



Experience in the Management of Pancreatic Adenocarcinoma with Whipple Procedure at the Institute of Social Security and Services for State Workers of Puebla

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ABSTRACT

Background: Currently, in the management of periampullary tumors, pancreatic carcinoma is the most frequent, considered a tumor with a poor prognosis. Approximately 95% of cases are exocrine cell tumors, most commonly pancreatic ductal adenocarcinomas (PDAC). According to INEGI, in Mexico, PDAC is the twelfth leading cause of cancer, with 4,489 cases diagnosed annually, accounting for 4.9% of oncological deaths. **Methods:** A retrospective descriptive observational study was designed for patients managed with pancreaticoduodenectomy during 2023 and 2024, at a tertiary care center in Puebla, Mexico. **Results:** A total of 16 patients went to surgery, with malignancy reported in 13 of them. A predominance of female-to-male ratio greater than 2:1 was observed, and the complication rate was 81%, with respiratory complications predominating, followed by biliopancreatic fistula. **Conclusions:** The Whipple procedure is considered a high-complexity surgery with a high risk of complications. However, in selected cases, it is the treatment of choice for periampullary tumors, showing better survival, especially in the early stages of pancreatic cancer.

Keywords: pancreatic adenocarcinoma, Whipple, periampullary tumor.

INTRODUCTION

Pancreatic carcinoma is considered a solid malignant tumor with a poor prognosis and a general 5-year survival rate of approximately 10%, which translates into a disease with a high fatality rate. [1] In our country, PDAC (Pancreatic Ductal Adenocarcinoma) represents the twelfth leading cause of cancer, with 5,822 new cases diagnosed in the last year, accounting for 5.5% of cancer-related deaths, according to Globocan 2024 data [2]; figures that highlight an opportunity area in prevention, diagnosis, and treatment.

It is expected that pancreatic ductal adenocarcinoma will be the second most lethal cancer by 2040, due to the high incidence of metastatic disease and limited treatment responses [3]. The average age at diagnosis for pancreatic cancer is 70 years, with it being more common in men than women. Due to its nonspecific symptoms, diagnosis is often delayed by an average of 10 years until obstructive or general symptoms appear, by which time up to 80% of cases will present with locally advanced and unresectable disease.

Regarding the surgical treatment of this type of neoplasm, the Whipple procedure has been considered the standard. Italian surgeon Alessandro Codivilla performed the first pancreaticoduodenectomy in 1898, with subsequent modifications by Walter Kausch in 1912. Allen Whipple further refined the surgical technique, making it a single-stage operation in 1940 [4]. In 1978, pancreaticoduodenectomy with pylorus preservation (PPPD) was introduced to reduce complications linked to gastric resection, such as diarrhea, emptying disorders, early satiety, marginal ulceration, and biliary reflux gastritis [5-8].

The refinement, standardization of techniques, and surgical experience at many centers have led to the Whipple procedure being considered the gold standard not only in the treatment of benign pathologies but also in the treatment of malignant tumors in the periampullary region, particularly pancreatic head tumors. However, it is also associated with significant early and late complications [9-12].

Currently, the goal of surgical therapy in asymptomatic patients is to prevent the growth of lesions that would complicate treatment further and are associated with worse prognosis. There are already care protocols for perioperative management, such as the Johns Hopkins Hospital protocol or the ERAS (Enhanced Recovery After Surgery) protocol for pancreatic surgery [13-14]. As well as models for describing complications like the Clavien classification. For this reason, this series highlights some aspects of the internal protocol of the unit for managing these patients, as well as the description of important postoperative outcomes.

METHODS

A descriptive, observational, retrospective study was designed, collecting information from a total of 16 patients who underwent pancreaticoduodenectomy between July 2023 and June 2024 at the "5 de mayo" Specialty Hospital, ISSSTEP, in the state of Puebla, Mexico. The study included presumptive cases of periampullary neoplasia based on imaging studies, laboratory tests, and clinical presentation, as well as patients with prior pathology reports showing atypia or suggesting malignancy.

The search was conducted in the unit's electronic medical records for patients with related diagnoses according to the International Classification of Diseases (ICD-10) and those who underwent the Whipple procedure.

The studied variables were: age, sex, clinical presentation symptoms, pre-surgical endoscopic retrograde cholangiopancreatography (ERCP), imaging studies, intraoperative findings, procedure with or without pylorus preservation, open or laparoscopic procedure, average surgical time, final pathology report, intensive care unit stay, complications, and deaths.

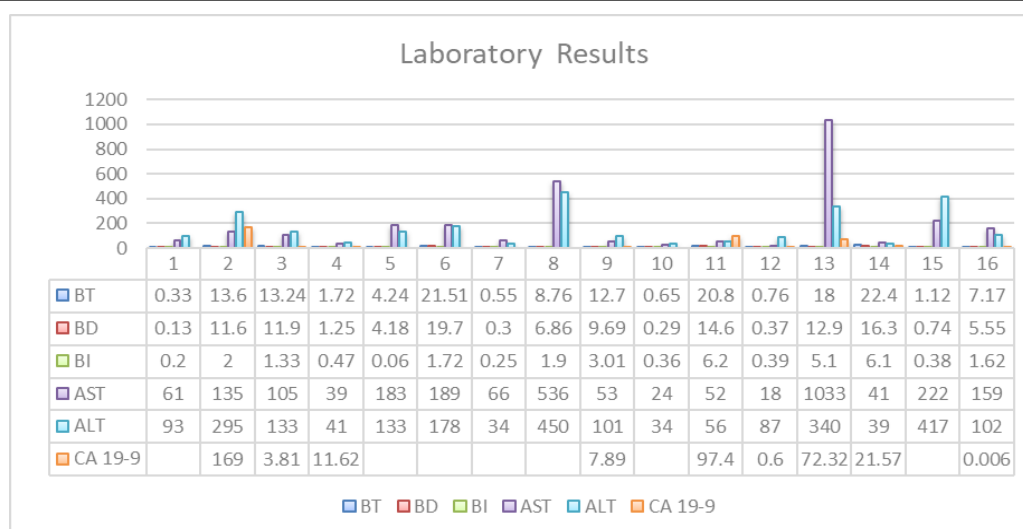
Patients who were not able to undergo the procedure due to locally advanced or metastatic disease at the time of surgery, as well as those with incomplete information in their medical records, were excluded.

Data was collected using a validated instrument based on expert methods, and statistical analysis was descriptive, using frequency tables and percentages with Microsoft Excel® software.

After approval by the ethics committee, a search of the literature related to pancreatic cancer was conducted using databases such as PubMed, Google Scholar, and Elsevier. Following the final review by experts in general surgery, oncological surgery, radiology, and pathology, the discussion and conclusions of this study were formulated.

RESULTS

A total of 16 patients underwent the Whipple procedure, 11 of whom were female and 5 male, representing 69% and 31%, respectively, with an average age of 65 years. The clinical presentation in most patients was progressive jaundice (81%), abdominal pain (56%), and weight loss (19%), with 12% of patients presenting with nonspecific symptoms. Laboratory tests mainly showed abnormalities in liver function tests, with prominent hyperbilirubinemia with an obstructive pattern expressed in mg/dl, as well as elevated AST, ALT, and CA19-9 levels expressed in U_i/l and U/l, respectively. The data is summarized in Graph 1.



Graph 1: Laboratory Results at the Time of Admission for Each Patient. (Horizontal axis: Patient number. Vertical axis: Laboratory values).

Regarding imaging studies, 16 ultrasounds, 11 contrast-enhanced CT scans, 6 magnetic resonance cholangiopancreatographies (MRCP), and one T-tube cholangiography were performed. The results for patients with malignancy are shown in Table 1, with some examples in Figures 1-3.

Table 1: Imaging study reports of each patient with malignancy results.

No.	Type of imaging study	Findings
1	contrast-enhanced CT scan	Neoplasm dependent on the head of the pancreas with dilation of the intrahepatic and extrahepatic bile ducts and dilation of the main pancreatic duct
2	contrast-enhanced CT scan	Dilation of the intrahepatic and extrahepatic bile ducts, with the presence of a migrated biliary stent
3	Magnetic resonance cholangiopancreatography (MRCP)	Dilation of the main pancreatic duct and bile duct with a filling defect due to a biliary stent
4	contrast-enhanced CT scan	Dilation of the common bile duct to 20mm and stenosed ampullary region
5	contrast-enhanced CT scan	Common bile duct with dilation of 15mm and abrupt decrease in the intrapancreatic caliber
6	contrast-enhanced CT scan	Neoplasm dependent on the head of the pancreas with extension to the uncinate process, causing dilation of the pancreatic and bile ducts
7	contrast-enhanced CT scan and ultrasound	Dilation of the common bile duct to 10mm and dilation of the pancreatic duct, with atrophic body and tail of the pancreas
8	contrast-enhanced CT scan	Neoplasm of the pancreatic head that borders the portal vein in less than 180 degrees
9	contrast-enhanced CT scan	Thickening of the duodenum in the first and second portions, dilation of the pancreatic duct and intrahepatic and extrahepatic bile ducts
10	contrast-enhanced CT scan	Common bile duct of 10mm and changes in the morphology of the pancreatic head due to a 10x11mm

		lesion with enhancement in both arterial and venous phases, pancreatic duct of 4mm
11	contrast-enhanced CT scan	Pancreatic head tumor that infiltrates the uncinate process and causes dilation of the common bile duct
12	contrast-enhanced CT scan and ultrasound	Narrowing of the intrapancreatic bile duct causing dilation of its extrahepatic portion
13	contrast-enhanced CT scan	Lesion in the ampullary region leading to dilation of the intrahepatic and extrahepatic bile ducts

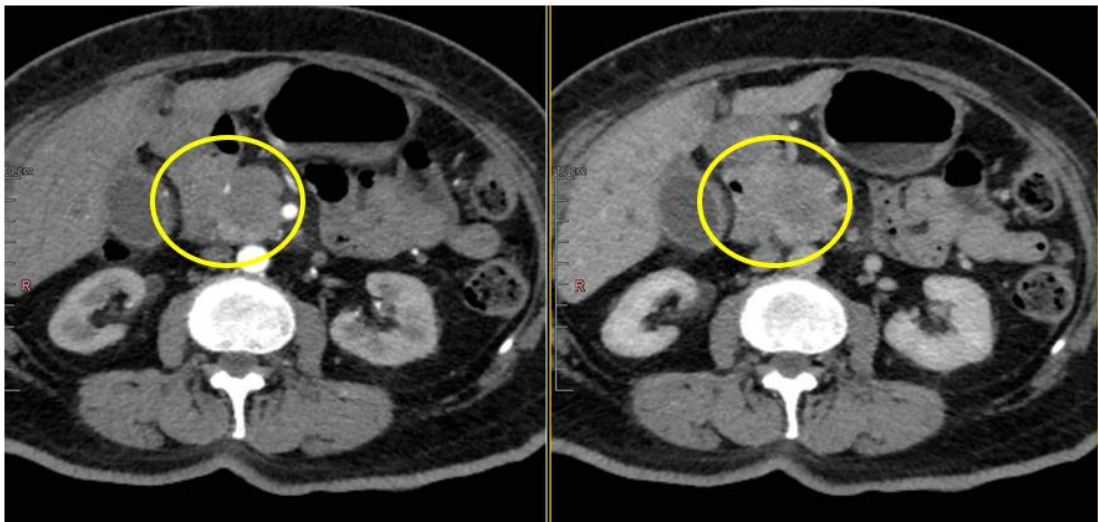


Fig 1: Tumor dependent on the pancreatic head with hypovascular behavior visualized in both arterial and venous phases, causing obliteration of the common bile duct and pancreatic duct, as well as involvement of the common hepatic artery (outlined by the yellow markers).

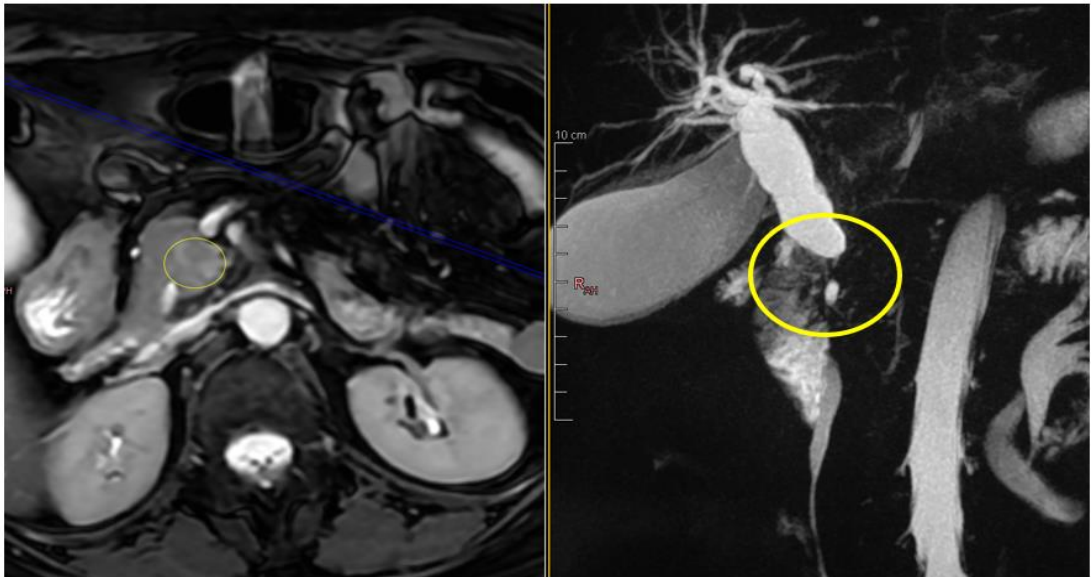


Fig 2: Magnetic resonance cholangiography showing a poorly defined area causing stenosis of the common bile duct in its intrapancreatic portion (outlined by the yellow markers).

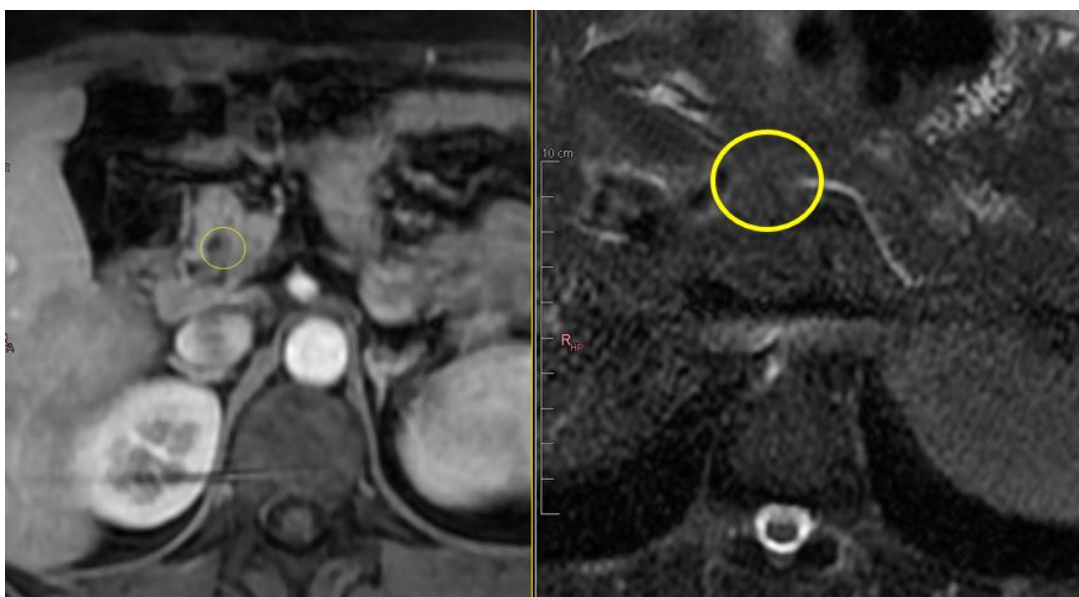


Fig 3: Magnetic resonance cholangiography showing a hypodense area molding the main pancreatic duct at the level of the pancreatic head, causing mild dilation of the rest of the pancreatic duct (outlined by the yellow markers).

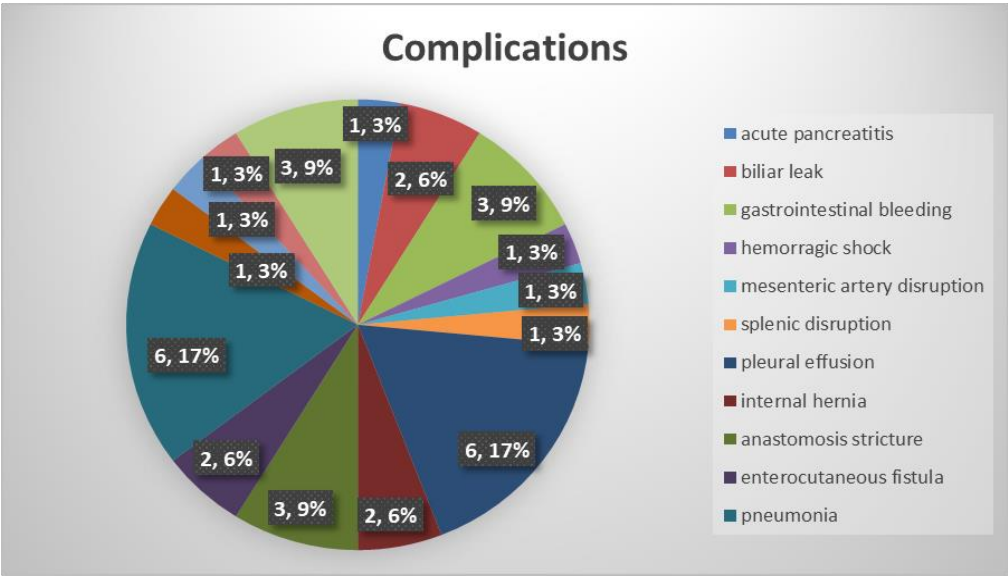
Regarding the surgical events, 14 Whipple procedures with pylorus preservation were performed, and 2 additional patients underwent total pancreatectomy. Of the total procedures, one was performed laparoscopically and the rest via open surgery. The average surgical time was reported as 4.6 hours, with a minimum of 3.5 hours and a maximum of 8.2 hours.

The most common findings were, in 13 procedures, tumor lesions with an average size of 3 cm, followed by two pancreases with a stone-like consistency without a localized focal lesion, and a 2x2 cm duodenal diverticulum in the second portion of the duodenum.

After the surgical procedure, only 4 patients (25%) were admitted to the Intermediate Care Unit, and 12 of them (75%) were admitted to the Intensive Care Unit.

The complications presented by the patients were related to the surgical procedure and the length of hospital stay, with a range of 81%, among which pneumonia associated with healthcare and pleural effusion were the most common at 46%, followed by pancreatic leak/fistula at 9% and biliary leak at 6%. Two cases of vascular disruption in the mesenteric artery and portal vein were also reported, as well as two cases of intestinal obstruction secondary to internal hernia. These and the rest of the complications are summarized in Graph 2.

The average hospital stay for this type of procedure was 15 days.



Graph 2: Shows the percentage of complications during postoperative follow-up.

The final pathology reports revealed 13 positive cases for malignancy, representing 81.25% of the cases, with the following locations: 11 in the pancreatic head, 1 distal cholangiocarcinoma, and 1 tumor of the Vater’s ampulla. The characteristics of the patients with malignancy reports are summarized in Table 2. Some examples of the surgical specimens are shown in Figures 4 and 5.

Age	Sex	Histopathology report	Tumor location
67	Female	Ductal adenocarcinoma well differentiated	Pancreatic head
66	Male	Ductal adenocarcinoma lymphovascular invasion	Pancreatic head
41	Female	Ductal adenocarcinoma moderately differentiated	Pancreatic head and ampulla
69	Female	Ductal adenocarcinoma moderately differentiated	Pancreatic head
77	Female	Ampulla adenocarcinoma	Ampulla
77	Female	Ductal adenocarcinoma moderately differentiated	Pancreatic head
74	Male	Ductal adenocarcinoma moderately differentiated	Pancreatic head
63	Male	Ductal adenocarcinoma moderately differentiated	Pancreatic head and Ampulla
47	Female	Cholangiocarcinoma	Distal common bile duct
65	Female	Ductal adenocarcinoma poorly differentiated	Pancreatic head
66	Female	Ductal adenocarcinoma poorly differentiated	Pancreatic head
66	Female	Ductal adenocarcinoma poorly differentiated	Pancreatic head
62	Female	Ductal adenocarcinoma poorly differentiated	Pancreatic head and uncinate process

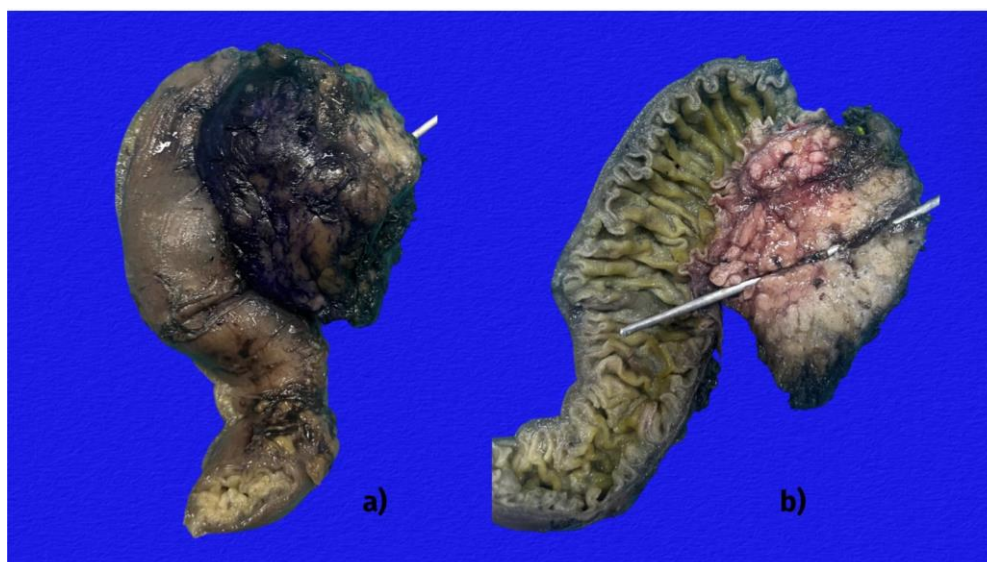


Figure 4: a) Surgical resection. Whipple procedure (Pancreaticoduodenectomy), stained anterior pancreatic margin (purple). b) Longitudinal section of the specimen, cannulated pancreatic duct.

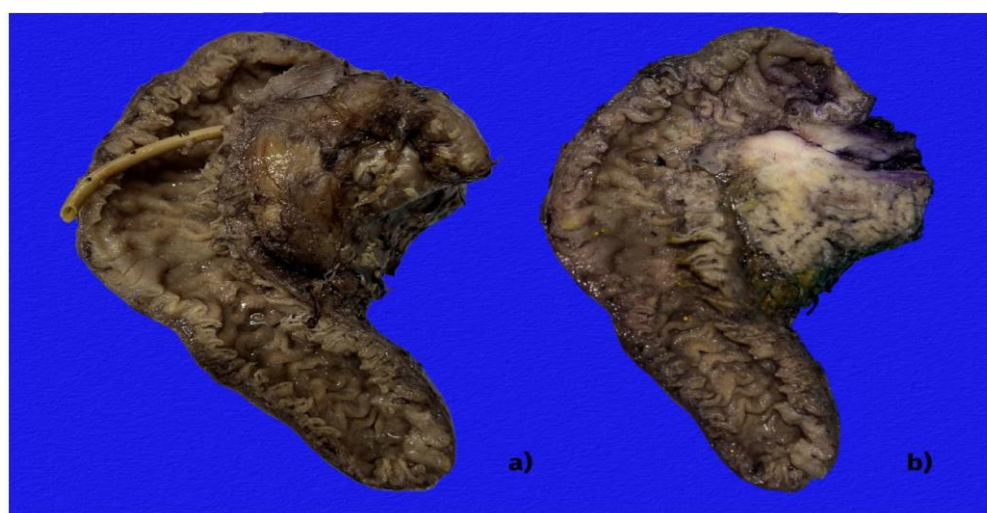


Figure 5: a) Surgical resection. Whipple procedure (Pancreaticoduodenectomy) with the presence of a cannula in the duodenal portion. b) Longitudinal section of the specimen, stained bile duct (purple).

Three cases negative for malignancy were also reported, including a diagnosis of a diverticulum in the second portion of the duodenum and another with chronic pancreatitis and chronic inflammatory process associated with autoimmune pancreatitis. Six deaths were recorded, representing a 36.5% mortality rate, of which two occurred in the immediate postoperative period, one in the intermediate period, two in the late postoperative period, and one at three months from causes unrelated to the surgical procedure.

DISCUSSION

In our study, we had a heterogeneous population with findings suggestive of periampullary tumors, so the purpose of our study is not to establish guidelines or standardized protocols for

the management of these patients, but rather to document the prevalence of this pathology in our setting, as well as to compare the characteristics and outcomes of our population with the data reported in the international literature.

When discussing periampullary tumors, four pathologies arising near the ampullary region are included, with pancreatic head tumors at the top of the list, without considering other possible neoplasms such as neuroendocrine tumors, lymphomas, metastases from other sites, etc. There is no effective screening, and most patients present with locally advanced disease (30-35%) or metastatic disease (50-55%) at the time of diagnosis [15-17]. This translates into a survival rate of no more than 10% at 5 years [18].

In our study, 16 patients were found with an average age of 65 years, which aligns with the general literature, reporting a higher prevalence in those over 50 years of age, with a peak between the sixth and seventh decades of life. Regarding gender predominance, we found a female/male ratio greater than 2:1, a finding that contrasts with those reported by Wungki Park et al., where a male/female predominance of 1.3:1.0 was mentioned [19].

When evaluating the clinical presentation, we found that the predominant symptoms were obstructive jaundice, abdominal pain, weight loss, and a small percentage presented with nonspecific symptoms, which aligns with the data reported in a review by Jorg Kleef et al. regarding the most common presenting symptoms [20]. In the laboratory abnormalities, hyperbilirubinemia and elevated CA 19-9 levels were found, which is consistent with a multivariate analysis in which the combination of bilirubin >3mg/dl, weight loss, and CA 19-9 >37U/l has proven to have a specificity and positive predictive value close to 100%, independent of imaging findings [21].

The post-surgical management pathway in our unit is as follows: in the case of patients who do not require mechanical ventilation, if possible, the nasogastric or nasoenteric tube is removed on postoperative day 1; on days 2 and 3, oral fluids are started if tolerated; on day 4, serum amylase levels are measured, as well as the output from abdominal drains; on days 5-7, the drains are removed and patients are discharged between days 7-10 if no biliopancreatic leak is detected. We found an overall complication rate of 81%, with pleural effusion and healthcare-associated pneumonia being the most frequently reported, followed by biliary or pancreatic leaks, which, in terms of complication frequency, aligns with the findings reported in a systematic review by Sherko et al [7].

Finally, the pathology reports were positive for malignancy in a total of 13 cases, resulting in pancreatic adenocarcinoma in 11 of them, consistent with global literature where more than 90% of cancer cases are due to pancreatic adenocarcinomas [22]. Of the remaining two cases of malignancy, one was reported as distal cholangiocarcinoma and the other as an ampullary tumor of the Vater's type adenocarcinoma. Regarding the 3 patients who presented benign pathology after the definitive report, it is important to highlight a case of autoimmune pancreatitis (AIP), which, although a rare diagnosis representing less than 5% of cases, has evidence in the literature of its association with pancreatic cancer, specifically AIP type 1 [22]. Although the diagnosis of pancreatic cancer is typically made at an advanced stage with distant disease in more than 50% of cases, timely intervention was performed, resulting in ten of these patients currently undergoing adjuvant treatment aimed at improving survival. After a

thorough evaluation of the reported complications or incidents, modifications have been made to the protocol used in the institution for patients with neoplasms of this type or suspected cases, implementing pancreaticoduodenectomy with pylorus preservation, as a reduction in complications was observed compared to the classic Whipple procedure [9-12]. Despite the lack of effective screenings, a more comprehensive approach is now adopted for patients with suspected pancreatic cancer or risk factors, with the aim of prioritizing care and offering a curative treatment.

CONCLUSION

The Whipple procedure, although considered complex and with a high risk of complications, has achieved improvements in quality of life and increased survival in selected cases. We recommend thorough evaluation and individualization according to each patient's case and institution. We emphasize the need for further research and more sophisticated studies, such as endoscopic ultrasound, along with excellent multidisciplinary pre, intra, and postoperative management, to increase early diagnosis rates and reduce morbidity, ultimately improving outcomes in the treatment of pancreatic adenocarcinoma.

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