**PANCREATICODUODENECTOMY: RETROSPECTIVE STUDY OF A SINGLE CENTER EXPERIENCE**

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**Abstract**

**Background:** Whipple surgery (pancreaticoduodenectomy) is a complex surgery with high postoperative complication rate. We aimed to demonstrate the outcomes and rates of complications from patients who had undergone PD in our hospital.

**Materials and methods:** Medical records of 22 patients, who underwent pancreaticoduodenectomy surgery between November 2018 and December 2022 at Department of Abdominal Surgery, City General Hospital 8th September in Skopje, North Macedonia, were examined retrospectively. Age, sex, localization of the lesion and pathohistological properties and postoperative morbidity and mortality were studied.

**Results:** A total of 22 patients (12 male, 10 female) with a mean age of 63,9 years who underwent pancreaticoduodenectomy were included in the study. Ten patients (45,45%) had pancreatic head malignancies, 7 patients (31,81%) had ampullarry malignancies, 1 patient (4,54%) had duodenal and also 1 patient (4,54%) had common bile duct malignancies. Two of our cases (9,08%) underwent surgery for gastric antrum carcinoma and one patient (4,54%) for colon carcinoma. The most frequently encountered complications were pancreatic fistula (18,16%), biliary leakage (13,64%) and pulmonary complications (13,64%). Surgery related mortality rate was 9,09% (2 cases).

**Conclusion:** We represent outcomes of our surgical team compared to the published data of some other centers. Prospective randomized studies are needed to adequately assess postoperative complications. To improve the postoperative outcome, appropriate monitoring, multidisciplinary approach and further improving of surgical techniques are needed.

**Keywords:** pancreaticoduodenectomy (PD),postoperative complications, Whipple procedure

**1. Introduction**

The pancreatoduodenectomy, also known as the Whipple procedure, is the surgical procedure of choice for the resectable and the borderline resectable pancreatic ductal adenocarcinomas It is commonly performed for malignant tumors of pancreatic head, ampulla, distal bile duct, but also may be performed for benign tumors, and trauma of pancreatic head and duodenum.[1,2,3] Only 10-20% of patients with diagnosed mass in pancreatic region, presenting with a tumor that can be resected [4]. Because of its complexity PD is associated with significant postoperative morbidity, rates of which range from 30% to 60% [5–7]. These complications include: pancreatic leak or fistula, intra-abdominal abscess, bile leak, postoperative hemorrhage, delayed gastric emptying, surgical site infection, pulmonary or cardiac complications and sepsis [5,8]. With the progress of surgical techniques and improvements in perioperative and critical cares, the mortality rate has been recently decreased from 25% to less than 5% [9].

In this study, we report our experience with pancreaticoduodenectomy with aim to evaluate the spectrum of postoperative complications and clinical outcomes.

**2. Materials and Methods**

This retrospective study was conducted at the Department of Abdominal Surgery, General City Hospital, Skopje, North Macedonia. The study included data from patients that underwent pancreaticoduodenenctomy in the period from November 2018 till December 2022 (including the period of Covid-19 Pandemia). It was performed on 22 patients with proven mass in the ampulary, periampulary or pancreatic head region who underwent a classic Whipple procedure, but also included patients with multivisceral resections due to multivisceral malignant tumor involvement.

**2.1. Data collection**

The patients data were colected from the medical records including demographic characteristics (gender, age), preoperative findings and comorbiditities (presence of DM, high billirubin level, tumor location), intraoperative data (including type of operation, operation time) and postoperative complications and early outcome were also studied. From this study were excluded patients with missing information from their data registries, unresectable patients and patients with distant metastasis.

**2.2 Preoperative workup**

All patients who were candidates for PD were admitted with symptoms of weight loss, obstructive jaundice, severe vomiting and anemia. Routine preoperative workup included ECG and chest x-ray and complete blood analysis including liver and renal functional test, serum electrolytes and coagulation profile. Tumor location and staging were assessed by computed tomography scanning, MRI, abdominal US (ultrasonography). In order to achieve preoperative patient optimization, ERCP with biliary stent insertion was carried out for some cases as a therapeutic biliary drainage measure for jaundice, especially in those patients where the hiperblirubinemia generate liver and brain function impairment.

**2.3. Surgical technique**

All patients received prophylactic antibiotics (Ceftriaxone) 30–60 min before the skin incision. For abdominal exploration was used upper midline or transverse incision most frequently and in some cases was used Mercedes Benz modification of Kocher’s incision. The peritoneum and liver were assessed for the presence of metastasis and the tumor for the resectability. In the most of the patients was performed standard Whipple procedure, which consists of 20%–40% distal gastrectomy, cholecystectomy, PD and also the technique of “triangle resection” was included. Regarding the reconstructions, all the anastomoses were performed using the appropriate size of Maxon sutures. First anastomosis is pancreaticojejunostomy in the form of end-to-side anastomosis with interrupted sutures. According to the size of pancreatic duct in all patients with ductal diameter smaller than 3 mm, pancreaticojejunostomy was performed and duct-to-mucosa anastomosis, when ductal diameter was bigger than 3 mm. The reconstruction was followed by end-to-side hepaticojejunostomy with interrupted single layer sutures. The third anastomosis is the gastrojejunostomy typically performed 40 cm downstream from the hepaticojejunostomy. Braun jejunojejunostomy, side-to-side, was added to other anastomoses at the end of the operation and it was performed using a standard, manual one-layer method. Some of the patients because of the tumor spreading, beside PD had other resection (right hemicolectomy, splenectomy, nephrectomy). In all patients closed suction drains were placed in Morrison pouch and in the vicinity of the pancreatic and biliary anastomosis. None of the operated patients received any types of neoadjuvant therapy. The samples were sent for histopathological examination to confirm the type and pathological characteristics of the tumor.

**2.4. Postoperative follow-up**

Postoperative period management includes keeping the patient with nothing by mouth for day 1 and advancing with clear liquids and then gradually to a low-fat diet in frequent small feeds. NG tube for stomach decompression usually stays on operative and first postoperative day if there is no high output, and then is removed. The drains are removed gradually once the output is minimal and there is no evidence of pancreatic fistula or biliary leakage, usually between postoperative days 5 and 8. Mortality and morbidity were estimated within 30 days postoperatively. Postoperative complications were classified as procedure-related (pancreatic fistula, biliary leakage, delayed gastric emptying, acute pancreatitis, wound infection, wound disruption, postoperative bleeding) or general (pulmonary complications, cardiac complications, ketoacidosis, sepsis).

In this study pancreatic fistula was defined as amylase level of drainage fluid on postoperative day 3 exceeding three times of the serum concentration. Biliary leak was defined by bilious aspect of the drainage fluid confirmed biologically. Both pancreatic and biliary leak were managed by drainage until resolution or reoperation.

Delayed gastric emptying was defined as intolerance to oral intake and need of gastric decompression after the seventh postoperative day. Other complications were defined as following: wound infection (purulent wound drainage); postoperative bleeding (requiring transfusion or endoscopic or operative intervention); acute pancreatitis (>3 fold increase in serum amylase or lipase from postoperative day four onward with a compatible clinical course or CT scan findings); pulmonary complications (pneumonia, effusion requiring drainage or re-intubation); postoperative mortality (death occurring in the first 30 postoperative days). Тotal hospital stay (number of days spent in hospital) was also evaluated.

**2.5. Data analysis**

SPSS (version 22) program was used for a statistical analysis. Data were analyzed using ꭕ2 test, student t-test and Fischer exact test as appropriate. A p-value of < 0.05 was considered as a statistically significant.

**3. Results**

In this study were included 22 patients, 12 male (54,54%) and 10 female patients (45,46%). The mean age was 63.9 ± 10.6 years with a range of 32 – 74 years. In preoperative period 16 patients (72,73%) had jaundice or higher level of serum bilirubin. The median of preoperative serum bilirubin was 118.03 ± 113.7 umol/L and preoperative ERCP with biliary stent insertion was carried out in 9 (40,91%) patients as a therapeutic biliary drainage measure for jaundice or cholangitis. Six patients had diagnosis of diabetes as comorbidity. Initial diagnosis of the patients was based upon baseline, clinical and radiological investigations. Further highlights regarding the tumor site, grade and other histopathological parameters are shown in **Table 1**.

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| **Parameter** | | **Frequency** | **Percentage** |
| Tumor site | Pancreatic head | 10 | (45,45%) |
| Ampullary | 7 | (31,81%) |
| Duodenal | 1 | (4,54%) |
| Choledochus | 1 | (4,54%) |
| Gastric antrum | 2 | (9,08%) |
| Colon | 1 | (4,54%) |
| Tumor type | Well-differentiated adenocarcinoma | 4 | (18,18%) |
| Moderately differentiated adenocarcinoma | 13 | (59,06%) |
| Poorly differentiated adenocarcinoma | 3 | (13,66%) |
| GIST (duodenum) | 1 | (4,54%) |
| Lymphoma malignum anaplasticum (large cell) | 1 | (4,54%) |
|  |  |  |
| Involvement of lymph nodes | Yes | 10 | (45,45%) |
| No | 12 | (54,55%) |
| Surgical margins | Positive | 2 | (9,08%) |
| Negative | 20 | (90,92%) |

**Table 1.** Histopathological details of the resected tumors.

In this study, 19 patients (86,26%) underwent standard pancreatico-duodenectomy (PD, i.e., Whipple’s procedure), 2 underwent PD with right hemicolectomy and one patient beside PD had splenectomy and nephrectomy of right kidney because of chronic pyelonephritis (End stage renal disease).

The average surgery time was 343.95 ± 98.5 minutes and mean length of hospital stay of the patients was 15.41 ± 7.5 days. Postoperative complications data are presented in **Table 2**. Four of the 22 patients (18,16%) were identified as having pancreatic leakage after operation. Other procedure-related postoperative complications included biliary fistula (13.64%, 3); delayed gastric emptying (4,54%, 1); wound infection (9,08%, 2); wound dehiscence (4,54%, 1); pancreatitis (4,54%, 1); hemorrhage/anemia (4,54%, 1); lung complications (13,64%, 3); ketoacidosis (4,54%, 1). Two of the patient died in the early postoperative period, because of pulmonary complications, one diagnosed with lymphoma malignum anaplasticum (large cell) and other was simultaneously complicated with ketoacidosis.

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| --- | --- |
| **Postoperative complications** | Cases (%) |
| Pancreatic fistula | 4 (18.16%) |
| Biliary fistula | 3 (13.64%) |
| Delayed gastric emptying | 1 (4.54%) |
| Wound infection | 2 (9.08%) |
| Wound dehiscence | 1 (4.54%) |
| Pancreatitis | 1 (4.54%) |
| Hemorrhage/anemia | 1 (4.54%) |
| Lung complications | 3 (13.64%) |
| Ketoacidosis | 1 (4.54%) |
| Postoperative death (in 30 days) | 2 (9.09%) |

**Table 2.** Postoperative complications after pancreatoduodenectomy

**4. Discussion**

Pancreaticoduodenectomy, modified and promoted in 1935 by Allen Whipple, has been burdened by a high morbidity and mortality rates and because of that resulted in initial reluctance to adopt this surgery for the management of pancreatic and periampullary tumors [10]. Because of its complexity, some of the surgeons had a concept that this procedure is better not be performed, because it is demanding and time-consuming procedure with poor long-term outcomes and necessitating the presence of an advanced critical care for its success. In our district, beside the fact that is not high-volume experienced center for pancreatic surgery, we decide to popularize PD and during the past 4 years of our experience in Whipple procedure we developed a progressive improvement in the different aspects of the surgical technique including less intraoperative bleeding, less pancreatic anastomosis failure, shorter operative time and decrease in hospital staying days.

We carried out a single-center retrospective study of 22 patients undergoing PD to present early postoperative outcome and complications. Nearly half of the patients (10 patients) had pancreatic head tumor, 7 had ampullary tumor, 1 duodenal, 1 patient with tumor in distal choledochus and 3 patients had carcinomas that infiltrate in pancreas or duodenum (gastric and colon carcinoma).

The goal of PD is to achieve comprehensive oncological resection. Thus it is considered as curative surgery for ampullary, periampullary and pancreatic head cancers which includes complete gross and microscopic resection of tumor elements [9, 11,]. We include the technique of “triangle operation”, which is radical artery-sparing approach, allowing a sharp dissection (adventitial layer of arteries is opened longitudinally) with removal of all lymphatic and neural tissue structures to the basis of celiac axis and superior mesenteric artery [12]. This results in an anatomic triangle bordered by superior mesenteric artery, celiac axis and portal vein, with complete lymphadenectomy and soft tissue removal in this area, in the light of a truly radical surgical approach [13,14]. In our study, patohistological analysis of specimens shown positive surgical margins (retroperitoneal) in two patients (9,08%) with carcinoma of pancreatic head and 20 patients (90,92%) with all negative surgical margins. Ten patients (45,45%) had positive lymph nodes for metastatic deposits.

In our series, the postoperative complications we came across were pancreatic fistula (18,16%), bile leak (13,64%), lung complications (13,64%), wound infection (9,08%) Complications like acute pancreatitis, ketoacidosis, wound dehiscence, postoperative bleeding and gastric atony were presented in 4,54% (which corresponds for one patient respectively). Yeo et al. in a pancreaticoduodenectomy series of 650 patients shown that the most common three complications were delay in gastric emptying (19%), pancreatic fistula (14%), and wound infection (10%), respectively [15]. Kargi E et al. in a study in Turkey, from a single-center, general hospital experience with small number of patients (71 patients) presented postoperative complications rate were pancreatic fistula (12%), lung infection (2.5%), wound infection (5.5%), postoperative bleeding (1%), and gastric atony (7%) [16]. Among these complications, pancreatic fistula is the most important complication of PD because, directly or indirectly, contributes to the other morbidity including DGE, postpancreatectomy hemorrhage and death. In our patients the rate of pancreatic fistula was 18,16%. Although, the rate of pancreatic leak is considerably variable among the centers that ranging from 13 to 35% [17-19], our result is acceptable. To control potential pancreas leaks, in most centres, during surgery, a drain is implemented around pancreatic anastomosis as we did in our cases. Most often, pancreatic leak comes to an ends with conservative treatment, with control of drain fluid output and if the patient is relatively asymptomatic and if, in spite of the normal diet, a fistula output below 200 ml/day is observed, the patient can be discharged with the drain. In most cases, the fistula closes in a few days.

Delay in gastric emptying (DGE) is not life threatening and usually resolves spontaneously with parenteral nutrition support and nasogastric decompression until the complication is resolved. The higher percentage of lung complications in our series probably is due previously suffered Covid-19 pneumonia and HOBB (all three patients had that in common in medical history). The overall perioperative mortality rate in this study was 9,09% (2 patients), which is higher than < 5% rate reported by other centers [17,19]. The higher percentage is probably due to small series of patients in our study compared with high-volume centers. The importance of an adequate perioperative complication management in pancreatic surgery is essential and it is important to include multidisciplinary team approach to this- including interventional radiologists and endoscopists for non-surgical complication management and anesthesiologists for adequate postoperative care in ICU [20].

Even though our analysis highlights important findings it has certain limitations. First, this work is a retrospective analysis, therefore, the possibility of bias cannot be eliminated and associations of complications with the cause could not be developed. Second, the study was performed at a single-institution which is not referral center for pancreatic surgery and it includes the limitations of performing this kind of operations during the period of Covid-19 pandemia in which our hospital functioned as Covid Hospital. Moreover, we used a convenience sampling technique for the selection of study participants. To overcome these limitations, a prospective multicenter study with more patients is necessary for better understanding of postoperative complications following pancreaticoduodenectomy.

**5. Conclusion**

We decide for the first time to publish data of our experience and we believe that our study contribute for the development of pancreatic surgery in our country. Appropriate postoperative monitoring, multidisciplinary approach and further improving of surgical team experience and surgical techniques can help in improving the postoperative outcomes.

**REFERENCES**

1. Scaife L. C, Hewitt C. K, Mone K. M, et al, Comparison of intraoperative versus delayed enteral feeding tube placement in patients undergoing a Whipple procedure, HBP 16 (2014) 62–69.

McGuigan A, Kelly P, Turkington RC, Jones C, et al: Pancreatic cancer: a review of clinical diagnosis, epidemiology, treatment and outcomes. World j Gastroenterol. (2018), 24:4846-61.

Leichtle W.S, Kaoutzanis C, Mouawad J.N, et al., Classic Whipple versus pylorus-preserving pancreaticoduodenectomy in the ACS NSQIP, JSR 183 (2013) 170–176.

1. Javed AA, Wright MJ, Sidddique QH, Rahim FH: Outcome of patients with borderline resectable pancreatic cancer in the contemporary era of neoadjuvant chemotherapy. J Gastrointest Surg (2019) 23:112-21.

Eric C.H. Lai, George P.C. Yang, Chung Ngai Tang. Robot-assisted laparoscopic pancreaticoduodenectomy versus open pancreaticoduodenectomy – a comparative study, Int. J. Surg. 10 (2012) 475–479.

Clancy E. T, Ashley S. W. Pancreaticoduodenectomy (Whipple operation), Surg. Oncol. Clin. N. Am. 14 (2005) 533–552.

Sahora K, Morales-Oyarvide V, Thayer P. S, et al., The effect of antecolic versus retrocolic reconstruction on delayed gastric emptying after classic non-pylorus preserving pancreaticoduodenectomy, Am. J. Surg. 209 (2015) 1028–1035.

Martignoni M, Friess H, Sell F, Buchler M W, et al. Enteral nutrition prolongs delayed gastric emptying in patients after Whipple resection, Am. J. Surg. 180 (2000) 18–23.

1. Perysinakis I, Avlonitis S, Georgiadou D, et al: Five year actual survival after pancreaticoduodenectomy for pancreatic head cancer. ANZ J Surg. (2015), 85:183-6.

O.A. Whipple, Pancreaticoduodenectomy for islet carcinoma: a five-years follow-up, Ann. Surg. 121 (1945) 847e852.

Sulzer JK, Sastry AV, Meyer LM, et al.: The impact of intraoperative goal-directed fluid therapy on complications after pancreaticoduodenectomy. Ann ed Surg (2018) 36:23-8.

Hackert T, Strobel O, Michalski CW, et al .The TRIANGLE operation – radical surgery after neoadjuvant treatment for advanced pancreatic cancer: a single arm observational study. HPB (2017) 19:1001–1007

Rosso E, Zimmitto G, Ianelli A, et al. The “TRIANGLE Operation” by laparoscopy: radical pancreaticoduodenectomy with major vascular resection for borderline resectable pancreatic head cancer. Ann Surg Oncol (2020). 27(5):1613–1614

1. Klotz R, Hackert T, Heger P, Probst P, Hinz U, Loos M, Berchtold C, Mehrabi A, Schneider M, Müller-Stich BP, Strobel O, Diener MK, Mihaljevic AL, Büchler MW . The TRIANGLE operation for pancreatic head and body cancers: early postoperative outcomes. HPB (Oxford) (2021); S1365–182X(21)00614–6

Yeo CJ, Cameron JL, Sohn TA, et al. Six hundred fifty consecutive pancreaticoduodenectomies in the 1990's- Pathology, complications, and outcomes. Ann Surg (1997);226:248-60.

1. Kargı E, Okay E, Gunes A, et al. Outcomes of pancreaticoduodenectomy surgeries: a single center experience with 71 cases. J Turgut Ozal Med Cent (2014);21:118-121.

John L. Cameron, One thousand consecutive pancreaticoduodenectomies and beyond: a personal series, Am. J. Surg. 194 (2007) S11–S15.

Castillo CF, Morales-Oyarvide V, McGrath D, et al., Evolution of the Whipple procedure at the Massachusetts General Hospital, Surgery 152 (2012) S56–S63.

Michael B. Ujiki, Mark S. Talamonti, Surgical management of pancreatic cancer, Semin. Radiat. Oncol. 15 (2005) 218–225.

Nießen A, Hackert T. State-of-the-art surgery for pancreatic cancer. Langenbecks Arch Surg. (2022) Mar;407(2):443-450.