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Original Article

Whipple's pancreaticoduodenectomy: Outcomes at a tertiary care hospital

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ABSTRACT

Background: Pancreaticoduodenectomy is a formidable surgery and was associated with high morbidity and mortality. Though the mortality rates have steadily improved, morbidity continues to be high. There is lack of published data on outcomes following pancreaticoduodenectomy in Armed Forces hospitals. The aim of this study was to analyze the short term outcomes at our center and to compare it with the published literature.

Methods: A retrospective review of prospectively maintained data base was done. Preoperative, intraoperative and postoperative data was analyzed with emphasis on the morbidity and mortality rates. Follow up data was analyzed to look at disease recurrence.

Results: Between Jan 2008 and March 2014, 69 patients underwent Whipple's pancreaticoduodenectomy with a median age of 64 years. All had a malignant etiology with periampullary carcinoma being the commonest (42%). Overall, intra-abdominal complications occurred in 46% of patients which included postoperative pancreatic fistula (20%) and delayed gastric emptying (24%). The mortality rate for the whole was 11% which reduced to 8% in the second half of the study.

Conclusion: The short term outcomes at our center were comparable to those in published literature. The mortality rates showed a decreasing trend with time.

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Introduction

Pancreaticoduodenectomy (PD) is a formidable surgery, commonly performed for pancreatic head and periampullary tumors and occasionally for benign conditions like chronic pancreatitis and pancreato-duodenal trauma. Before 1980s, this was being performed infrequently due to concerns regarding the morbidity and mortality rates associated with this complex surgery. In the series of 12 cases published by

Whipple himself, the mortality rate was 43% and remained in the region of 25% till 1970s.^{1,2} Since the 1980s, experience with this surgery increased and high volume centers were established. This along with improvements in perioperative and critical care management resulted in a steady and consistent fall in mortality rates and currently reported rates are below 5% in high volume centers.³

The morbidity, though, has not fallen significantly and reported rates in literature vary between 22 and 57%.^{4,5} The

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bulk of this morbidity consists of post operative pancreatic fistulas (POPF), delayed gastric emptying (DGE) and post pancreatectomy hemorrhage (PPH).

PDs are being done in hospitals of Armed Forces Medical Services for a long time now and there is a need to look at the outcomes of this surgery in our hospitals. However, there is lack of published data from our centers in this regard. The aim of this article was a surgical audit of all PDs done at our center with primary objectives being the morbidity and mortality rates and secondary objectives was to compare the outcomes with the available literature.

Material and methods

This was a retrospective review of prospectively maintained database of patients undergoing PD at our center between Jan 2008 to March 2014. Follow up of these patients was done and data incorporated in to database. Patients who had not reported were contacted by telephone calls where ever it was possible. Those reporting for review underwent detailed evaluation directed at detection of recurrence.

Preoperative work up: A detailed history was taken and clinical examination done for all patients. Diagnosis and resectability was assessed with ultrasound, contrast enhanced computed tomography scan (CECT) and side viewing endoscopy as indicated.

Preoperative fitness was evaluated with complete blood count, liver function test, renal function test, serum electrolytes, prothrombin time, electrocardiogram, chest radiographs and pulmonary function tests. The patient's condition was then optimized with regard to pulmonary function and other comorbid conditions. Preoperative biliary drainage was done if the serum bilirubin at the time of presentation was more than 20 mg/dl or if the patient had cholangitis.

Operating technique: All patients were explored using a bilateral subcostal incision. Once dissemination/unresectability was ruled out by visual inspection and palpation, the operation proceeded to a PD. All patients underwent a standard Whipple's PD. Reconstruction was be done by either a pancreaticojejunostomy (PJ) or pancreaticogastrostomy (PG). This was followed by hepaticojejunostomy (HJ) and finally an antecolic Gastrojejunostomy. Distal to this anastomosis a feeding jejunostomy (FJ) was routinely done.

Adjuvant therapy: All operated patients, irrespective of their pathological stage were referred for adjuvant chemotherapy.

Data collection

1. **Preoperative data:** This included age, sex, hemoglobin, liver function tests, serum albumin, weight loss, presence of jaundice, occurrence of cholangitis in recent past, preoperative biliary drainage, comorbid conditions, imaging, indication for surgery – benign or malignant and biopsy report if any.
2. **Operative data:** This included operative findings particularly duct size, pancreatic texture (as determined by the operating surgeon), total operation time, blood loss, blood transfusions.

3. **Postoperative clinical data:** The morbidity and mortality, if any was recorded. The length of hospital stay was noted. The need for re-exploration and readmission were also noted.

Definitions

1. **Morbidity:** Procedure or non-procedure related complication requiring medical/surgical intervention.
2. **Perioperative mortality:** All deaths within 30 days of surgery or in the same admission, irrespective of cause.
3. **Postoperative pancreatic fistula:** Defined according to the definition of the International Study Group of Pancreatic Fistula that included three grades (grades A, B, and C).⁶

Criteria	No fistula	Grade A	Grade B	Grade C
Drain amylase: Normal serum amylase	<3 times	>3 times	>3 times	>3 times
Clinical condition	Well	Well	Often well	Ill
Specific treatment	No	No	Yes/no	Yes
US/CT if obtained	Negative	Negative	Negative/positive	Positive
Persistent drainage (>3 weeks)	No	No	Usually yes	Yes
Signs of infection	No	No	Yes	Yes
Readmission	No	No	Yes/no	Yes/no
Sepsis	No	No	No	Yes
Reoperation	No	No	No	Yes
Death related to fistula	No	No	No	Yes

4. **Delayed Gastric Emptying:** As proposed by the International Study Group for Pancreatic Surgery (ISGPS), DGE was classified into three grades based on their clinical impact.⁷
 - Grade A: need for intubation of NGT for 4 days or reinsertion of the NGT after postoperative day (POD) 3, or inability to tolerate a solid diet by POD 7.
 - Grade B: need for intubation of NGT for 8 days or reinsertion of the NGT after postoperative day (POD) 7, or inability to tolerate a solid diet by POD 14.
 - Grade C: need for intubation of NGT for 15 days or reinsertion of the NGT after postoperative day (POD) 14, or inability to tolerate a solid diet by POD 21.
5. **Postpancreatectomy hemorrhage:** Bleeding in the form of fresh blood in the NGT and/or melena necessitating treatment such as transfusion of blood, embolization or relaparotomy. This definition corresponded to the definition of grade B or C post pancreatectomy hemorrhage that was proposed by the ISGPS.⁸

Results

During this period, 224 patients were evaluated for a PD. Of these 69 patients were found to be resectable and underwent a PD.

Patient characteristics and preoperative factors: The median age of all patients was 64 years (Range 42–78 years) with

Table 1 – Patient characteristics and preoperative factors.

Variables	Values (n = 69)
Age ^b	64 (42–78) years
Sex (%)	
Males	46 (67)
Females	23 (33)
Symptoms (%)	
Jaundice	64 (92)
Anorexia/wt loss	59 (85)
Pain abdomen	32 (46)
Cholangitis	10 (14)
Gastric outlet obstruction	05 (7)
GI bleed	03 (4)
Laboratory parameters	
Hemoglobin (g/dl) ^a	11.1 ± 2.4
Total leukocyte count (cells/cmm) ^a	8632 ± 3375
S. Creatinine mg/dl ^a	0.7 ± 0.2
Serum bilirubin at presentation (mg/dl) ^b	14.5 (0.5–29)
Preoperative serum bilirubin (mg/dl) ^b	9.9 (0.4–17.4)
S. ALP IU/dl ^b	915 (148–3602)
S. AST IU/dl ^b	54 (19–141)
S. ALT IU/dl ^b	50 (12–128)
S. Albumin g/dl ^b	3.85 (2.5–5)

^a Mean ± SD.^b Median (Range).

the commonest age bracket being 60–70 yrs. The male to female ratio was 2:1 with 46 males and 23 females (Table 1 and Fig. 1A). All patients had a malignant etiology, with periampullary carcinoma (42%) being the commonest indication followed by carcinoma of the head of pancreas (30%) (Fig. 1B). Among the presenting complaints, jaundice (92%) was the commonest symptom followed by anorexia weight loss (84%) and pain abdomen (46%). The median serum bilirubin at presentation was 14.5 mg/dl (Range 0.5–29). Eighteen patients (26%) underwent a preoperative biliary drainage; the modality in all was an ERC/stent. The median preoperative serum bilirubin was 9.9 mg/dl (Range 0.4–17.4).

Intraoperative factors: The mean operative time was 309 ± 59 min. The mean blood loss was 655 ± 398 ml and median blood transfusion was 1 (Range 0–5) units. Two patients underwent an extended resection; one had a portal vein resection and the other, a colectomy. In 83% of the patients,

Table 2 – Intraoperative and postoperative factors/complications.

Variable	Total (n = 69)	%
Operative time (min) (mean ± SD)	309 ± 59	–
Blood loss (ml) (mean ± SD)	655 ± 398	–
Transfusion (units) (median; range)	1 (0–5)	–
Extended resection (n) (%)	2	3
Pancreatic texture (n) (%)		
Soft	33 (48)	48
Firm	36 (52)	52
Pancreatic duct size (median) (range)	4.5 (1–20)	
<3 mm (n) (%)	19 (25)	25
≥3 mm (n) (%)	50 (75)	75
Type of pancreatic anastomosis (n) (%)		
PJ	57 (83)	83
PG	12 (17)	17
Intra-abdominal complications	32	46
POPF	14	20
Grade A	05	7
Grade B/C	09	13
DGE	17	24
Grade A	5	7
Grade B/C	12	17
Hemorrhage		
Grade A	0	–
Grade B/C	01	
Pulmonary complications	12	17
Wound infection	16	23
Reoperation	5	7
Postoperative stay (days) (median) (range)	17 (9–67)	–
Readmission	2	3

the pancreaticoenteric anastomosis was in the form of PJ and in the rest it was a PG (Table 2). The various techniques of PJ used are given as Fig. 2A.

Postoperative factors/complications: Overall 46% of patients had an intra-abdominal complication. The commonest complication was DGE (24%) followed by POPF (20%). The rates of clinically relevant (Grade B/C) DGE and POPF were 17% and 13% respectively. PPH occurred in only one patient (Table 2). The breakup of POPF according to the various techniques used is given as Fig. 2B. The rates of pulmonary complications and wound infections were 17% and 23% respectively. The reoperation and readmission rates were 7% and 3% respectively with no significant difference between the two arms. The

Fig. 1 – A. Distribution of patients according to age groups. B. Histopathological diagnosis.

Fig. 2 – A. Various techniques of pancreaticojejunostomy used in the patients. B. Pancreatic fistula in the various techniques of pancreatic anastomosis done.

indications for reoperation are given as Fig. 3A. The median postoperative hospital stay was 17 (9–67). The mortality rate was 11%. The mortality in the first half of this period was 15% while it was 8% in the second half (Table 3). All but 1 of the death were attributable to POPF (Fig. 3B).

Follow up: Follow up was available for 31/61 (52%) of the patients. The median duration of follow up was 29 months (Range 2–57 months). Thirteen patients were detected with disease recurrence, 8 were patients with carcinoma head of pancreas, 4 with periampullary carcinomas and one with cholangiocarcinoma. The recurrences in patients with carcinoma of the head of pancreas were more common and occurred earlier as compared to periampullary or cholangiocarcinomas (Fig. 4). The stage-wise break down of recurrences is given at Table 4.

Discussion

Though Alessandro Codivilla was the first person to perform a PD,⁹ it was Allen Whipple who popularized this surgery.¹⁰ The complexity of the surgery and its associated high morbidity and mortality resulted in initial reluctance in adopting this surgery for the management of pancreatic and periampullary

tumors. Whipple himself had performed only 37 PDs by the end of his career.¹¹

Things have steadily improved and many centers have brought out their outcomes. High volume centers are now reporting mortality rates below 5%,³ though morbidity rates still remain high. There is a definite need for Armed Forces hospitals to bring out their outcomes individually and collectively. So the purpose of this article was dual; one was to look at the short term outcomes and the other was to compare the outcomes with the available literature.

During this period, 69 PDs were performed by gastrointestinal surgeons and oncosurgeons. Overall, our morbidity rates were comparable to those in published literature. The commonest morbidity in our series was DGE (Overall 24%, grade B/C 17%). The reported rates of DGE by studies using the ISGPS definition are between 33 and 45%.^{12–14} The clinically significant DGEs were managed with prokinetics with addition of Erythromycin. Those not responding to this were started on parenteral nutrition along with prolonged nasogastric drainage. No patient needed reoperation for this indication though, in one patient, these measures needed to be continued 9 weeks before his DGE resolved.

The 'Achilles heel' of all PDs is the pancreatic anastomosis. POPF in our study was 20% with the clinically relevant (Grade B/C) POPF being 13%. The POPF rates reported in literature is

Fig. 3 – A. Indications for reoperation. B. Causes of mortality.

Table 3 – Mortality rates in the two periods.

Period	n	Mortality	%
Overall	69	08	11
2008–10	33	05	15
2011–2014	36	03	8

Fig. 4 – Recurrence pattern.

6–25%.¹⁵ POPF, directly or indirectly, contributes to the other morbidities including DGE, PPH, sepsis etc., and consequently is the commonest cause of mortality. To address this problem, many techniques of pancreatic anastomosis have been described. Although some of them may have shown better results in individual cohorts, no convincing evidence exists to choose one over the other. We, over a period of time have changed our technique of pancreatic anastomosis. Initially, if the pancreas was soft and/or the duct was small, we used the dunking method and in all others we did a ‘duct to mucosa’ PJ. During the second half of this period we have abandoned the dunking technique in favor of a PG in such cases and have used the binding technique described by Peng¹⁶ occasionally. However the numbers are small to draw any firm conclusion from the various techniques that we have used.

We had just one case of PPH in our cohort. This patient actually had a bleed from the drain insertion site and had to be re-explored. The reported rates of PPH in literature is 5–12%.^{17,18}

The re-exploration rates was 7%, the most common reason being POPF (3/5 patients). The rates of re-exploration in the range of 4–11% have been reported in different series.¹⁹

Our mortality rates overall was 11%. This is higher than those reported by large volume centers but comparable to reports from other centers. As our experience increases, both with the surgery as well as critical care management along with better intervention radiology support, the mortality rates

Table 4 – Stage-wise break down of recurrences.

Diagnosis	Recurrences	Stages		
		I B	II A	II B
Pancreatic adenocarcinoma	08	01	02	05
Periapullary carcinoma	04	0	01	03
Cholangio carcinoma	01	0	0	01

Table 5 – Comparison of our outcomes with those from other tertiary care centers of India.

Author	n	POPF (%)	DGE (%)	PPH (%)	Mortality (%)
Jagannath et al ²⁰	144	16	29	11	7
Balachandran et al ²¹	218	16	–	20	10
Mistry et al ²² and Chaudhary et al ²³	132	13	–	25	8
Lakshmanan et al ²⁴	212	7	14	8	3
Gangavatiker et al ²⁵	72	13	31	3	–
Present study	69	20	24	1	11

will become lower as evidenced by the lower mortality in the second half (8% vs. 15%). As expected, the commonest cause leading to death was POPF (7/8 deaths). We compared our outcomes with those from other tertiary care centers of India. The comparison is shown as Table 5.

Conclusion

Whipple's pancreaticoduodenectomy is a complex and a formidable surgery. Large series with good results are being reported by large volume centers with experienced surgeons. At our center, we have a reasonable volume. Our results are comparable to published data, though the mortality rates need to be better. However, notwithstanding the socio-economic and logistical problems, we need to have a more rigorous follow up in order to look at long term outcomes. Last, but not the least, we need to pool our data from all tertiary care centers in Armed Forces to look at our outcomes as a whole which can then form a basis for a multicenter randomized trials.

Conflicts of interest

All authors have none to declare.

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