

Experience of Pancreatic Resection for Pancreatic Cancer an Audit of 75 Cases

Aditya Parakh^{1*}
Prabhat B. Nichkaode²

¹Assistant Professor, Department of Surgery Government Medical College, Rajnandgaon, CG, India

²Professor, Department of Surgery, D.Y. Patil Medical College & Research Centre, D.Y. Patil Vidyapeeth, Pune, India

Abstract

Introduction: Different pancreatic pathologies, needs resection of pancreatic tissue. Adenocarcinoma of the pancreatic duct is the most frequently seen malignancy, presenting with early metastasis and seen as resistant to alternative treatment regimens currently available [1,2]. Management and handling of such tumors is a complex and challenging task for a surgeon [1-3]. surgical resection offers improved prognosis, with a median survival after resection of 14-20 months and up to 25% 5-year survival rates [4,5]. This study is aimed at presenting data of 75 pancreatic resections for various malignant pancreatic lesions.

Methods: This is an ongoing longitudinal study which started in 2009 at teaching institute in central India. Though we had 122 patients for pancreatic resection, only 75 patients were considered suitable for the present study. All patients after admission were thoroughly investigated and then considered for surgery. 53 patients were male and 22 patients were female. Age group was ranging from 34 to 67 years with mean age between 46 to 56 yrs. Spectrum of various malignancies and different types of pancreatic resections were done and results are presented in this study.

Results: Pancreatic adenocarcinoma is one of the most aggressive malignancy, responds to surgical treatment better than other alternative modalities. In our series out of 75 patients 32 patients with pancreatic head cancer, 28 patients with Periampullary cancer, 2 patients with duodenal cancer, 8 patients with distal cholangio carcinoma, 1 patient with mucinous cystadenocarcinoma. 4 patients with body and tail of pancreas cancer. Average age 34 to 67 years, 53 males and 22 females. Commonest procedure was Whipple's operation, and distal pancreatectomy. Survival in our series was 18 -24 months and 5-year survival was 12 % that is seen mainly with Periampullary cancer.

Conclusion: Surgery is the only chance of cure or long term survival in pancreatic cancer. Chemo radiation as a primary therapy is ineffective. But some reports suggest the improved quality of life with palliative chemotherapy. Biology of the disease is the king and dictates the outcome, the type of surgical procedure had no impact on survival, nor on morbidity and mortality.

Keywords: Pancreatic cancer, Pancreatic resections, Complications, Outcomes.

Abbreviations: SWS: Standard Whipple's surgery; PPPD: Pylorus preserving pancreaticoduodenectomy; DCC: Distal Cholangiocarcinoma; CT: Computed Tomogram; MRCP: Magnetic Resonance Cholangio Pancreaticogram; ERCP: Endoscopic Retrograde cholangio Pancreaticogram; RCT: Randomized controlled Trials.

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***Corresponding author:** Dr. Aditya Parakh, Assistant Professor, Department of Surgery Government Medical College, Rajnandgaon, CG, India. Tel: +9770724242; Email: aadityaparakh83@gmail.com

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Introduction

A variety of pancreatic pathologies, malignant and benign, may need to remove the pancreatic tissue to varying extent. Resection of head includes standard Pancreaticoduodenectomy or but less extensive resections can also be performed in the form of central pancreatectomy or distal pancreatic resection. Pancreatic ductal carcinoma is the most common malignancy of pancreas, presents with early metastasis which is resistant to alternative treatment regimens available currently. Handling of such a disease is a complex and challenging task for operating surgeon or his conservative medicine team [1-3]. Surgical resection offers significantly improved prognosis with a median survival 14-20 months and 5-year survival rates 8% [4,5]. When surgical resection was compared with radio chemotherapy for resectable pancreatic cancer, patients in operative group done fairly well with median survival of 17 months versus 11 months in chemo-radiation group [6,7]. Few studies report improvements especially with regard to quality of life, are primarily due to use of gemcitabine as first line chemotherapy [8]. Standardized surgical treatment for head of pancreas cancer, duodenal cancer, distal cholangiocarcinoma, Periampullary cancer was Whipple's or it's pylorus preserving modification. While for Tumors of body and tail of pancreas needs distal pancreatectomy. Many studies report the role of adjuvant chemotherapy is advantageous in prolonging the overall survival, while the neo adjuvant chemotherapy is still in the phase of infancy [9]. With this in mind we aimed our study to present the data of 75 cases of various pancreatic resections for cancer of pancreas.

Methods

This is an ongoing longitudinal study which started in 2009 at teaching institute in central India. Though we had 122 patients of pancreatic cancer only 75 patients were considered suitable for the study. As other 46 patients had pancreatic cancer with metastasis, or locally inoperable disease found during imaging investigations, and one patient was diagnosed as adenocarcinoma of tail of pancreas, but after resection proved to be neuroendocrine tumor (Glucagonoma) so excluded from our study. 53 patients were male and 22 patients were female. Age group was 34 to 67 years with mean age between 46 to 56 yrs. Detail history was obtained from all patients and all necessary investigations were done with emphasis on Liver function, kidney function, coagulation profile, CA 19-9, USG abdomen, Upper GI endoscopy and biopsy whenever indicated. CT scan of abdomen to see the extent of disease and involvement of vascular structures around pancreas. (In Patients with the tumor is fixed to Portal vein or SMV, patients with liver metastasis, Ascitis, peritoneal metastasis were excluded from study) where ever necessary MRCP/ERCP with biliary stenting was done (bilirubin levels have gone >22% mg) and then considered for surgery. We did not have the facility of endoscopic ultra-sound; all patients were subjected for preoperative laparoscopy to assess the operability. Preoperative preparation was done as for any major case, all patients who had major

pancreatic resections were closely observed in Surgical ICU for 48 to 72 hours. Drain amylase was done on 3rd, 5th, 10th.postoperative day, to see any pancreatic leak. Chest physiotherapy started immediately on 2nd postoperative day. All patients were given DVT (Deep Venous Thrombosis) prophylaxis by LMH (Low molecular wt. Heparin) Spectrum of various malignancies and pancreatic resections done, evaluated and results are presented in the study, relevant differences in morbidity and mortality of the surgery, i.e., Standard Whipple's procedure over Pylorus preserving Pancreatico- duodenectomy (PPPD) and survival between two procedures. Some standard definitions were followed during the study, A POPF (Post-operative Pancreatic Fistula) was defined as a drain output of any measurable volume of fluid after POD 3 with amylase content greater than three times the serum amylase activity. Post-operative mortality was defined as death occurring in the first 30 postoperative days, or before discharge from hospital. Delayed gastric emptying was defined as intolerance to oral intake and need for nasogastric decompression after 7 post-operative days. Other complications were categorized and defined as any of the following intra-abdominal abscess (fluid requiring drainage and with post bacterial culture) wound infection, post-operative bleeding (requiring transfusion, endoscopic or operative intervention) Bile leakage (bilious drainage from intraoperatively placed drains or bile collection requiring drainage). Cardiac (Myocardial infarction or new onset of arrhythmia requiring intervention) Pulmonary (Pneumonia, effusion requiring drainage, or reintubation. Sepsis (Fever, leukocytosis, or bacteremia requiring medical or surgical intervention) reoperation in the first 30 postoperative days or before discharge from the hospital.

Technicalities of Surgery

Pancreaticoduodenectomy has evolved since Walter Kausch, Allan Whipple who performed first successful operation in 1912 but it was associated with lot of morbidity and mortality. Pancreaticoduodenectomy consists of three basic steps, Exploration, resection and reconstruction of the gastrointestinal continuity. As of now because of the modification in the technology the procedural morbidity has come down considerably. Classical whipple's operation consists of removal of head of pancreas with duodenum with pylorus with 1st. few cms of jejunum. Today we have lot many modifications including major vascular resections, multivisceral operations, and extended lymphadenectomy. But Pancreaticoduodenectomy is still considered to be standard operating procedure for cancer head of Pancreas. Various complications like gastric dumping, Postoperative pancreatic fistula, bleeding, chest complications associated with this procedure. In present series 32 patients with diagnosis of head cancer, 28 patients with Periampullary cancer, 8 patients with distal cholangiocarcinoma, 2 patients with duodenal cancer underwent Whipple's operation or its modification, PPPD (Pylorus preserving Pancreaticoduodenectomy) 5 patients with body and tail tumors had distal pancreatectomy with or without splenectomy. In all 70 patients who underwent whipple's operation, the pancreas was transected about 2 cm. left to the portal vein, R-0 resection was achieved in all patients.

Standard anastomosis between Pancreas and Jejunum (Duct to Mucosa Pancreatico Jejunostomy, Pacreatico Jejunostomy by dunk in method, on antimesenteric boarder, followed by Biliary enteric anastomosis and then Gastrojejunal anastomosis). The distances between all these anastomoses were almost 8 cm. From each other, Gastrojejunostomy was almost 25 cm from PJ (Pancreatico Jejunostomy).

Anastomosis was done in two layers by 4-0 PDS sutures. All anastomosis was done by a surgeon of at least of the level of Associate Professor and above who is experienced in doing these anastomoses. The method of anastomosis depends on whether the pancreas is soft or fibrosed. Wherever it is soft (good exocrine function) pancreas dunk in method was followed, otherwise it was duct to mucosa anastomosis.

Results

Out of 75 patients 53 (70.7%) males, 22 patients (29.33%) females, Age group was 34 to 67 years with mean age between 46 to 56 yrs. Our study group was consisting of 75 patients, of 75 patients, 32 (42.66%) with pancreatic head cancer, 28 patients (37.33 %) with Periapillary cancer, 2 patients (2.66 %) with duodenal cancer, 8 patients (10.66%) with distal cholangio carcinoma, 1 patient (1.33%) with mucinous cystadenocarcinoma involving body and tail. 4 patients (5.33%) with body and tail of pancreas cancer. (Table 1) 67 patients (89.33%) presented with jaundice. 2 patients (2.66%) presented with signs of gastric outlet obstruction. On upper GI endoscopy followed by histopathology, confirmed the diagnosis of adenocarcinoma of duodenum. Pain in abdomen with or without mass and vague abdominal symptoms was the presentation in patients with body and tail of pancreas cancer in 5 patients (6.66%). Initial USG followed by CT Scan complementing the diagnosis along with ERCP/MRCP, in properly selected patients. We did not do Endoscopic ultrasound and guided biopsy, because of financial constraints, MRI for lymph node mapping was not done in our study. CT Scan was basically aimed to assess extent of disease around the major vascular structures. We did not favor major vascular resections in our series. Of 75 patients 70 (93.33%) underwent Whipple's Pancreaticoduodenectomy. Of 70 patients 37 (52.85%) had classical whipple's and 33 patients (47.14 %) had PPPD operation. 5 patients (6.66%) underwent distal pancreatectomy with 4 patients had splenectomy because of close proximity of the tumor to splenic hilum. Average operating time 180 to 270 minutes in Whipples, time required for distal pancreatectomy was between 180 to 220 minutes. Average blood loss was 150 ml to 200 ml. not a single patient had blood transfusion intraoperatively. All patients had histopathological diagnosis of adenocarcinoma- 1 had mucinous cystadenocarcinoma. One patient in the study had an CT guided FNAC from the mass in the tail of Pancreas diagnosed as adenocarcinoma patient was diabetic, distal pancreatectomy with splenectomy was done. Surprisingly patient landed in hypoglycemia with a migrating Necrolytic rash on upper and lower limbs. This confirmed the diagnosis of Glucagonoma later on confirmed by Histopathology and Immuno-histochemistry- so excluded from the present series.

Morbidity and Hospital mortality was calculated and Survival was estimated by the Kaplan-Meier method using the date of operation as the starting point and death as the end point. In our series we had Pancreatic leak in Whipples in 6 (8.57%) patients. All 6 patients had hospital mortality. All pancreatic leaks were demonstrated by wound discharge and subsequent wound dehiscence with presence of high levels of amylase in drain fluid done from 3rd and 7th Post-operative day. Pancreatic Leak was demonstrated on day 4 to day 6. One patient (1.75%) with bile leak from Hepatico Jejunostomy, was treated conservatively stopped after 2 weeks. All remaining patients were followed up and average survival in patients with head cancer was 16 to 20 months. With no patients survived for five years but we noted 3 years' survival in head cancer group. Not a single patient with cholangio carcinoma survived more than 12 to 16 months. While Periapillary cancers were surviving from 24 to 40 months. It is this group where we had 5-year survival after surgery in 4 patients (14.28%) Patients with distal pancreatic resection for body and tail of pancreas- Mucinous cystadenocarcinoma the patient is still surviving after 5 years. Average survival for adenocarcinoma of body and tail of pancreas in our series was 12 to 18 months. No patients survived after 18 months. 2 patients with duodenal cancer also died within 18 months.

Discussion

Pancreatic resections are described for various pancreatic and peri-pancreatic tumors since the era of Kausch and Whipple. Pancreatic ductal adenocarcinoma is found to be one of the commonest pathology, followed by ampullary or Periapillary cancer, Distal cholangio carcinoma, needs Whipple's procedure, tumors of body and tail are treated by distal pancreatectomy [1-3]. Surgical resection offers significantly improved prognosis with a median survival 14-20 months and 5-year survival rates less than 7%-10% [1,4,5] (Table 1). Current scenario in such a complex situation is a difficult proposition, as outcome with other alternative therapies are not acceptable in terms of survival and quality of life [6-8]. Some recent reports show improved survival with Gemcitabine as a first line of therapy [9]. In our series males are the sufferers of pancreatic cancer, out of 75 patients, 53 (70.7%) males, 22 (29.33%) females. 32 Patients (42.66%) were with Pancreatic head cancer, 28 patients (37.33%) with Periapillary cancer, 2 patients (2.66%) with duodenal cancer, 8 patients (10.66%) with distal cholangio carcinoma, 1 patient (1.33%) with mucinous cystadenocarcinoma involving body and tail, 4 patients (5.33%) with body and tail of pancreas cancer. Age group was 34 to 67 years with mean age between 46 to 56 years. As per available literature incidence of pancreatic head cancer is between 0.3 to 13.7/100000 [9]. Duodenal cancer is a relatively uncommon neoplasm, which accounts for approximately 6% of Periapillary malignancies with an incidence estimated at 2.9 cases for million population and accounts for approximately 0.2% of gastrointestinal tract carcinomas. SWS 50% done for duodenal adenocarcinoma had overall 5 year survival varies widely according to the series published, but is generally reported to be >50% in case of curative resection [10,11]. Distal cholangio carcinoma

(DCC) In a study of 56 DCC-mean age was 65 ± 15 years. The median Overall Survival (OS) was 36.9 months, recurrence occurred in 35 patients (67%) mostly in the liver (37%) median Disease free Survival (DFS) was 14.6 months [12,13] (Table 2,4). In our study group of 75 patients, 70 (93.33%) underwent Whipple's Pancreaticoduodenectomy. Of 70 patients 37 (52.85%) had classical whipple's and 33 patients (47.14%) had PPPD operation. 5 patients (6.66%) underwent distal pancreatectomy with 4 patients had splenectomy because of tumor reaching splenic hilum. A 2014 Cochrane review examined six randomized controlled trials (RCTs) comparing classic Whipple Pancreaticoduodenectomy with PPPD in a total of 465 patients with Periampullary or pancreatic carcinoma [14]. The authors found no relevant differences in mortality, morbidity, or survival between the two operations. This review was updated in 2016 to include eight RCTs with a total of 512 participants. Again,

the investigators found no evidence of any relevant differences in mortality, morbidity, and survival between the two operations, though some perioperative outcome measures favored PPPD to a significant degree [15]. Postoperative pancreatic fistula (POPF) is the main cause of fatal complications after whipple's operation (Table 3). There is still no universally accepted technique for Pancreaticoenterostomy, especially in patients with soft pancreas. Modified Blumgarts method is safe and simple and improves postoperative outcomes [15]. In our series average operating time 180 to 270 minutes in Whipples, Median duration of the SWS was 265 (range 203-475 mins). with median blood loss was 570 (50-850) ml (Table 5). Time required for distal pancreatectomy was between 180 to 220 minutes. Average blood loss is between 150 ml. to 200 ml. In our series, not a single patient had blood transfusion intraoperatively. Average hospital stay after SWS was, 17.5

Table 1: Location of Pancreatic Cancer, Number of Patients, Operation performed, Survival.

Pancretic resection for	Number of Patients	Operation performed	3-5 year survival
Cancer Head of Pancreas	32 (42.66%)	Classical Whipple's	Nil
Periampullary Cancer	28 (37.33%)	Pylorus preserving Pancreato duodenectomy	4- Patients (18%)
Duodenal Cancer	2 (2.66%)	Classical whipple's	No patient surviving
Distal Cholangiocarcinoma	8 (10.66%)	Classical Whipple's	No patient surviving
Cancer Body and Tail of Pancreas	4 (5.33%)	Distal Pancreatectomy	No patient surviving
Mucinous cystadenocarcinoma	1 (1.33%)	Distal Pancreatectomy	1 patient surviving

Table 2: Survival Data of Pancreatic resection for pancreatic cancer patients.

References	Time period	Additional treatment	Number of patients	Median survival in Months	5year survival
Capussotti <i>et al.</i> 2003 [20]	1988-1998	No adjuvant	100	----	8.4%
Carpelan –Holmatorm – <i>et al.</i> 2005	1990-1996	Not documented	10	----	0.25%
Mosca <i>et al.</i> 1997 [21]		No adjuvant treatment	69	16.9	11%
Neoptolemos <i>et al.</i> (2004) [9]	2000	Chemoradiation	73	13.9	7%
Our study	2009-2017	No adjuvant therapy	75	12-18	6%
					Periampullary group.

Table 3: Mortality and Morbidity after pancreatic resections for pancreatic cancer.

References	Time period	Number of patients	Mortality	Morbidity
Buchler <i>et al.</i> 2003 [5]	1993-2001	468SW/PPPD	1.3%	36%
Capussotti <i>et al.</i> 2003 [20]	1988-1998	149 whipple's SW	5.4% (60 days)	37.5 %
Richter <i>et al.</i> 2003 [6]		PPPD	Nil	34.4%
Fahy BN, Frey CF [22]	1997-2002	51- patients Distal Pancreatic resection	0-4%	47%
Our study	2009-2018	75, patients SW, PPPD, DPR	8%	36%

Table 4: Surgical Procedure for a Pancreatic Cancer Patients.

S. No	Diagnosis	Operation Performed	Number of Patients
1	Cancer Head of Pancreas	Classical Whipple's	32 (45.71%)
2	Periampullary Cancer	Pylorus Preserving Pancreatico Duodenum	
3	Adenocarcinoma Duodenum	Classical Whipple's	2 (2.85 %)
4	Cholangiocarcinoma Distal CBD	Classical Whipple's	3 (4.28 %)
5	Cancer Body & tail of Pancreas	Distal Pancreatectomy	
6	Cystic Mucinous Adenocarcinoma of Body	Distal Pancreatectomy	

Table 5: Surgical Procedure, Operating time, Average Blood Loss, Hospital Stay in days.

S. No	Surgical Procedure	Operation Time in Minutes	Blood Loss in ML	Hospital Stay Days
1	SW surgery	180 to 270 Avg-265 Mins.	50 ml.-850ml.	17.5 to 19.5
2	PPPD	165 to 270 mins	100-450 ml.	12 to 19
3	Distal Pancreatectomy	180 to 220 mins	150 to 200 ml	12 to 14
4	Distal Pancreatectomy with Splenectomy	180 to 230 mins.	200 -250 ml	13 to 17

to 19.7 days, with about 27 patients discharged within 12 days' time. Study published in 2013, reports hospital stay (19.7 ± 7.7) days. Post-operative complications occurred in 62.5% (95/152) and mortality was 3.29% (5/152) delayed discharge is associated with postoperative complications. Age, BMI, Surgical procedure, Blood Transfusion, fluid input are few factors associated with complications [16,17]. In the patients who had PPPD, median operating time was 232 (165-270) min. and median blood loss was 100-1300 cc. Pancreatic leak 5.5% delayed gastric emptying was observed more frequently with PPPD 6/14 than after SWS none of 19 patients ($p < 0.05$) There is no significant difference between the SWS and PPPD in terms survival and 5 year survival rate. Recent reports suggest median survival was 16 months and 5 year survival was 9.4% in 36 patients. Blood loss during the operation influenced the prognosis [18-21]. All patients had histopathological diagnosis of adenocarcinoma-1 had mucinous cystic adenocarcinoma. Distal pancreatectomy was first performed by Billroth in 1884, accounts for approximately 25 percent of all pancreatic resections. Distal Pancreatic resections can be performed with low rate of mortality, though incidence of pancreatic leak is a common cause of morbidity. the method of pancreatic stump closure may influence postoperative morbidity [22] (Figure 1-6).

Conclusion

Pancreatic resections are performed with some morbidity and mortality, technical differences in managing both the resection and reconstructive parts of operation depend on surgeons preference rather than actual guidelines. In current scenario pancreatic resection for pancreatic cancer seems to be the best possible option in terms of quality of life and survival. Earlier diagnosis as a result of more

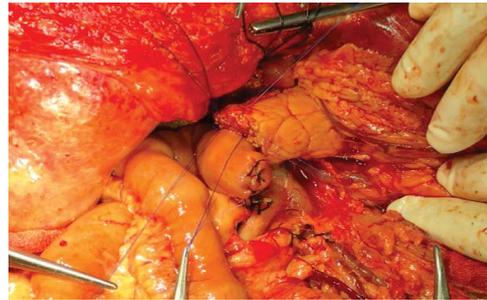


Figure 3: Duct to mucosa Pancreatic Jejunostomy. PV is in picture.

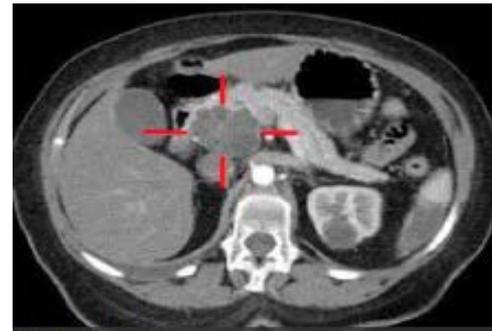


Figure 4: CT Scan Pancreatic head cancer.



Figure 5: Septate lesion in the pancreatic body and tail.



Figure 1: Specimen of Periampullary cancer (Pancreaticoduodenectomy).



Figure 2: Specimen of Periampullary cancer (Pancreaticoduodenectomy).

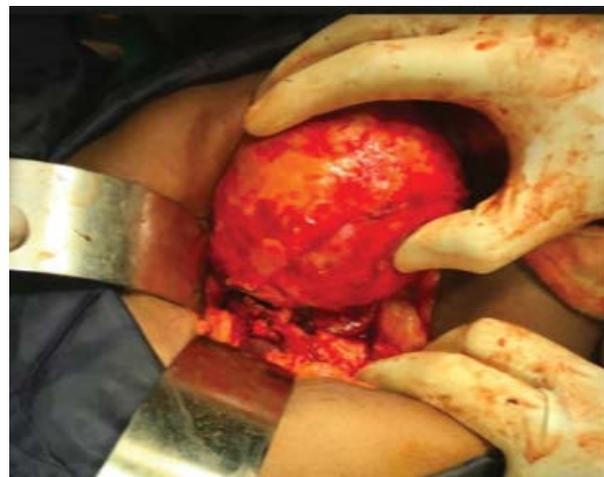


Figure 6: Mucinous cystadenocarcinoma of body and tail of pancreas.

sophisticated investigations, Improved neo adjuvant or adjuvant chemotherapy together with targeted therapies are likely to improve the dismal prognosis with pancreatic cancer patients in near future. However all these surgical resections and newer treatment modalities have to be evaluated in controlled clinical trials with optimal statistical analysis.

Ethical committee permission:

Obtained.

Informed consent:

Was obtained from Patients.

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