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A Comparison Study Between Classical Whipple's Resection and Pylorus Preserving Pancreaticoduodenectomy in Carcinoma Pancreas

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ABSTRACT
The aim of this study was to compare the results of Pylorus-Preserving Pancreatico-Duodenectomy (PPPD) and Classical Whipple's operation, especially with respect to duration of surgery, blood loss, hospital stay, and complications, in carcinoma pancreas.A prospective, non-randomized study was done to compare the results of Pylorus-Preserving Pancreatico-Duodenectomy (PPPD) (Group A) and Classical Whipple's operation (Group B) in carcinoma pancreas, especially in terms of the length of surgery, the amount of blood lost, the length of time spent in the hospital, and the number of complications. Each study group included 25 individuals who underwent pancreatic cancer surgery and were followed up on for six months afterward. The study results suggest that people who received Whipple resection exhibited a greater average time of surgery and a higher need for blood transfusions in comparison to those who underwent pylorus-preserving pancreatico-duodenectomy. Group B (WHIPPLES) had superior post-operative weight gain and overall outcome in comparison to other groups. The study found that there were comparable rates of complications and deaths in both groups. The postoperative pathological examination indicated that both groups achieved margin-free excision, according to oncological criteria. Therefore, a surgical approach that preserves the pylorus and aligns with physiological considerations would be a more acceptable alternative for treating carcinoma of the pancreas.The study suggests that, when possible, pylorus-preserving pancreatic duodenectomy should be used as the preferred management approach for all operable instances of pancreatic and peripancreatic cancer.

INTRODUCTION

Pancreatic cancer is responsible for 4.8% of cancer-related fatalities in males and 5.5% in females. The formidable characteristics of these tumors, including their aggressive behavior, propensity for early metastasis, and elevated local recurrence rate, have resulted in unsatisfactory five-year survival rates after surgical removal, which range from 11% to 21%[1-6]. The development of the partial pancreaticoduodenectomy technique is attributed to German surgeon Kausch and Italian surgeon Godivilla[7]. Subsequently, this technique was improved by Whipple *et al*.[8].

Several modifications have been recorded, including the pylorus-preserving pancreaticoduodenectomy (PPPD), first reported by Watson in 1944 [9]. Pancreaticoduodenectomy, a surgical excision method, is the only option for survival for patients with periampullary and pancreatic cancer[4-6]. In high-capacity healthcare establishments, advancements in surgical proficiency have resulted in a reduction in the likelihood of mortality during surgical procedures to below 5%[6-8]. However, it is noteworthy that operational morbidity remains significantly elevated, with rates sometimes exceeding 30 to 40% and the primary factors contributing to this morbidity are pancreatic fistulas, intra-abdominal abscesses, sepsis, and delayed gastric emptying (DGE)[9].

The primary treatment approaches for periampullary and pancreatic head cancer consist of two surgical techniques: the pylorus-preserving Whipple procedure (PPPD), first described by Watson and subsequently popularized by Traverso and Longmire, and the traditional Whipple operation (CW), which was established by Kausch and Whipple[7].

For almost six decades, Classical Whipple's Resection has been widely regarded as the benchmark in surgical interventions for the treatment of pancreatic and peri-ampullary cancer. Furthermore, it has been suggested as a treatment option for those suffering from chronic pancreatitis accompanied by a mass located in the head of the pancreas. The CW procedure involves the complete excision of the pancreatic head, duodenum, common bile duct, gall bladder, and distal section of the stomach, along with the surrounding lymph nodes[10]. This procedure has the potential to result in particular problems, including early and late dumping, postoperative weight loss, and postoperative reflux. The surgical procedure known as pylorus-preserving gastrectomy (PPW) is gaining popularity among surgeons since it offers an alternate approach while maintaining the functionality of the pylorus at the gastric outlet[11-12].

The concept of PPPD was introduced in 1978 as a potential alternative, with both benefits and drawbacks. Postoperative Postprandial Pain and Discomfort (PPPD) has been linked to an increased prevalence of delayed stomach emptying, leading to an extended duration of postoperative naso-gastric suctioning. The use of the pylorus preservation approach results in a streamlining of the surgical intervention, resulting in reduced duration of procedures and decreased levels of intraoperative blood loss[11-12].

The PPPD procedure is designed to maintain the functioning of the stomach and pylorus, both of which play a crucial role in the physiologically regulated movement of chyime, the partially digested food[2,13]. Nevertheless, comparable rates of survival have been reported for both methodologies.

The goal of this study was to conduct a comparative analysis of Pylorus-Preserving Pancreatico-Duodenectomy (PPPD) and Classical Whipple's operation, specifically focusing on the length of surgery, blood loss, hospital stay, and complications in patients diagnosed with cancer of the pancreas.

MATERIALS AND METHODS

Study design: The design of this prospective study consists of a pre-treatment evaluation and a non-randomized treatment with either a classical whipple's resection or a PPPD. All the patients were closely monitored post-operatively. The postoperative morbidity and mortality data was evaluated every month up to 6 months of follow-up. The study protocol was approved by the research committee and ethical committee of the Medical College. Informed consent was obtained according to the local rules prevailing at the institution.

Inclusion criteria: All patients admitted to the hospital with diagnosed pancreatic or peri-ampullary cancer underwent curative resection.

Exclusion criteria:

- Patients with distant metastasis or local unresectable tumors
- Patients with direct invasion of the pylorus or stomach
- Patients with positive peripyloric lymph nodes
- Patients with lesions other than pancreatic or periampullary adenocarcinoma
- Patients with a previous gastric resection
- Patients with additional major procedures and who underwent emergency surgery without preoperative follow-up were excluded
- Patients who underwent palliative surgery

Preoperative evaluation: The preoperative workup was standardized for all patients. A CT scan of the upper abdomen and a chest x-ray were requested. In most cases, an ERCP, percutaneous transhepatic cholangiography, angiography, CT-angiography and MRI were optional.

Surgical procedure:

- All patients underwent Classical Whipple's Resection, or PPPD, in a standard manner
- After PPPD reconstruction is done either by Traverso's or by Watson's methods, A biliary stent was kept in all cases
- The decision regarding the type of surgery and the type of reconstruction was taken by the operating surgeon

Technique:

- **Pancreaticojejunostomy:** either dunking or duct to mucosa anastomosis as per duct size and the operating surgeon's preference
- **Hepaticojejunostomy:** single layer using interrupted 2.0 polyglactin sutures
- **Duodenojejunostomy:** single-layer extramucosal interrupted by 2.0 silk sutures

Postoperative Management: All patients were managed according to a standard postoperative pathway. All patients were given histamine H2-receptor antagonists as prophylaxis against stress ulceration, and octreotide treatment was continued for 7 days. At the end of the operation, a drain was left in the area of the pancreaticojejunostomy and the hepaticojejunostomy. The drain was removed if the amylase concentration was less than 300 μL^{-1} (less than twice the serum concentration) and production was less than 50 ml per day or after postoperative day 10. The nasogastric tube is removed when the aspiration has decreased to less than 200 mL per 24 hrs.

Pathologic review: All pathology specimens were reviewed to determine the primary pathologic diagnosis and the extent of the disease. The tumor stage was determined according to the UICC classification system and the TNM system resection margins of the specimen to be stained and to be considered positive if the neoplasm was present at the pancreatic neck, uncinate process, common bile duct, duodenum/gastric resection area, mesenteric artery, portal vein, and the circumferential margin.

Follow-Up: Patient follow-up was obtained via office records from the outpatient clinic. Patient demographics, intra-operative factors, pathologic findings, and postoperative course were evaluated. Parameters such as blood loss, duration of operation, delayed gastric emptying, intra-operative and postoperative complications, hospital stay, and hospital mortality were recorded at discharge. Follow-up evaluations were conducted every month following discharge. When signs of recurrent disease occurred during the interval, a CT scan or MRI was performed.

Statistical methods: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements were presented as mean ± SD (min-max), and results on categorical measurements were presented as number (%). Significance was assessed at the 0.05 level of significance. The student t-test (two-tailed, independent) has been used to find the significance of study parameters on a continuous scale between two groups (intergroup analysis). The chi-square and Fisher exact tests have been used to find the significance of study parameters on a categorical scale between two groups. The student t-test (two-tailed; independent) has been used to test the homogeneity of samples based on age (or continuous parameters) and the chi-square test to test the homogeneity of samples based on parameters on a categorical scale between two groups.

The statistical software, namely SPSS 15.0, Stata 8.0, MedCal 9.0.1, and Systat 11.0, was used for the analysis of the data, and Microsoft Word and Excel were used to generate graphs and tables.

RESULTS

A comparative study with 25 patients in Group A (PPPD) and 25 patients in Group B (WHIPPLES) was undertaken to study the results of Pylorus-Preserving Pancreatico-Duodenectomy (PPPD) and Classical whipple's operation, especially with respect to duration of surgery, blood loss, hospital stay, complications, and survival in carcinoma pancreas.

Comparison of age in years and gender: Out of 50 patients with 25 patients in each group the distribution of age and sex was matched between the two groups of study. Study subject's age and gender were matched with $p = 0.251$ and with $p = 0.395$ (Table 1).

Comparison of clinical features and diagnosis: Presenting complaints were statistically similar between the two groups of patients with $p = 1.000$. Duration of symptoms was statistically similar between tthe wo groups of patients with $p = 0.824$. Distribution of Co-morbid conditions were statistically similar b/w two groups of patients with $p = 1.000$. The presenting complaints, duration of symptoms, and the associated co-morbid conditions were also statistically similar between the two groups of patients. The preoperative albumin and bilirubin values were also comparable with respect to disease in both groups of study. CAHOP were significantly more in Group B while PAC were significantly more in Group A with $c2 = 5.128$; $p = 0.024$* (Table 2).

Table 1: Comparison of age in years and gender

		Group A		Group B		Pooled	
Variables	Characteristics	No	%	No	%	No	%
Age in years	Up to 40	2	8.0	2	8.0	4	8.0
	41-50	8	32.0	8	32.0	16	32.0
	51-60	6	24.0	9	36.0	15	30.0
	61-70	5	20.0	6	24.0	11	22.0
	>70	4	16.0	0	0.0	4	8.0
	Total	25	100.0	25	100.0	50	100.0
	Mean ± SD	56.80±13.46	52.90±9.59	54.88±11.73			
Gender	Male	10	40.0	13			
	Female	15	60.0	12			

Table 2: Comparison of clinical features and diagnosis

		Group A		Group B		Pooled	
Variables	Characteristics	N	%	N	%	N	%
Presenting complaints	Abd pain	7	28.0	8	32.0	15	30.0
	Jaundice	14	56.0	15	60.0	29	58.0
	Pruritis	3	12.0	2	8.0	5	10.0
	Wt loss	1	4.0	0	0.0	1	2.0
Duration of symptoms	Up to 5 weeks	16	64.0	16	64.0	32	64.0
	5-10 weeks	7	28.0	5	20.0	12	24.0
	>10 weeks	2	8.0	4	16.0	6	12.0
Co-morbid conditions	Absent	13	52.0	13	52.0	26	52.0
	Present	12	48.0	12	48.0	24	48.0
	DM	6	50.0	6	50.0	12	50.0
	HTN	2	16.7	3	25.0	5	20.8
	DM/HTN	4	33.3	0	0.0	4	16.7
	COPD	0	0.0	1	8.3	1	4.2
	CCP	0	0.0	1	8.3	1	4.2
	PTB	0	0.0	1	8.3	1	4.2
Diagnosis	CAHOP	9	36.0	17	68.0	26	52.0
	PAC	16	64.0	8	32.0	24	48.0
	Total	25	100.0	25	100.0	50	100.0

		Group A	Group B	Significance
Pre-operative Bilirubin and albumin	Bilirubin	9.75±7.40 (0.70-25.0)	8.39±6.16 (0.20-20.0)	t = 0.701; p = 0.486
	Albumin	3.56±0.59 (2.70-4.70)	3.90±0.67 (2.70-5.10)	t = 1.911; p = 0.062

Table 3 : Comparison of intra and post-operative parameters

MOT	Group A	Group B
Range	3.50-6.00	4.00-8.00
Mean ± SD	4.84±0.89	5.45±0.93

Table 4: Comparison of intra and post-operative parameters

		Group A		Group B		Pooled	
Variables	Characteristics	N	%	N	%	N	%
Blood transfusions	Nil	3	12.0	0	0.0		36.0
	1-2	14	56.0	12	48.0	26	52.0
	2-4	4	16.0	10	40.0	14	28.0
	>4	4	16.0	3	12.0	7	14.0
	Mean ±SD	2.24±1.50		3.24±1.78		2.74±1.71	
	Total	25	100.0	25	100.0	50	100.0
Duration of hospital stay in days	<5	0	0.0	0	0.0	0	0.0
	5-10	13	52.0	6	24.0	19	38.0
	10-15	9	36.0	18	72.0	27	54.0
	>15	3	12.0	1	4.0	4	8.0
	Mean ± SD	12.28±7.16		12.08±2.63		12.18±5.33	

Comparison of intra and post-operative parameters: Mean operating time was 4.89 hrs in Group A and 5.45 hours in Group B and so the mean operating time was significantly more in Group B with t = 2.372 and p = 0.02 (Table 3).

The average number of blood transfusion in Group A was 2.24 units whereas in Group B it was 3.24 units. Average blood transfusion was more in Group B with t = 2.139 and p = 0.038.

The mean distribution of hospital stays in Group A was 12.28 days whereas in Group B it was 12.08 from the study the hospital stay was statistically similar between two groups of patients with p = 0.896 (Table 4).

The incidence of complications were statistically similar between the two groups with p = 0.747. 18 patients (72%) in Group A did not have any complications and had an uneventful postoperative period whereas this was 19 patients (76%) in Group B the distribution of complication in Group A was asctic leak-one patient (14.3%), bile leak-2 patients (28.6%0, pancreatic leak-one patient (14.3%) hemorrhage-2

Table 5: Comparison of complications

Complications	Group A (n = 25)	Group B (n = 25)
Absent	18 (72.0%)	19 (76.0%)
Present	7 (28.0%)	6 (24.0%)
ASC leak	1 (14.3%)	3 (50.0)
BILE leak	2 (28.6%)	1 (16.7%)
PAN leak	1 (14.3%)	0
Hemorrhage	2 (28.6%)	1 (16.7%)
Infection	1 (14.3%)	1 (16.7%)

Table 6: Comparison of post-operative Mortality, follow up, 30 day outcome and weight gain

Variables	Characteristics	Group A N (%)	Group B N (%)
Mortality	yes	1 (2)	4 (8)
	No	24 (96)	23 (92)
Outcome	Improved	20 (80)	23 (92)
	Not improved	5 (20)	2 (8)
	Mortality	1	2
	Critical	1	0
	DGE+	1	0
	HS	1	0
	Readmitted	1	0
Follow up	Good	21 (84.0)	22 (88.0)
	Poor	2 (8.0)	0
	Death	2 (8.0)	3 (12.0)
Weight gain	Range	1.50-8.00	1.50-5.00
	Mean±SD	3.24±1.65	2.83±0.97

Table 7: Pathology

Pathology	Group A (n = 25)	Group B (n = 25)
MD-AD MF	6 (24.0%)	6 (24.0%)
PD-AD MF	3 (12.0%)	2 (8.0%)
WD-AD MF	16 (64.0%)	17 (68.0%)

patients (28.6%) and wound infection-one patient (14.3%). In Group B complications were seen in 6 patients. Ascitic leak in 3 patients, bile leak in one patient, haemorrhage in one patient and wound infection in one patient (Table 5).

Comparison of post-operative Mortality, follow up, 30 day outcome and weight gain: Occurrence of mortality was found to be statistically similar between the two groups of study with p = 1.000. The outcome on follows up in group 20 patients improved on treatment and in Group B 23 patients improved on treatment. Mortality 4% = one patient was seen in Group A ,one patient was critical, one patient had delayed gastric emptying and one patient and one patient required readmission and over all 5 patients were expired on follow up and the mortality was 8% (2 patients) in Group B. Post operative weight gain over six months of follow up was 3.24 kg in Group A and 2.83 in Group B this was statistically significant with p = 0.307 (Table 6).

Pathology: The pathology of both groups were statistically similar between the two groups with p = 1.000. All patients had a margin free resection all specimen were adenocarcinoma pancreas with well differentiated to poorly differentiated forms (Table 7).

DISCUSSION

The preservation of the pylorus in patients undergoing duodenopancreatectomy for cancer has been a controversial issue for the last decade. Numerous studies have been performed, including several RCTs, but the cumulative knowledge gained from these studies needed to be captured in a quantitative summary of the results to establish whether the pylorus-preserving pancreaticoduodenectomy (PPPD) is a better technique than the classic whipple (CW). A prospective, non-randomized comparative study was conducted to compare the results of PPPD and CW Operation, especially with respect to the duration of surgery, blood loss, hospital stay, and complications in the carcinoma pancreas.

The mean operating time was 4.89 hrs in Group A and 5.45 hrs in Group B, so the mean operating time is significantly higher in Group B with t = 2.372 and p = 0.022. The average number of blood transfusions in Group A was 2.24 units, whereas in Group B it was 3.24 units. That is, the average blood transfusion was higher in Group B, with t = 2.139 and p = 0.038. The mean distribution of hospital stays in Group A was 12.28 days, whereas in Group B it was 12.08 days. From the study, the hospital stay is statistically similar between the two groups of patients, with p = 0.896.

Other studies show that meta-analysis of perioperative parameters such as blood loss, red blood cell transfusion, operating time, and length of hospital stay in 3 RCTs demonstrated a significant reduction in operating time [min] for the pylorus-preserving Whipple group [PPW][14-16]. Intraoperative blood loss (mL) could be extracted in an analyzable way from only one trial and was significantly reduced in the PPW group[17]. In contrast, the summarized effect estimates of blood replacement units indicated similar application of blood products intraoperatively. Length of hospital stay (days) showed similar results in both groups, with only one article providing adequate data for pooling[18].

The incidence of complications was statistically similar between the two groups (p = 0.747). 18 patients (72%) in Group A did not have any complications and had an uneventful postoperative period, whereas 19 patients (76%) in Group B did. The distribution of complications in Group A was asctic leak in one patient (14.3%), bile leak in two patients (28.6%), pancreatic leak in one patient (14.3%), hemorrhage in two patients (28.6%), and wound infection in one patient (14.3%).

In Group B, complications were seen in 6 patients. Ascitic leak in three patients, bile leak in one patient, hemorrhage in one patient, and wound infection in one patient. The outcome on follow-up in Group A was that 20 patients improved on treatment, and in Group B, 23 patients improved on treatment. Mortality of 4% was seen in Group A; one patient was critical; one patient had delayed gastric emptying; and one patient required readmission. Over all, 5 patients expired on

follow-up, and the mortality was 8% (2 patients) in Group B. Warshaw *et al*.[16] show PPPD has been associated with delayed gastric emptying, an increase in morbidity, and prolonged hospital stays.

The incidence of mortality was found to be statistically similar between the two groups of study, with p = 1.000 (overall 12%, Group A 2%, and Group B 8%). The overall operative mortality in the Tran *et al*.[20] study shows 5.3%. Multicenter studies were often associated with a higher mortality rate, ranging from 5% in Italy[18] to 10% in France[17] and 17.2% in the United States[22]. In Taran study shows PPPD has been associated with delayed gastric emptying, an increase in morbidity, and prolonged hospital stays. As per the present study findings, postoperative pathological analysis revealed margin-free resection in both groups obeying oncological principles, so a more physiological procedure preserving the pylorus would be a more acceptable surgical option in carcinoma pancreas.

CONCLUSION

This study showed that the mean operating time and blood transfusions were higher in patients who underwent whipple resection compared to those in the pylorus-preserving pancreatico-duodenectomy group, whereas postoperative weight gain and overall outcome were better in the later group. The complications and mortality were similar in both groups in this study.

Postoperative pathological analysis revealed margin-free resection in both groups obeying oncological principles, so a more physiological procedure preserving the pylorus would be a more acceptable surgical option in carcinoma pancreas. Therefore, this study recommends all operable cases of pancreatic and peripancreatic carcinoma be managed with pylorus-preserving pancreatic duodenectomy whenever feasible.

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