

## Original Research Article

# Outcomes of Whipple procedure/pancreaticoduodenectomy- an eighteen-year experience at a tertiary cancer care centre in south India

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## ABSTRACT

**Background:** Early postoperative mortality rates after pancreaticoduodenectomy are in the range of 2-5%. Nonetheless, morbidity rates are still at 30-50% calling for apt strategies. The goal of this study was to examine the outcomes in terms of postoperative morbidity and 30-day mortality while additionally reviewing the demographic, clinical and pathological features of patients undergoing Whipple procedure at our government institution and comparing the outcomes with literature.

**Methods:** Data about demographic characteristics, intraoperative findings, postoperative histopathology, postoperative course, early post-operative outcomes, complications, and causes of postoperative death in patients who underwent pancreaticoduodenectomy for periampullary and pancreatic carcinoma between September 2006-August 2023 were collected and analysed.

**Results:** 45 patients were analysed. Mortality rate was 15.6%. Seven patients died perioperatively; three from cardiac cause (myocardial infarction), two from bile leak and sepsis, one from pulmonary embolism, and one as a result of postoperative hemorrhage. The morbidity rate was 54%. The most common early postoperative complication was delayed gastric emptying (31%) followed by postoperative pancreatic fistula (22%). The median overall survival of 39 patients was 21±6.5 months. The 5-year survival was 17 months.

**Conclusions:** Considering the fact that postoperative morbidity after Whipple procedure was similar to other centres, but the mortality rate being high, better knowledge about salvage techniques, improvements in perioperative care, use of interventional radiology, and running quality improvement projects to standardize postoperative recovery protocol could help in reducing the mortality and improve the outcome.

**Keywords:** Delayed gastric emptying, Morbidity and mortality, Pancreaticoduodenectomy, POPF, Whipple procedure

## INTRODUCTION

Pancreaticoduodenectomy (Whipple procedure) is a complex surgery commonly performed for malignant tumors of pancreatic head, ampulla, distal bile duct, second part of duodenum and less frequently performed for benign tumors and trauma of pancreatic head or duodenum, while rarely performed for chronic pancreatitis. Pancreatic head adenocarcinoma carries a dismal

prognosis compared to periampullary tumors. Most of the patients at presentation have advanced disease, and only 15% to 25% have operable tumors. Despite being associated with significant morbidity, surgery remains the cornerstone of the management plan in the era of multimodal management. Although Codivilla (1898) and Kausch (1909) performed pancreaticoduodenectomy (PD) successfully, the procedure secured its name as Whipple procedure after Allan Oldfather Whipple

publicized it for periampullary tumors in his publication in 1935.<sup>1</sup> As per his published case series, the postprocedural mortality was high, estimated to be 25 percent.<sup>2</sup> In recent times, high-volume centres have reported a significant reduction in mortality rates, in the range of 2-5%, due to advancements in surgical techniques, instrumentation, perioperative care, and intensive care facilities.<sup>3-5</sup> Nonetheless, morbidity rates are still at 30-50% calling for apt strategies.<sup>6,7</sup>

Major postoperative complications include: delayed gastric emptying, pancreatic leak or fistula, intra-abdominal abscess, bile leak, postoperative haemorrhage requiring blood transfusion or reopening, and complications related to the surgical site such as infection and wound dehiscence. Most of the studies are from western countries, where there is a substantial difference with respect to socio-economic conditions, treatment facilities, and perioperative care, which may affect the rate of complications and their management.<sup>8-10</sup> Ours is a government tertiary cancer care centre in south India doing pancreaticoduodenectomies for two decades. The goal of this study was to examine the outcomes in terms of postoperative morbidity and 30-day mortality while additionally reviewing the demographic, clinical and pathological features of patients undergoing Whipple procedure at our institution and comparing the outcomes with literature.

## METHODS

This was an observational study done in Government Royapettah Hospital, a tertiary cancer care centre in south India. Information on patients who had pancreaticoduodenectomy for pancreatic cancer and periampullary carcinoma between September 2006 and August 2023 was gathered from the Hospital record database.

### *Inclusion and exclusion criteria*

Data of all consecutive patients who were operated in the study period were collected using patients' records focusing on demographic characteristics, clinical history and investigations, intraoperative findings, postoperative histopathology, postoperative course, early post-operative outcomes and complications, and causes of postoperative death. Some data were gathered through telephone calls with the patients or accompanies, where-ever it was possible.

Patients with missing information from their data registries were excluded.

The study was approved by the Institution ethics committee, Government Kilpauk Medical college. After excluding patients with missing information, the final sample size was 45. Statistical Package for the Social Sciences (SPSS version 24) software was used to analyse the data. The qualitative variables were expressed by

number and percentage, whereas, the continuous data were expressed by mean, median, and standard deviation (SD). Multivariate data analyses were performed for following variables: demographics, intraoperative blood loss, postoperative histopathology, early post-operative outcomes such as morbidity and 30-day mortality. Survival function was estimated by Kaplan-Meier survival curve.

## RESULTS

### *Demographics, presenting symptoms, and preoperative factors*

45 patients who underwent Whipple procedure (PD) were analysed. Twenty-eight patients were males and seventeen patients were females. Maximum incidence was seen in the age group of 45-65 years (mean 54.5±14.7) with male preponderance (62%). Jaundice (74.7%) was the most common symptom, followed by anorexia with weight loss (60.6%), while the least presenting symptom was gastrointestinal bleeding. Preoperative biliary stenting through ERCP was performed in 4 patients. One patient with solid pseudopapillary tumor was operated after chemotherapy and radiation (SBRT) due to unresectability. None of the procedures were done after neoadjuvant therapy for malignant tumors. The demographics and presenting symptoms are shown in Table 1.

**Table 1: Demographics, presenting symptoms, and preoperative factors.**

Variables	Values	
Age	54.5±14.7 (21-77)	
Sex	Male	28 (62%)
	Female	17 (28%)
<b>Symptoms (%)</b>		
Jaundice	74.7	
Anorexia/weight loss	60.6	
Abdominal pain, vomiting	33.2	
Pruritus	16.5	
Fever	6.1	
Gastrointestinal bleeding	2.2	

### *Intraoperative factors and postoperative histopathology*

The mean operation time was 325±37.3 minutes and the mean blood loss during surgery was 550±130 ml. Vascular resection and reconstruction was performed in one patient with solid pseudopapillary tumor. On histopathology five (11.1%) patients had chronic pancreatitis, two patients had neuroendocrine tumors (one well differentiated and other neuroendocrine carcinoma), one patient has solid pseudopapillary tumor while 37 (82.2%) patients had malignant disease with adenocarcinoma of the pancreas being the most prevalent pathology (Figure 1).

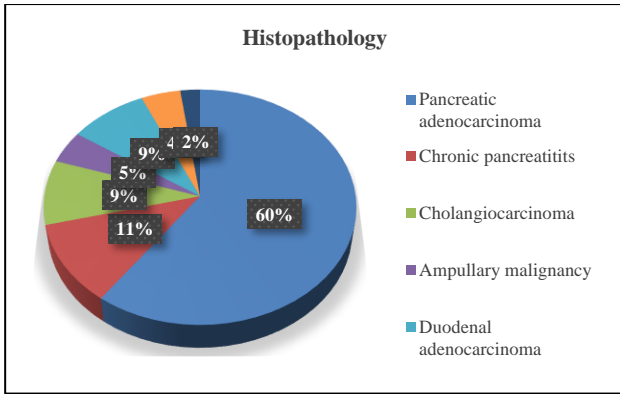


Figure 1: Postoperative histopathology.

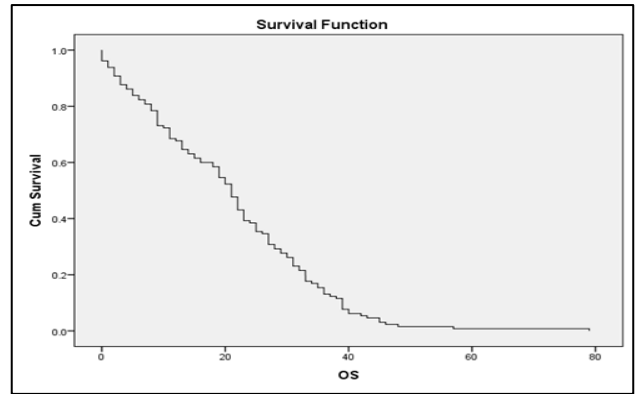


Figure 2: Survival.

**Postoperative outcomes**

30 days early postoperative outcome was analysed. Mortality rate was 15.6%. Seven patients died perioperatively; three from cardiac cause (Myocardial infarction), two from bile leak and sepsis, one from pulmonary embolism, and one as a result of postoperative hemorrhage (Table 2). The morbidity rate was 54%. The most common early postoperative complication was delayed gastric emptying (31%) followed by postoperative pancreatic fistula (22%). Reoperation was done in two patients with post-pancreatectomy hemorrhage and one died postoperatively. The morbidities are listed in Table 3.

Table 2: Postoperative outcomes- mortality.

Cause of mortality	Number (%)
Cardiac complication	3 (6.7)
Bile leak/sepsis	2 (4.4)
Pulmonary embolism	1 (2.2)
Hemorrhage	1 (2.2)

Table 3: Postoperative outcomes- morbidity.

Complication	Number (%)
Delayed gastric emptying	14 (31.1)
Pancreatic fistula	10 (22.2)
Infection and intra-abdominal abscess	5 (11.1)
Cardiac events	4 (8.9)
Respiratory complications	4 (8.9)
Bile leak	4 (8.9)
Haemorrhage	3 (6.7)
Reoperation	2 (4.4)

**Survival**

Leaving aside benign conditions, the median overall survival of 39 patients was 21±6.5 months (Figure 2). Most of the patients died of distant metastases (78%) and less commonly of locoregional recurrence (38%). The 5-year survival rate was 19%.

**DISCUSSION**

Pancreaticoduodenectomy is a complex and demanding surgical procedure requiring high dexterity. Once considered as a high mortality procedure is now being practiced in major hepatobiliary centres with mortality declining to less than 5%. However, the morbidity is still significantly high. Morbidity and mortality have improved recently with developments in intensive care management and surgical techniques. The postoperative mortalities have dramatically reduced, but the prevalence of postoperative complications is still high.<sup>11</sup> Therefore, it is imperative to achieve enough skills to avoid these complications and diagnose them in an expeditious manner to treat patients accordingly. This study describes our eighteen-year experience of Whipple’s procedure in terms of preoperative, operative, and postoperative parameters of patients undergoing surgery.

Delayed gastric emptying was the most common complication (31.1%) encountered. Most of them were ISGPS grade B or C requiring prokinetics and nutritional support. With poorly understood aetiology and no difference relating to pylorus resection or preservation, there seems to be no preferred method to prevent delayed gastric emptying after pancreaticoduodenectomy.<sup>12,13</sup>

The rate of pancreatic leak/postoperative pancreatic fistula (POPF) was 22.2%. We used monofilament, non-absorbable (3/0 to 5/0) sutures for the pancreatic duct reconstructions by varied approaches over the years with or without an internal pancreatic duct stent (infant feeding tube 6 Fr). Our result is in accordance with reports from varying centres ranging from 15 to 35%.<sup>14</sup> Among the 10 patients with POPF, 4 patients had ISGPF Grade B fistula with signs of infection or bleeding and no mortality. One patient with Grade C POPF died due to bleeding. Factors that may have effect on the pancreatic leak rate include age, nutrition, pathology of the tumor (malignant or benign), pancreatic duct size, soft or bulky pancreas (texture), operative time, and type of surgical technique.<sup>15</sup> The risk of POPF is elevated in patients having a small diameter/nondilated main pancreatic duct and soft pancreas. Several methods have been advocated

to prevent the pancreatic anastomotic leak, but none are standardized.

4 patients had bile leak/fistula (BF) and two succumbed to sepsis and organ failure. Patients with small size of the extrahepatic bile duct has the greatest risk of postoperative BF. Apart from the texture and calibration of the bile duct, the resection level of the bile duct and the vascularity is of importance. To get optimal vascularization, the resection of the bile duct should be at the hepatic duct level, superior to the cystic duct but below the confluence. Ischemic cholangiopathy is commonly caused by skeletonization, division, and anastomosis with the CBD and ligation of the hepatic arteries. Proper surgical technique with consideration of the texture and diameter of the hepatic duct could help reduce the risk of BF.<sup>16</sup> We also observed that preoperative ERCP makes the bile duct dissection and its separation from the portal vein and hepatic artery difficult leading to longer operating time and increased chance of BF.

In our analysis, we found that pulmonary complications such as pneumonia, pleural effusion, and reintubation occurred in 8.9% of patients. This result is in accordance with the findings of other studies, which reported rates of 6-15%. Adequate prehabilitation and postoperative chest physiotherapy with good pain control has helped us achieve these rates. In our study, we had three patients (6.7%) with intra-abdominal bleeding postoperatively. Because of lack of percutaneous angiographic intervention facility at our centre, we explored two of the patients surgically and one patient died eventually.

30 days early postoperative mortality rate was 15.6% which was double that of standard rates. Mortality after pancreaticoduodenectomy has decreased considerably from as high as 25-30% in the 1970-1980s to less than 2-4% in the modern era. The decline in short-term, perioperative mortality is observed across different indications for resection and variations of surgical technique. Improvements in operative and anaesthetic techniques, regionalization to high-volume centres, implementation of standardized recovery pathways, and better understanding and management of common complications have all contributed to the dramatic decline in postoperative mortality.<sup>17</sup> Further reduction in postoperative mortality can be achieved by improving patient selection, mitigating postoperative malnutrition, and optimizing preoperative management strategies.<sup>18</sup> In our study, out of seven patients, four patients died in the early postoperative period due to cardiorespiratory cause (myocardial infarction-3, pulmonary embolism-1) indicating that we need to rejuvenate our patient selection, improve prehabilitation, and standardize postoperative recovery protocol by running quality improvement projects.

Radiologic intervention was applied to 9 patients. All were drainage of intraabdominal abscess/collection and

no vascular intervention could be carried out due to lack of infrastructure. Angiographic intervention could have helped in preventing the death of one patient with postoperative intra-abdominal bleeding.

Several studies have reported the effect of treating at high volume centres on post-operative outcomes taking into consideration both the technical expertise and postoperative management protocols. The definition of high and low volume varied among all these studies from 15 to 40 patients per year. Birkmeyer et al. have reported a marked difference in mortality rates of Whipple procedure in very low-volume (zero or one patient per year) and low-volume (one or two per year) hospitals compared with higher-volume hospitals (less than five per year).<sup>19</sup> In very low-volume and low-volume hospitals, mortality rates were significantly higher than those at high-volume hospitals. Surgeons who performed fewer than four resections per year had more complications than those who performed more than four.<sup>20</sup>

Although this study gives insight into the clinical details, postoperative complications, and early mortality of patients who underwent Whipple procedure in a public sector tertiary care centre, the retrospective nature of this study with small sample size is a limitation. The study did not compare the outcomes of different surgical techniques. A comparison of stage, age-related, tumour marker related, and performance status related outcomes of Whipple procedure was also not performed. The surgical procedures were not standardized or uniform, with varied techniques and surgeons performing the procedure over years.

## CONCLUSION

Considering the fact that postoperative morbidity after Whipple procedure was similar to other centres, but the mortality rate being high, better knowledge about salvage techniques, improvements in perioperative care, use of interventional radiology, and running quality improvement projects to standardize postoperative recovery protocol could help in reducing the mortality and improve the outcome.

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