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Pancreaticoduodenectomy Procedure - A Tertiary Care Centre Experience.

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ABSTRACT

Background: Pancreaticoduodenectomy, also referred to as Whipple's resection, refers to the en bloc surgical resection of the pancreatic head, uncinate process, duodenum, gall bladder, and common bile duct. Though generally done for oncologic indications, the procedure can be warranted in benign or pre-neoplastic conditions of the peri-ampullary region also. Pathologic assessment of surgical specimens from pancreaticoduodenectomy needs special attention in order to accurately evaluate many factors that are prognostically important. The objective of the study was to analyze the clinical as well as histopathological profile of patients who underwent Whipple's resection over a 3-year period at a tertiary level institution. **Methods:** This descriptive study included patients from the General Surgery and Surgical Gastroenterology wards of Medical College Trivandrum, who underwent pancreaticoduodenectomy from January 2012 to January 2015. **Results:** The mean age was 55.18 years, with the majority of patients being females. Jaundice was the most common symptom, followed by itching. Among tumour markers, CA 19-9 was elevated in majority of patients, followed by CEA. Majority of the patients underwent PPPD rather than classical Whipple's resection. Head of the pancreas was the most common primary site followed by bile duct, ampulla of Vater and duodenum respectively. Adenocarcinoma was the most common pathological type among all sites with the majority being well-differentiated tumours. **Conclusion:** Adenocarcinoma of the head of the pancreas is the most common tumour for which majority of the patients undergoes pancreaticoduodenectomy at this institution. Majority of surgeons prefer the pylorus preserving type over the classical Whipple's procedure.

Keywords: Cholangiocarcinoma, Pancreaticoduodenectomy, Pancreatic Ductal Carcinoma, Periampullary carcinoma, pylorus preserving pancreaticoduodenectomy.

INTRODUCTION

Periampullary cancers refer to a group of malignant neoplasms arising in the vicinity of the head of pancreas or the ampulla of Vater. They are usually discovered because of symptoms of obstructive jaundice or pain. The first successful resection of a periampullary tumour was performed by Halsted in 1898. He described a local ampullary resection, with re-anastomosis of the pancreatic and bile ducts into the duodenum, in a female patient, who presented with obstructive jaundice.[1] Codivilla is often credited with performing the first en-bloc resection of the head of the pancreas and duodenum for periampullary carcinoma. Unfortunately, the patient did not survive the postoperative period.

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The first successful two stage pancreaticoduodenectomy was reportedly performed by Kausch in the year 1909. In 1914, Hirschel reported the first successful one-stage pancreaticoduodenectomy. In the first third of the 20th century, most periampullary cancers were managed by a trans-duodenal approach similar to the one first reported by Halsted.

Pancreaticoduodenectomy did not gain popularity until 1935, when Allen Oldfather Whipple and his colleagues reported on three successful cases of two stage, en bloc resections of the head of pancreas and duodenum.[2] Over the next few decades, a number of modifications and technical refinements were made in the operative procedure. This included the first one-stage pancreaticoduodenectomy, reported in the United States by Trimble in 1941. The first pylorus preserving pancreaticoduodenectomy (PPPD) was performed by Watson in 1944. PPPD was popularised by Traverso and Longmire so as to preserve gastrointestinal function in 1978. Nevertheless, pancreaticoduodenectomy procedure was rarely performed until the 1980s, because of the

formidable operative morbidity, mortality, as well as poor prognosis associated with these cancers.

Classic Whipple's as well as its PPPD variant are the most widely employed surgical procedures for the treatment of pancreatic head and periampullary tumours. While a classic Whipple's procedure includes resection of the pancreatic head, duodenum, gallbladder, distal common bile duct, partial jejunum and distal stomach, in a PPPD the proximal duodenum is transected 3 to 4 cm distal to the pylorus ring. Though some randomized controlled trials (RCTs) and meta-analyses have suggested that these two procedures are comparable in terms of postoperative complications, long-term survival rates and quality of life, other studies have reported that PPPD is superior to classic Whipple's pancreaticoduodenectomy as it results in less occurrence of dumping, diarrhoea and bile reflux gastritis.[3,4] Hence PPPD is claimed to provide the patients with an improved nutritional status.[5,6]

However, during the last few decades, significant advances have been made in the understanding of the pathogenesis of periampullary neoplasms. There have been improvements in the ability to diagnose and stage these diseases, as well as in the surgical and non-surgical approaches for managing these patients. Developments in adjuvant therapies and critical care management have made the disease itself and the surgical procedure less formidable. This has improved the volume of radical duodeno-pancreatic surgeries by leaps and bounds. So much so that it is being done by many General surgeons also, and not just by Gastro-onco-surgeons.

With this background, we aimed to analyze the pattern of patients who underwent pancreaticoduodenectomy in our institution. Being a tertiary level referral institution, we get a large number of patients referred to us from the southern districts of both Tamilnadu and Kerala states. While the Surgical Gastroenterology department contributes to the lion's share of the surgery in the hospital, General Surgery department also has its own contribution. The objectives of this study were to analyze the clinical profile of patients undergoing pancreaticoduodenectomy at our institution as well as to analyze the histopathological profile of pancreaticoduodenectomy specimens of these patients.

MATERIALS AND METHODS

The study was designed as a Descriptive study. Study setting was the General Surgery and Surgical Gastroenterology wards of Government Medical College, Trivandrum. The study was vetted by the Institutional Review board and approved by the Ethics Committee of the institution. Confidentiality of patient details was maintained and informed consent obtained before starting the study. Study population included all patients who underwent pancreaticoduodenectomy during the time period from January 2012 to January 2015.

Inclusion criteria

All patients who underwent pancreaticoduodenectomy during study period.

Exclusion criteria

Those patients who had history of previous pancreatic/duodenal surgeries.

Data collection tool included oral history and details from case sheets. The variables studied included clinical profile of patients with pancreaticoduodenal masses and histopathological specimens of pancreaticoduodenectomy. Data was recorded into a structured Performa and subsequently entered into Microsoft Excel sheet. The relevant data were collected using pre written proforma and entered into Microsoft Excel data sheets. All the statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) software version 18 by IBM Inc, USA. Data is being presented as mean ± standard deviation and proportions as appropriate. The case with a p value of less than 0.05 was considered to be statistically significant wherever relevant.

RESULTS

A total of 79 patients underwent pancreaticoduodenectomy during the study period. Out of these 43 (54.4%) were females and 36 (45.6%) were males. Among the 79 patients, the youngest patient was 32 and the oldest was 76 years. The mean age in the study group was 55.43 +/- 9.24 years.

The most common symptom was jaundice (93.7%) followed by itching (63.3%), weight loss (46.8%) and abdominal pain (45.6%) [Figure 1]. Out of the 79 subjects, 23 (29.1%) were diabetic and 18 (22.8%) were hypertensive. None of the female patients were smokers or alcoholics, but among the 36 males, 14 (17.7%) were smokers and 10 (12.7%) were alcoholics.

The mean total bilirubin was 14.72 +/-5.26 mg/dl. The mean direct bilirubin was 8.68 +/- 3.25 mg/dl. The mean alkaline phosphatase was 621.59 +/- 201.91 IU/L. Majority of the patients (63 or 79.7%) had albumin levels between 2 – 3 mg/dl. CEA was elevated in 51 (64.6%) patients. CA 19-9 was elevated in 64 (81%) patients.

Among the 79 patients, 56(70.9%) underwent PPPD, while 23 (29.1%) underwent classical Whipple's resection. The site of malignancy was the pancreas in 48 (60.8%) patients followed by bile duct (12 or 15.2%), Ampulla of Vater (10 or 12.7%) and duodenum (9 or 11.4%) [Figure 2]. In the pancreas (N=48) itself, majority of the tumours were pathologically found to be adenocarcinomas (87.5%) [Table 1]. In the bile duct (N=12), all were

adenocarcinoma with majority (58.3%) being well differentiated. In the Ampulla of Vater also all (N=10) were adenocarcinoma with majority being well differentiated (60%). In the duodenum (N=9), majority were adenocarcinoma (88.9%). The mean tumour size was 1.75 +/- 0.66 cm.

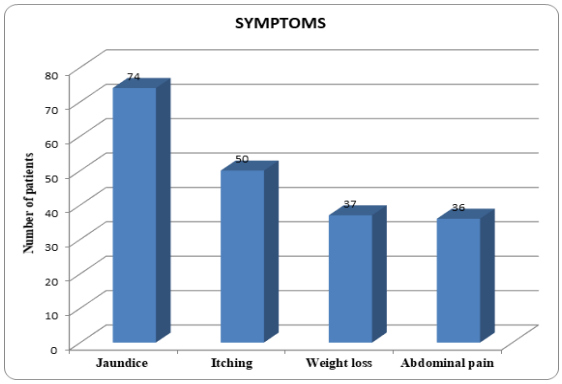

Figure 1: Distribution of Symptoms

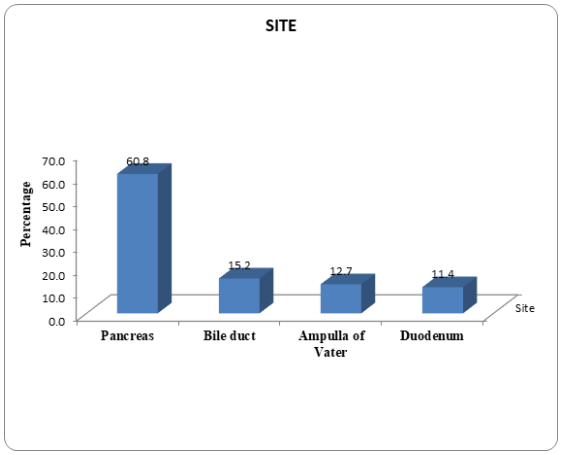

Figure 2: Distribution of site of primary tumour.

Table 1: Pathological types of malignancy in Pancreas

Types Of Malignancy In Pancreas	Frequency
Well differentiated adenocarcinoma	29
Moderately differentiated adenocarcinoma	6
Poorly differentiated adenocarcinoma	5
Mucin secreting adenocarcinoma	2
Neuroendocrine tumour	2
Signet ring cell carcinoma	2
Acinar cell carcinoma	1
Malignant IPMN	1
Total	48

DISCUSSION

This was a descriptive study conducted to analyse the clinical and histopathological profile of patients who underwent pancreaticoduodenectomy at a tertiary care institution. 79 patients underwent pancreaticoduodenectomy during the study period of 3 years.

Out of the 79 patients majority were females (54.4%). The minimum age was 32 years and the maximum was 76 years with a mean age of 55.43 +/- 9.24 years. This is in consensus with the study conducted by Chauhan et al.[7] In that retrospective record-based descriptive study, epidemiologic data of all patients diagnosed with periampullary carcinoma in Kasthurba Medical College Hospital for a period of 3 years (n=92) were collected. From this analysis, 24 patients who were managed exclusively by the Department of GI Surgery were identified, and their records analyzed for detailed clinical profiling. In that study, majority were in the 50–60–year age group (28.3%), followed closely by the 60–70 year age group (27.2%). The study population included 58.7% males and 41.3% females. Ibrahim et al analysed the records of all the patients who had Whipple's resection during a two year period.[8] The mean age incidence of ampullary carcinoma calculated was 44 years. The sex ratio of ampullary carcinoma was 1:1. Grizas et al performed 55 radical operations on the pancreas because of periampullary carcinoma in Kaunas Medical University Hospital during 1998-2000.[9] There were 50 pancreatoduodenal resections (PDR) and 5 total pancreatectomies (PE). Age of patients ranged from 28 to 78 years, mean age was 61.9 years. Thirty six percent (36.4%) of patients were older than 70 years. Graf et al retrospectively analysed the 70 patients who underwent Whipple duodenopancreatectomy in their center and found that 36 were men and 34 women, with a mean age of 64 (33-84) years.[10]

In our study, the most common symptom was jaundice (93.7%) followed by itching (63.3%), weight loss (46.8%) and abdominal pain (45.6%) In the Kasthurba medical college study also, besides jaundice, pruritus was the major presenting complaint in female patients (81.8%), while both weight loss (53.8%) and pruritus (53.8%) were major complaints in male patients.[7] Ceuterick M et al performed pancreaticoduodenectomy in 79 patients for pancreatic or periampullary tumours.[11] Fifty-five patients were icteric (55/79: 70%); among these 33 patients underwent preoperative biliary decompression (endoscopic procedures 29, percutaneous trans-hepatic drainage 3, laparotomy and T-tube placement. After biliary drainage, bilirubin levels decreased from 12.4 +/- 1.3 mg/dl at admission to 5.1 +/- 1.1 mg/dl before surgery.

CA 19-9 was elevated in 81% patients of our study, while CEA was elevated in 64.6% patients. Literature evidence shows 75% elevation in CA 19-9 levels in patients with periampullary carcinoma. Majority of the patients underwent PPPD (70.9%) than Whipple's resection as it is being increasingly considered more physiological.

In our study, pancreas (head) was the most common (60.8%) site of malignancy followed by the bile duct, ampulla of Vater and duodenum respectively. This is in consensus with the study conducted by Grizas et al.[9] However, in the study conducted by Graf et al, though pancreas was the most common site, it was followed by ampulla of Vater, bile duct

and then only the duodenum.[10] In the study by Ibrahim et al when the histopathology records of Whipple's resection were reviewed and the parameters were calculated, out of thirty cases, on which Whipple's resection was done, twenty one had ampullary and periampullary carcinoma.[8] Three had pancreatic tumours and six had chronic pancreatitis. Out of the three cases with pancreatic tumour, two had pancreatic endocrine tumours. They both were female. One patient had a solid pseudopapillary pancreatic tumour. Wu et al reported 150 cases of patients with periampullary carcinoma, among which the cancer in 85 cases was in the head of pancreas, 26 in the lower part of common bile-duct, 21 around the Ampulla of Vater and 18 in the duodenal papilla.[12] In 150 patients, pancreaticoduodenectomy was performed in 53 cases but one had total pancreatectomy. The total resection rate was 36%. Resectability was high with cancer in ampulla and duodenal papilla, with a resection rate of 89.5% and 83.3%, respectively, while the lowest resection rate of 14.1%, was seen in patients with cancer in the head of the pancreas.

According to the study by Grizas et al, carcinoma of the head of the pancreas was diagnosed in 48 (87.3%) cases, common bile duct carcinoma in 3 (5.5%) cases, ampulla of vater carcinoma in 2 (3.6%) cases and carcinoma of duodenum in 2 (3.6%) cases.[9] Twenty five (45.5%) patients were suffering from first or second stage cancer, and 28 (50.9%) from third stage. Stage IV was diagnosed for 2 (3.6%) patients, due to invasion to the portal, mesenteric or splenic veins. For those patients resection of portal, mesenteric or splenic veins was performed. Malignant invasion to the resection margin of the pancreas was found in 4 (7.3%) patients. Regional lymphadenectomy (D1) was also performed in 23 cases while radical lymphadenectomy (D2) in 32 cases. When Ceuterick et al performed a review of pancreaticoduodenectomy in 79 patients, 44 tumours were found to be pancreatic and 35 were periampullary tumours (ampulla 18, common bile duct 9, duodenum 8).[11] In the study by Graf et al, 36 patients had carcinoma of the head of the pancreas, 13 had carcinoma of the ampulla of vater, 9 had carcinoma of choledochus, 4 had duodenal carcinoma and 8 had benign disease of the pancreas.[10] Chandrasegaram et al performed a retrospective review of PD between January 2000 and December 2012 at a public metropolitan database.[13] Of the 142 cases, 116 were for periampullary cancers. There were 65 (56%) pancreatic, 29 (25%), ampullary, 17 (15%) biliary and 5 (4%) duodenal cancers. Irrespective of the site, adenocarcinoma remained the most common pathological type of malignancy.

During the past two to three decades, significant advances have been achieved in pancreatic resection surgery. Postoperative pancreatic fistula (POPF) remains the most challenging and life threatening complication despite the introduction of numerous techniques and preventive strategies.[14] A recent analysis of 424 patients who had undergone pancreatic resection showed a very low 90 day mortality rate of 1.7%, and one and five year survival rates of 76% and 23% respectively.[15] Outcomes following pancreatic surgery have been largely tied to surgeons' experience. Recently, there have been several reports demonstrating that surgeons' exposure to the procedure and increased hospital volume correlate with lower death rates following pancreatic resections.[16,17] These data show that this surgery has become relatively safer and is no longer the anathema it was considered to be.

CONCLUSION

We acknowledge that our study has several limitations. First, our design being descriptive in nature does not allow for detailed analysis. Also the sample size is not sufficiently large. However our study was highlights the various clinical and biochemical parameters relevant in the population of patients who undergo pancreatic resection at our centre.

To conclude, in our study, alike many other previous studies, adenocarcinoma of the head of the pancreas was the most common malignancy among the patients who underwent pancreaticoduodenectomy. Even after the advent of many advanced investigations, it is difficult to accurately diagnose preoperatively the site and type of malignancy in periampullary tumours. The exact site of tumour and the type of malignancy can be ascertained for sure only after the histopathological examination of the resected specimens. These factors retain the enigma associated with this sophisticated procedure.

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