed by pathologic examinations. Malignancy was the most common indication for pancreaticoduodenectomy (84.62%). Of the malignancy, ampullary adenocarcinoma was the most common (45.45%), followed by pancreatic (31.82%), other periampullary tumors (13.64%), gastric (6.82%), and duodenal adenocarcinoma (2.27%). The other six benign disorders, chronic pancreatitis being the most common (50%), followed by chronic gastric ulcer (16.67%), cystadenoma of pancreas (16.67%), and leiomyoma of the duodenum (16.67%).

Preoperative symptoms, physical signs, and associated conditions recorded, the most common were jaundice (80.8%), abdominal pain (34.62%) and abdominal mass (7.69%). Thirty-nine patients in whom the serum bilirubin level was measured, 82.5% had an elevated level (> 2 mg/dL), suggesting that many patients had a component of obstructive jaundice. Serum albumin concentration was below the reference range (< 3 U/L) in 17.95% of the patients tested. CA 19-9, a serum tumor marker in the diagnosis of pancreatic cancers, was used only in two patients. This serologic test was not available in the past. Pretreatment diagnostic evaluation with ultrasonography, CT, and ERCP were performed in 73.08%, 36.54%, and 46.2%, respectively. All patients with advanced cancers in the preoperative evaluation were prevented needless laparotomy. Computed tomography was not accurate in predicting resectability in most patients and sometimes it was not always known whether the diagnosis is malignant or benign periampullary lesions, so surgery was undertaken for intraoperative management of this condition. A quarter of these patients had medical diseases, and diabetes was the most common comorbidity (61.54%). In forty-three patients with pathologic diagnosis of adenocarcinoma, 79.07% were well-differentiated adeno carcinoma, 18.6% metastatic to at least one lymph node, and 30.23% invaded to adjacent organ.

The overall postoperative morbidity rate was 40.38%, which is similar to 36%-41% in experienced centers[19-22]. No postoperative complication in patients under the age of 50 years, which is not consistent with previous studies showing that age did not significantly impact on the overall complication rate or any type of complications by severity[23].

Surgical complications were about three- fold more common than medical complications (76.2% vs. 23.8%). Complications included minor deteriorations from the normal postoperative course that can be treated with noninvasive therapy (19.1%), complications require invasive therapy (23.8%), and life-threatening complications (57.1%). The most common complications were intra-abdominal sepsis (28.57%), pancreatic fistula (14.29%), and acute renal failure (14.29%). These complications, for the most part, were major and life threatening.

Three patients (14.29%) had postoperative pancreatic fistula, similar to recent literature that reported the broad range of pancreatic fistula rates of 0%-28%[24-25]. Pancreatic fistula is the most problematic and feared common complication, there is still no consensus on a uniform definition of pancreatic fistula. In the present study, no postoperative pancreatic fistula in three patients with chronic pancreatitis, supporting the conventional thinking that a soft pancreas is more likely to develop a pancreatic fistula than one that is firm and holds sutures more reliably[26].

Although postoperative morbidity is similar to recent literature reports, the incidence of postoperative mortality is still high, with the overall postoperative mortality rate of 23.08%, which was comparable to a hospital mortality in the range of 25% in about fifty years ago (during the 1960s and 1970s)[27]. In recent literature, the operative mortality rate for pancreaticoduodenectomy has decreased to less than 5% in high volume centers[28]. Pancreaticoduodenec-tomy can be performed safely with a mortality of 0.7%-3% in experienced centers[19-22]. Analysis did not show any correlation between the age of patients and mortality after pancreaticoduodenectomy ($p = 0.65$). Duration of surgery was not a statistically significant mortality predictor ($p = 0.95$). After a mean follow-up of 3.37 months in the resection, six patients (15%) were found to recur within the 3-year follow up.

The division of general surgery of Sawanpracharak Hospital provides primary, secondary and tertiary care for the entire spectrum of general surgical diseases, performed 4-13 procedures of pancreaticoduodenectomy in 1 year, performed by six surgeons, 39 patients (75%) were performed by two surgeons, so variations in technique in the collected series were minimal. The mean operative time decreased significantly after the first year, being 6 hours in year 2000 and 3.4-4.12 hours in the following year, but mortality was not decreased. Hospital's annual procedure of 4-9 procedures performed was defined as medium volume hospitals, and in-hospital mortality rate in medium volume hospital was 8.2%-9.4%[27]. These results lead many surgeons to question whether pancreaticoduodenectomy should be performed for the treatment of pancreatic cancer at Sawanpracharak Hospital or refer patients to hospitals that do a high volume of the same procedure. There are obviously many factors responsible for the significant drop in hospital mortality, besides high volume. The best results can be achieved by careful attention to patient selection, preoperative assessment of resectability, surgical technique, critical care anesthesia and postoperative care remains an important factor in minimizing the perioperative mortality from this operation. The author believes that with improved preoperative assessment, strict patient selection, and excellent intensive care units, mortality rates will be decreased. As operative mortality rates have become acceptable, this procedure can be continued.

Conclusion

Pancreaticoduodenectomy is a complex procedure, and associated with an appreciable risk of operative death. In high-volume centers, this procedure can be conducted with acceptable mortality and provide better results. In Sawanpracharak Hospital, proper patient selection, careful technique and good critical care continue to be the most important factors in minimizing morbidity, mortality, and improve short-term and long-term results from this operation.

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ประสบการณ์ 7 ปีของการผ่าตัด pancreacticoduodenectomy ในโรงพยาบาลสวรรค์ประชารักษ์

สุชาติ วิภาสกรวราวุธ

ภูมิหลัง: *ในอดีตการผ่าตัดด้วยวิธี pancreaticoduodenectomy เป็นหัตถการที่ซับซ้อนและยุ่งยาก มีผลแทรกซ้อนค่อนข้างมาก และมักต้องทำในโรงพยาบาลที่มีความชำนาญขั้นสูง ปัจจุบันการผ่าตัดด้วยวิธีนี้มีความปลอดภัยมากขึ้น แต่ก็ยังเป็นที่หวาดกลัวสำหรับศัลยแพทย์ทั่วไป*

วัตถุประสงค์: *เพื่อศึกษาผลการผ่าตัด pancreaticoduodenectomy ในผู้ป่วยที่มีพยาธิสภาพบริเวณ periampula ในช่วง เดือนกุมภาพันธ์ พ.ศ. 2543 ถึง พฤศจิกายน พ.ศ. 2549 นำข้อมูลทางคลินิก ผลการรักษารวมทั้งโรคแทรกซ้อนและอัตราตายภายหลังการผ่าตัดมาวิเคราะห์เปรียบเทียบและหาปัจจัยที่เกี่ยวข้องกับการเสียชีวิตหลังการผ่าตัด*

วัสดุและวิธีการ: *เป็นการศึกษาในผู้ป่วยที่ได้รับการผ่าตัดจำนวน 52 ราย โดยไม่รวมผู้ป่วยที่มีสาเหตุจากอุบัติเหตุในโรงพยาบาลสวรรค์ประชารักษ์ ซึ่งเป็นโรงพยาบาลศูนย์ขนาด 800 เตียง ระหว่างเดือนกุมภาพันธ์ พ.ศ. 2543 ถึงเดือนพฤศจิกายน พ.ศ. 2549*

ผลการศึกษา: *จากผู้ป่วยทั้งหมดจำนวน 52 ราย พบว่าเป็นเพศชาย 29 ราย เพศหญิง 23 ราย โดยมีอายุเฉลี่ย 61.15 $\pm$ 10.86 ปี สาเหตุจากมะเร็ง 44 รายและไม่ใช่มะเร็ง 6 ราย ไม่พบรายงานผลทางพยาธิวิทยา 2 ราย ได้รับการผ่าตัดซ้ำ 7 ราย (13.46%) เกิดภาวะแทรกซ้อน 21 ราย (40.38%) เสียชีวิตหลังผ่าตัด 12 ราย (23.08%) ระยะเวลาติดตามผลการรักษาเฉลี่ย 8.71 $\pm$ 13.66 เดือน*

สรุป: *การผ่าตัด pancreaticoduodenectomy เป็นหัตถการที่มีความเสี่ยงสูง การคัดเลือกและประเมินสภาพผู้ป่วยที่เหมาะสมและพัฒนาการดูแลผู้ป่วยวิกฤติในระหว่างและหลังการผ่าตัด จะช่วยลดอัตราเสียชีวิตหลังการผ่าตัดได้*