Whipple's Operation without an Operative Mortality in 37 Consecutive Patients: Thai Surgeons' Experiences

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Objective: *Pancreaticoduodenectomy (Whipple's operation) represents a considerable surgical challenge. The operative mortality rate after Whipple's operation is still less than 5%. Recent studies show pancreaticojejunostomy (PJ) anastomosis is the "Achilles heel" of the procedure. The authors present the results of Whipple's operation without mortality which were performed in the Division of General Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.*
Material and Method: *From January 1991 to December 2003, thirty-seven consecutive patients who underwent Whipple's operation were enrolled in the present study. The ages ranged from 33 to 79 years (mean 57.13). There were 19 male and 18 female patients. Twenty-nine of them underwent a pylorus preserving pancreaticoduodenctomy (PPPD). Construction of the PJ anastomosis was mostly performed by a dunking technique, that is, the invagination of the pancreatic resected end into the jejunum.*
Results: *There was no postoperative mortality from anastomotic leakage. Surgical wound infections occurred in 7 patients, gastric atony in 2 patients, and PJ anastomosis leakage which created a fistula in 1 patient. All 37 patients were discharged in an improved condition following surgery. The median follow-up was 2 years (range: 4 month-11 years). Eighteen patients died from liver failure. Until now 19 patients are doing well.*
Conclusion: *The authors demonstrated that the dunking technique used for PJ anastomosis in Whipple's operation provided a good result without any mortality rate.*

Keywords: *Whipple's operation, Dunking technique*

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The first successful pancreaticoduodenectomy was performed by the German surgeon Kausch in 1912[1]. After Whipple et al[2] reported pancreaticoduodenal resection for ampullary cancer in 1935, pancreaticoduodenectomy has become popularized as the standard treatment for various benign and malignant diseases of the periampullary region. At present, pancreaticoduodenectomy (Whipple's operation) is still characterized by high mortality and morbidity rates. The authors recently showed the results of 37 patients who underwent Whipple's operation without any mortality rate in a single Thai institution.

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Material and Method

From May 1991 to June 2003, 37 consecutive patients underwent pancreaticoduodenectomy for periampullary disease at the Division of General Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. All pancreaticoduodenectomies were performed by a team of surgeons (Subdivision A), specialized in hepatobiliary surgery, with experience in hepato-biliary tract surgery for benign and malignant diseases. During the past 13 years, 19 males and 18 females patients, between the ages of 38 and 79 (median 58) were operated on. There were 28 periampullary malignancies, 5 benign lesions, and 4 neuroendocrine tumors of the pancreas.

All hematologic, biochemical and nutritional abnormalities were corrected preoperatively. Chronic anemia and malnutrition were treated with blood

transfusions and the administration of total parenteral nutrition (TPN) before the patients' surgery. All patients were in class I or II according to the American Society of Anesthesiologists (ASA) risk classification. Preoperative assessment was based mainly on imaging studies; helical contrast computed tomography (CT) scans, endoscopic retrograde cholangio-pancreaticography (ERCP), ultrasonography. The present resection criteria were (1) periampullary adenocarcinoma; (2) the absence of distant metastasis; (3) no evidence of tumor extension to portal vein or superior mesenteric vein; (4) periampullary mass which malignancy couldn't be rule out.

(1) Demographics, (2) preoperative presenting symptoms and preoperative imaging studies (Table 1), (3) details of surgical therapy (including blood loss and blood transfusion), (4) pathological reports, (5) the hospital course (including complications) and (8) postoperative survival were recorded.

In 29 cases (78.38%), pylorus-preserving pancreaticoduodenectomy (PPPD) was performed. The classical Whipple's operation was performed in 8 cases of which one patient underwent an extended resection (including a right half colectomy) owing to the extent of the disease (Table 2).

Follow-up consisted of personal contact with the patients or a questionnaire by mail and was terminated on August 30th, 2003. The median follow-up was 24 months (range 3-136) after the operation. Any death that occurred within 30 days after surgery or while the patient was still in hospital was classified as a surgical mortality.

Surgical Technique and Postoperative Management

Standard pancreaticoduodenectomy was carried out according to the classical description (removing only the peripancreatic lymph nodes en bloc with the specimen, Fig. 1). From the recent literatures[3-7], the addition of an extended resection of retroperitoneal lymph nodes to standard pancreaticoduodenectomy does not significantly increase morbidity and mortality rate. However the authors didn't performed the retroperitoneal lymph nodes dissection cause the data failed to indicate any survival benefit from the procedure.

The authors mostly performed pancreaticojejunostomy in an intussusceptive end-to-end fashion (dunking technique). The pancreatic stump should be adequately isolated for a distance of 3 cm. The end-to-end invagination of anastomosis was first performed in two layers (Silk No. 3/0 outside, Dexon No. 3/0 inside, Fig. 2).

After pancreatic reconstruction, hepaticojejunostomy (end-to-side anastomosis) was fashioned with a single row of interrupted 3/0 absorbable sutures. Finally, gastro-/duodeno-jejunostomy (end-to-side anastomosis) was done in an anticolic type without the Braun jejunojejunostomy. No vagotomy was performed in any procedure. A nasogastric tube was routinely used to decompress the stomach postoperatively, and it was removed when the gastric output from the tube was less than 500 ml per day.

Double soft plastic (Penrose) drains were placed behind the pancreatic and biliary anastomosis and are brought out through a stab wound, 3 cm in length, on the right side. The drain was shortened on the third postoperative day and removed in one week.

All patients received an H2-receptor antagonist or proton pump inhibitor during their postoperative course as a prophylaxis for stress ulceration. Somatostatin or analogues were not used as prevention for pancreatic stump-related complications. A pancreatic leak was defined as amylase-

Table 1. Symptoms and preoperative imaging studies (n = 37)

Symptoms and Imaging studies		No. (%)	
Sex	M	19	(51.35)
	F	18	(48.65)
Age, mean (range), yr		57.13	(38-79)
Presenting symptoms			
	Jaundice	23	(62.16)
	Ascending cholangitis	9	(24.32)
	Weight loss	5	(13.51)
	Abdominal mass	3	(8.11)
	Gastric outlet obstruction	3	(8.11)
	Upper GI bleeding & anemia	2	(5.41)
Preoperative imaging studies			
	Ultrasonography	15	(40.54)
	ERCP with biliary drainage	16	(43.24)
	CT	10	(27.02)
Total		37	(100.00)

Table 2. Operative procedure (n = 37)

Operation	Number of patients (%)
PPPD	29 (78.38)
Dunking technique	27 (72.97)
Duct to mucosa	2 (5.41)
Classical Whipple's operation	8 (21.62)
(With right half colectomy = 1)	
Dunking technique	8 (21.62)

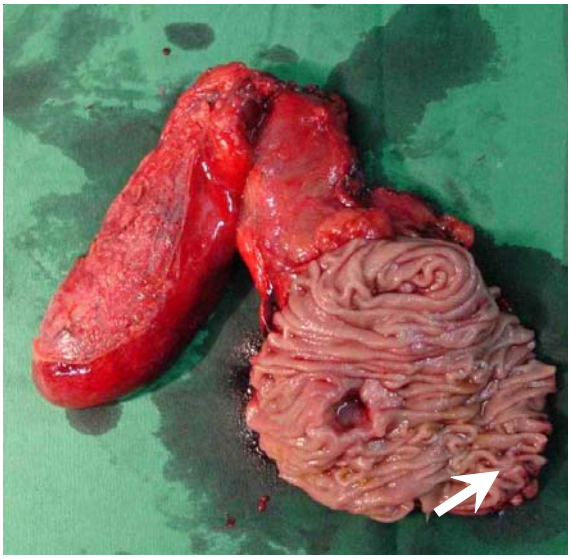

Fig. 1 Ulceroproliferative lesion of CA ampulla in an enbloc specimen of the duodenum, head of pancreas and common bile duct, gallbladder and peripancreatic lymph nodes

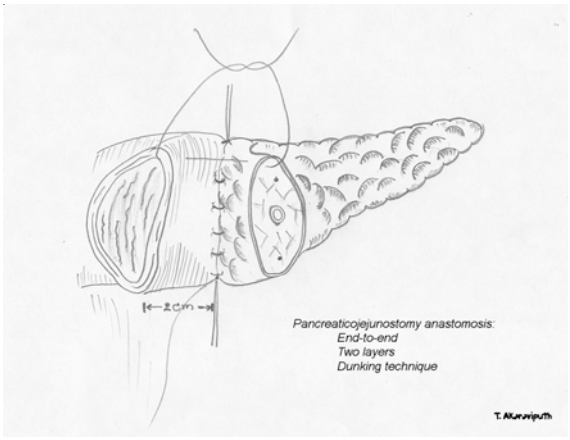

Fig. 2 The PJ anastomosis was performed in an end-to-end, dunking technique

rich fluid greater than 50 cc in volume (drain amylase greater than 3 times serum amylase). A pancreatic fistula was defined as a pancreatic leak that persisted beyond 14 days[8]. If no leak was determined, then the drains were removed prior to the patient's hospital discharge.

Delayed gastric emptying is defined as either persistent emesis after nasogastric tube removal, reinsertion of the nasogastric tube after the 10th day necessity to leave the nasogastric tube in for more than 10 days after the operation[9], failure to tolerate oral diet necessitating hyperalimentation, or radiologic evidence of delayed gastric emptying. Erythromycin or supplemental parenteral nutrition was not routinely used.

A biliary fistula was diagnosed if bilirubin-rich fluid was drained for more than 5 days. Bleeding was defined as the need for more than 2 units of packed red blood cells more than 24 hours after the operation, or reoperation for intra-abdominal bleeding.

Results

During this 13-year period, the authors performed a total of 37 Whipple's operations. Of these, there were 5 patients with benign lesions, 2 of whom had chronic pancreatitis, 2 patients with impact CBD stones, and one patient with an adenomatous polyp of Ampulla who underwent pancreatico-duodenectomy owing to clinical suspicion of malignancy (Table 3).

The operations lasted an average of 6.51 hours, with a median of 6 hours (range 3.5 to 10). The mean operative blood loss was 671.62 ml, with a median of 500 ml (range 250 to 3,000). The blood transfusion was 1.86 units, with a median of 2 units (range 0 to 4).

In the present series of 37 cases, complications occurred in 16 patients (43.2%) (Table 4). One

Table 3. Histolopathology of periampullary tumors resected by Whipple's operation

Histopathology	Patients (n)
Duodenum	
Carcinoma	1
Head of pancreas	
Carcinoma	4
NET	4
Chronic pancreatitis	2
Vater's papilla	
Carcinoma	17
Adenomatous polyp	1
Distal commom duct	
Carcinoma	4
Impact stones	2
Miscellaneous	2
(e.g. CA Gallbladder, CA stomach)	

Table 4. Complications after pancreaticoduodenectomy

Complications	Number of patients (%)
Surgical site infection	7 (18.92)
Delayed gastric emptying	5 (13.51)
Intraabdominal collection	3 (8.11)
Pancreatic fistula	1 (2.70)

patient (2.7%) had pancreatic leakage developing pancreatic fistula which spontaneously stopped after two weeks. Seven patients had surgical site infections (18.9%). Three patients had intraabdominal collections (8.1%) which didn't need a second operation. Five patients had delayed gastric emptying (13.5%) and were treated conservatively. No patient had biliary leakage. No hemorrhage or cholangitis was observed during hospitalization. The post operative length of the hospital stay was 9 to 84 days (median 16), with an average of 18.4 days. There was no postoperative mortality. Eighteen patients developed liver metastasis and died from liver failure. All the other patients are being followed up regularly.

Discussion

The surgical history of the treatment of periampullary tumors encompasses the past 100 years. Halsted reported the first successful resection of an ampullary tumor in 1899, describing a local ampullary resection with associated reanastomosis of pancreatic and bile duct into the duodenum. In 1912, Kausch[1], a German surgeon from Berlin, performed the first successful partial pancreaticoduodenectomy in two stages. In 1914, Hirschel reported a successful one-stage pancreaticoduodenectomy. In 1935, Whipple completed the one-stage pancreaticojejunostomy that is today called "Whipple's procedure"[2].

The Whipple's procedure was enthusiastically undertaken throughout America and Europe. The enthusiasm, however, was not unanimous, since the operative mortality rate remained high.

Pancreaticojejunostomy anastomosis has long been to be the critical step in Whipple's operation, and it represents the main cause of morbidity and death. A major problem was the complication of leakage of the pancreaticojejunostomy anastomosis. Regards the operative technique, the management of the pancreatic stump, the anastomosis procedure and a meticulous technique are the important points to prevent anastomotic leakage. As a matter of fact, some of the aforementioned risk factors - soft pancreatic texture, non-dilated pancreatic duct and high pancreatic juice secretion - are closely correlated. In other words, soft pancreatic texture is the basic risk factor since the other conditions frequently coexist with normal (soft) pancreatic texture. It might be the sutures that tend to lacerate the fragile pancreatic parenchyma. Thus, if sutures are not placed carefully and properly, the suture itself lacerates the gland and a pancreatic fistula may occur in the area of the suture placement.

In the present study, the most frequent surgical complication was surgical site infection (18.9%). The incidence of postoperative pancreatic fistula was only 2.7% (n = 1) and stopped spontaneously. No patient underwent another operation. Preoperative nutritional support and careful surgical technique are mandatory to reduce operative morbidity and mortality.

Preoperative biliary drainage may be a risk factor for infectious complications[10-13]. In the present study, the authors performed endoscopic retrograde cholangiopancreatography (ERCP) with biliary drainage in 16 patients (43%). In this group, we could not document a positive effect of a preoperative biliary drainage on morbidity, infection and survival rates.

Recent data from the literature seem to suggest that duct-to-mucosa anastomosis may be associated with a lower leakage rate than invagination anastomosis. However, there is still no consensus on the choice of anastomotic techniques, and currently both techniques (duct-to-mucosa versus invagination PJ anastomosis) find their application among different groups of surgeons. Marcus et al[14] found that duct-to-mucosa anastomosis was associated with a low pancreatic fistula rate in low risk patients with a dilated pancreatic duct or firm fibrotic pancreas. Whereas, the end-to-end invagination technique was safer in high risk patients with a small duct or soft friable pancreas.

Technical improvement on the part of the surgeons may be a more important approach to prevent pancreatic anastomotic leakage than relying on an expensive drug. The finding that the anastomotic leakage rate is related to the operative volume of the surgeon is a testimony to the importance of the surgeon's technique and experience in deciding the anastomotic leakage rate[15]. Many technique modifications for pancreaticoenteric anastomosis to decrease the pancreatic leakage rate have been suggested. Unfortunately, randomized trials on these technical measures are scarce. It is possible that gentle handling and proper mobilization of the pancreatic stump together with precise placement of the sutures, may have a greater effect on the postoperative outcome than the type of anastomosis performed[16].

Thus, by the early 1990s it was clearly demonstrated that, with a concentration of experience, the mortality rate could be reduced to below 5%[17]. There have been reports of long consecutive series of

Whipple's operation without any mortality at all[18-21]. However, the present study is the first one in Thailand which shows the excellence result of Whipple's operation without any operative mortality.

Conclusion

The present study demonstrates that a complicated procedure like Whipple's operation can be performed with excellent results (zero mortality). The dunking technique used for PJ anastomosis in Whipple's operation provided good results. The most important prerequisite is that the surgeon be adequately trained and have much experience in the procedure. In low-volume hospitals, the case load should be restricted to a minimal number of trained surgeons in order to concentrate the skill experience or the patient should be referred to an experienced surgeon in a hospital center.

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การผ่าตัด Whipple's operation ในผู้ป่วย 37 รายโดยไม่มีผู้ป่วยเสียชีวิต: ประสบการณ์ของศัลยแพทย์ชาวไทย

วิรุณ บุญนุช, ธวัชชัย อัครวิพุธ, ดรินทร์ โล่ห์สิริวัฒน์

คณะผู้วิจัยได้ศึกษาย้อนหลังถึงผลการผ่าตัด Whipple's operation ในผู้ป่วย 37 ราย ของหน่วยศัลยศาสตร์ทั่วไป ภาควิชาศัลยศาสตร์ โรงพยาบาลศิริราช มหาวิทยาลัยมหิดล ตั้งแต่เดือนมกราคม พ.ศ. 2534 ถึงเดือนธันวาคม พ.ศ. 2546 เป็นผู้ป่วยชาย 19 ราย ผู้ป่วยหญิง 18 ราย อายุระหว่าง 33-79 ปี โรคที่พบคือมะเร็งบริเวณ ampulla of vater (periampullary carcinoma) 33 ราย chronic pancreatitis 2 ราย และ impact CBD stone 2 ราย ผู้วิจัยได้ทำผ่าตัดแบบ pylorus preserving pancreaticoduodenectomy (PPPD) ในการต่อตับอ่อนกับลำไส้เล็กส่วนเจจูนัม จะใช้เทคนิคฝังตับอ่อนเข้าไปในลำไส้เล็กส่วนเจจูนัม (Dunking technique) ซึ่งได้ผลดี มีภาวะแทรกซ้อนคือ surgical site infection 7 ราย (18.9%) delayed gastric emptying 5 ราย (13.5%) intraabdominal collection 3 ราย (8.1%) pancreatic fistula 1 ราย (2.7%) โดยที่ไม่มีผู้ป่วยเสียชีวิตจากการผ่าตัด

***สรุป**: การผ่าตัด Whipple's operation โดยฝังตับอ่อนเข้าไปในลำไส้เล็กส่วนเจจูนัม (Dunking technique) น่าจะเป็นเทคนิคการผ่าตัดที่ได้ผลดีที่สุด*