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# Functional Results Following Pylorus-Preserving Pancreatoduodenectomy with Pancreaticogastrostomy

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## Rezumat

***Rezultatele funcționale după duodenopancreatectomia cefalică cu prezervare de pilor și anastomoză pancreatico-gastrică***

*Introducere:* Duodenopancreatectomia cu prezervare de pilor prezintă beneficii în ce priveşte durata mai scurtă a intervenției chirurgicale şi statusul nutrițional postoperator mai bun dar cu riscul apariției în postoperator a tulburărilor de evacuare gastrică.
*Metode:* Am efectuat un studiu retrospectiv în care au fost incluşi pacienții la care s-a efectuat duodenopancreatectomie cefalică în perioada mai 2012 - mai 2018 în cadrul Clinicii I Chirurgie a Institutului Regional de Oncologie Iaşi la care au fost analizați principalii parametri postoperatori
*Rezultate:* Au fost 47 de pacienți la care s-a practicat duodeno-pancreatectomie cefalică; la 42 din aceştia a fost folosită tehnica cu prezervare de pilor şi anastomoză pancreatico-gastrică. Tumora a fost localizată la nivelul pancreasului cefalic (n=21; 44,68%), ampulei lui Vater (n=14; 29,78%), coledocului distal (n=7; 14,89%), duodenului (n=2; 4,25%), şi la nivelul colonului drept (n=3; 6,38%). 10 pacienți (21,2%) au dezvoltat postoperator complicații de grad III-V în clasificarea Dindo Clavien. 12 pacienți (25,5%) au dezvoltat postoperator fistulă pancreatică: 8 (17%) pacienți cu fistulă de grad A, 3 (6,4%) cu fistulă de grad B şi 1 (2,12%) pacient cu fistulă de grad C. Tulburările de evacuare gastrică s-au întâlnit la 17 pacienți (36,17%): grad A la 9 (19,15%) pacienți, grad B la 6 pacienți (4,5%) şi grad C la 2 pacienți (2,25%). 3 pacienți au dezvoltat fistulă biliară postoperatorie. 4 pacienți au necesitat o relaparotomie.
*Concluzii:* Rezultatele studiului nostrum sunt concordante cu rezultatele din literatură şi arată că duodenopancreatectomia cu

prezervare de pilor asociată cu anastomoza pancreatico-gastrică nu creşte riscul de tulburare de evacuare gastrică.

**Cuvinte cheie:** duodenopancreatectomie, morbiditate, cancer pancreatic, fistulă pancreatică, evacuare gastric întârziată

**Abstract**

*Background:* Pylorus preserving (PP) pancreaticoduodenectomy (PD) has several advantages in terms of shorter operation time and improved nutritional status but with an increased risk for delayed gastric emptying.

*Methods:* We performed a retrospective study on all patients in which PD was performed from May 2012 to May 2018. It was analyzed early postoperative outcomes and the incidence of delayed gastric emptying (DGE) syndrome for patients with pylorus PP PD technique and pancreatico-gastrostomy (PG).

*Results:* There were 47 PD, in which PP technique was performed in 42 cases. The tumour location was in the pancreatic head (n=21, 44.68%), periampullary (ampulla of Vater) (n=14,29.78%), distal bile duct (n=7,14.89%), duodenum (n=2, 4.25%) and advanced right colon cancer (n=3, 6.38%). There were 10 cases (21.2%) of grade III-V complications, grade A pancreatic fistula (PF)8 cases (17%), grade B in 3 cases (6.4%) and grade C in 1 case (2.12%). DGE was encountered in 17 cases (36.17%), grade A 2 cases (4.25%), grade B in 4 cases (8.5%) and grade C in 2 cases (4.25%). Biliary fistula occurred in 3 cases (6.4%) and in 4 cases relaparotomy was needed.

*Conclusions:* The results of our study are concluding with the previous studies, the addition of PG to PP PD does not increase the risk of DGE.

**Key words:** pancreaticoduodenectomy, morbidity, pancreatic cancer, pancreatic fistula, delayed gastric emptying

## Background

PD remains the single radical treatment option for patients diagnosed with malignant tumours located in the pancreatic head, periampullary region or the duodenum, in addition the procedure is performed for some benign conditions. In a limited number of cases this procedure is performed for tumours originating in surrounding organs invading the duodenum or the pancreas. Pancreatic cancer (PC) represents the fourth cause of deaths in the world (1) and the estimates are that in the next decades will become the third one (2). Pancreatic surgery remains a highly demanding surgical procedure for the surgeon, the anesthesiology team and nevertheless for the patient. Even in highly experienced centers there are postoperative morbidity rates up to 50% with a mortality rates below 5%, mainly due to the standardized surgical technique and perioperative care (3).

Although it was first imagined and described by Kausch in the beginning of the 20$^{th}$ century, the original technique consisted only in the resection of some portions of the duodenum and the head of the pancreas. Once with the discovery of vitamin K, the advances in anesthesiology and of the intensive care, Allen O. Whipple refined the procedure, initially presented the first 3 cases, and in the 1946 presented his first 10 year experience of radical excision of the head of pancreas and duodenum (4).

A standard PD involves a distal gastrectomy

with removal of the pancreatic head, duodenum and first 10 to 15 cm of the jejunum, common bile duct and gallbladder followed by reconstruction of gastrointestinal route. Watson was the first surgeon that modified the standard Whipple procedure by preserving the pylorus in a patient with carcinoma of the papilla of Vater. Traverso and Longmire presented the first large series of patients with chronic pancreatitis and duodenal cancer with PP technique (5). This was the moment from which a debate whether or not to preserve the pylorus was born, the advocates of this modification states that patients present an improved nutritional status, the major argument against pylorus preservation is that the pylorus plays a central role in the occurrence of a DGE due to the devascularisation and denervation that induces pylorospasm.

One of the most important debate subjects in pancreatic surgery is the treatment of the pancreatic stump. Postoperative PF is the most common and severe complication after pancreatic head resection and it can lead to serious consequences such as hemorrhage, sepsis, need for reintervention, prolonged hospital stay and increased mortality. Pancreticojejunostomy was preferred anasthomosis with several variations: end-to-end, end-to-side pancreticojejunalanasthomosis, either duct-to-mucosa or with invagination. PG was proposed as an alternative to this technique especially in patients with soft pancreatic gland and small duct. Several randomized studies were published in order to compare the superiority of each method with conflicting results regarding the risk of mortality and PF, but the results of a meta-analysis from 2015 showed that the rate of pancreatic fistula was significantly lower in the PG (11.2% vs. 18.7%, p=0,0003) with the same mortality rates (3.7% vs. 3.9%) and lower biliary fistula rate (6).

The purpose of our study is to present the early postoperative outcomes in terms of mortality and morbidity (postoperative pancreatic fistula, septic complication) and also the functional results following a single center continuous series of patients in which PD was performed.

## Methods

We performed a retrospective review of all patients who underwent PD in the 1st Surgical Unit of the Regional Institute of Oncology Iasi during May 2013 and May 2018. Patients' data were recorded in a prospectively maintained database, for all the patients an informed consent for surgical procedure and data management was obtained. We included in the study patients diagnosed with pancreatic head tumours, ampullary tumours, duodenal cancer and right-sided colon tumours invading the duodenum.

Preoperative workout included clinical assessment, laboratory investigations including tumoral markers and radiological investigations (abdominal ultrasound, abdominal computed tomography, magnetic resonance cholangiopancreatography, chest X-ray). Preoperative biliary drainage was performed in a limited number of cases by endoscopic retrograde cholangiopancreatography.

Surgical technique consisted in an approach using extended right subcostal incision or a midline laparotomy based on patients characteristics or surgeon choice. In all of the cases the anterior approach was used in surgical dissection, standard regional lymphadenectomy was performed harvesting all the nodes between the hepatoduodenal ligament, right side of the superior mesenteric vessels and the inferior vena cava. Division of the pancreatic neck was performed using surgical scalpel with diathermy hemostasis on pancreatic stump surface. Transection of the duodenum is performed a centimeter distal to the pylorus. The cut end of the pancreas is mobilized from the retroperitoneal tissues for a distance of 2 to 3 cm, which requires ligation of several vessels tributaries to splenic vein. The pancreatic duct is probed with a 5 or 6 French tube and its patency assured. The posterior surface of the stomach is freed from the posterior bursa omentalis and a serous incision is performed on the posterior face corresponding to the topography of the pancreatic stump. The two layer anastomosis is performed by placing a 4-0 polydioxanone continuous suture between the

pancreatic capsule and the serosa of the stomach. A small incision is performed in the center of denudated area on the stomach and a duct to mucosa anastomosis is performed using the stent. A further single layer continuous suture is performed in a fashion similar with the posterior row. The cut end of the small bowel is passed through the mesocolon and a single layer duodeno-jejunostomy is performed, the biliary anastomosis is usually performed at a distance of at least 15 cm from the latter in a termino-lateral fashion. A feeding jejunostomy is inserted for postoperative nutritional support and a gastric tube is inserted.

Postoperative care included routinely administration of octreotide analogues, early enteral feeding using jejunostomy, continuous proton pomp inhibitors. The output of drainages and of the nasogastric tube is monitored. The nasogastric tube is removed between the 3rd and the 5th postoperative day, and a clear liquid diet is started.

Complications were defined as any adverse event from the normal postoperative course in the first 30 days after surgery. Major complications that required endoscopic, radiologic or surgical intervention were defined as class 3 or higher according to Clavien classification system (7). PF was defined according to the 2016 update of the International Study Group (8). Delayed gastric emptying was defind as an output of nasogastric tube greater than 500 ml per day that persisted after the 10th postoperative day, the failure to maintain oral intake or the reinsertion of a nasogastric tube and it was graded according actual recommendations (9).

Statistical analysis of the data was performed using MedCalc v9.2.0.1. The quantitative variables were done using mean and standard deviation, the categorical variables by way of percentages.

## Results

During our study period there were 47 cases of PD (25 males and 22 females) with a mean age of 62 years. Patient's characteristics are summarized in *Table 1*. The most frequent tumour localization was in the pancreatic head (21 cases, 44.68%) and ampullary carcinoma (14 cases, 29.78%). Less frequent tumour localization were: distal bile duct in 7 cases (14.89%), duodenal cancer in 2 cases (4.25%) and in 3 cases (6.38%) right sided colon cancer with direct invasion of duodenum or with direct communication. There were no patients diagnosed with chronic pancreatitis. Despite the fact that most of the patients with bile duct obstruction presented elevated levels of bilirubin (mean levels 6.24 mg/dl), preoperative stenting was performed only in 2 cases. The mean Charlson Comorbidity score

**Table 1.** Patients' characteristics

| n | |
|---|---|
| Age | 62 (51-73) |
| Gender Male/Female | 25/22 |
| ECOG performance status 0/1 | 32/15 |
| Charlson Comorbidity index | 4 (3-5) |
| BMI (kg/m2) | 27.3 (21.8-32.8) |
| Serum albumin (g/dl) | 4,26 (3.83-4.69) |
| Ca19.9 (U/ml) | 442 (8.9-886) |
| Preoperative bilirubin (mg/dl) | 6,59 (5.48-7.70) |
| Preoperative biliary drainage | 2 (4,2%) |
| Preoperative chemotherapy | 1 (2,12%) |
| Primary cancer | |
| Pancreatic cancer | 21(44.68%) |
| Ampullary carcinoma | 14(29.78%) |
| Distal bile duct cancer | 7(14.89%) |
| Duodenal cancer | 2(4.25%) |
| Others | 3(6.38%) |

**Table 2.** Intraoperative findings and technique

| | |
|---|---|
| Pylorus preserving | 42 (89.36%) |
| Whipple | 5 (10.63%) |
| Pancreatic duct stenting | |
| Yes | 47 (100%) |
| No | 0 |
| Mean operating time (minutes) | 240 (160-320) |
| Mean no. of red cell units transfused intraoperative | 1 |
| Pancreatic consistency | |
| Soft | 20 (42%) |
| Firm | 15 (32%) |
| Unknown/Missing | 12 (26%) |
| Pancreatic duct diameter | 3,2 (1.2-5.2) |

**Table 3.** Postoperative outcomes

| | |
|---|---|
| Mean length of in hospital stay | 23,6 (12.6-34.6) |
| Median intensive care stay | 6 (2-10) |
| Grade III-V complications (Dindo-Clavien) | 10 (21,2%) |
| Pancreatic fistula | 12 (25,5%) |
| Biochemical leak | 8 (17%) |
| Grade B | 3 (6,4%) |
| Grade C | 1 (2.12%) |
| Biliary fistula | 3 (6.4%) |
| Delayed gastric emptying | 17 (36.17%) |
| Grade A | 9 (19.15%) |
| Grade B | 6 (12.76%) |
| Grade C | 2 (4.25%) |
| Postpancreatectomyhemorrhage (31) | 8 (17.02%) |
| Grade A | 2 (4.25%) |
| Grade B | 4 (8.5%) |
| Grade C | 2 (4.25%) |
| Mean days NGT required | 5 (1-9) |
| NGT reinserted | 8 (17%) |
| Wound infection | 7 (14,9%) |
| Intra-abdominal abscess requiring reintervention | 1 (2,12%) |
| Other infections | 15 (32%) |
| Clostridium difficile infection | 9 (19,15%) |
| Cholangitis | 3 (6,38%) |
| Reoperation | 3 (6,38%) |
| In hospital mortality | 2 (4,26%) |
| 30 day mortality | 2 (4,26%) |

was 3.6 (standard deviation 1.2), with a mean BMI of 27.3 (SD 5.5).

In 42 cases (89.36%) it was performed pylorus PP PD. As recorded intraoperative, the duration of surgery was 240 minutes (SD 80 min), most of the patients presented a soft consistency of pancreatic parenchyma, 20 cases (42%), with a mean pancreatic duct diameter of 3,2 mm. intraoperative findings and technique details are presented in *Table 3*. In all patients a pancreatic duct stenting during the anastomosis was performed. Vascular resection was performed in two cases, a resection of portal vein, with termino-terminal anastomosis and a superior mesenteric artery resection and anastomosis.

Outcomes after surgery are summarized in Table 3. Overall severe complications following surgery occurred in 10 cases (21.2%). PF appeared in 12 cases, most of them were grade I (biochemical leak), 8 cases (17%), grade B in 3 (6,4%) and grade C in1 case. Biliary fistula occurred in 3 cases (6.4%), no biliary collection was encountered after surgery on abdominal imaging, and in all of those cases a conservatory treatment protocol was applied. Postoperative hemorrhage occurred in 8 cases (17.02%), and in 2 cases it required relaparotomy for hemostasis, of those cases all patients developed PF. Abdominal septic collection that required surgical drainage was developed in one case. Other significant postoperative complications included *Clostridium difficile* infection in 9 cases (19.15%) and cholangitis in 3 cases (6.38%), of those in 2 cases a preoperative endoscopic stenting was performed.

In patients with PP technique the naso-gastric tube was maintained for 5 days, delayed gastric emptying occurred in 17 cases (36.17%), in 8 patients (17.02%) it was necessary to reinsert the nasogastric tube, and in 2 patients a failure to tolerate oral liquids beyond the 10$^{th}$ postoperative day was encountered. The last cases were patients that also presented a PF.

Overall hospital stay was 23.6 days (SD 11 days) with a median intensive care stay of 6 days. Postoperative and 30 days mortality was 4.26% (2 cases), one patient with superior mesenteric artery resection and anastomosis developed in the 10$^{th}$ postoperative day a small bowel ischemia with necrosis and another patient developed pulmonary sepsis.

## Discussions

Although the DGE is not the most severe complication following PD, it is still the most frequent one. The late onset of oral feeding in patients after PD has several short-term consequences such as prolonged hospital stay, impaired quality of life and also long-term oncological consequences, such as the delay of initiation of chemotherapy that can influence overall survival of patients with pancreatic cancer.

The main purpose of this retrospective study is to evaluate the morbidity and functional results after PD in our service. Although there was a 5-year study period, the relatively

limited number of cases was explained by the lack of centralization of cases. All those patients represent the initial experience of a newly opened oncological surgical department. The advantages are that there is a uniform preoperative protocol, an accurate intraoperative assessment of pancreatic consistency, pancreatic duct diameter and a standardized technique for anastomosis. Furthermore, there was a unique protocol for postoperative treatment, surveillance and management of complications (same criteria for PF, hemorrhage or delayed gastric emptying).

The PP PD has the advantages of a shorter operation time with lower blood transfusion rates, but with an increased risk for DGE. The pathogenesis of this complication seems to be multifactorial: early enteral feeding, postoperative complications, PF occurrence and reconstruction route. The presence of a postoperative complication is the most significant risk factor for DGE, this can be explained by some degree of gastro paresis due to local inflammation or an abscess formation (10). One of the most frequent complications following PD is PF that itself increases and prologues the risk of DGE (11). Furthermore, a DGE could be the early sign of a possible abdominal complication, especially PF formation or a fluid collection, prior to other clinical sign or abdominal drain discharge. In our series, of the 17 cases of DGE, in 12 cases a clinical significant PF preceded or was developed in the same time with the onset of this complication. In another case a fluid collection was demonstrated on abdominal ultrasound without signs on infection. In all the cases the evolution of PF output and the DGE syndrome had a parallel evolution, the remission of symptoms were synchronous with the drop of fistula debit.

The reconstruction method was found to be another factor associated with DGE. Antecolic reconstruction, based on the results of a meta-analysis, avoids the risk of mechanical outflow obstruction, with an increased motility of the stomach and a lower pressure on pancreatic anastomosis, and thus a reduced risk of PF (11, 12). In our study a retrocolic route was chosen for the passage of the small bowel, with a wide opening of the transverse mesocolon and without angulation of the small bowel, those were the rationale for this technique. All of the anastomosis are located in the supramesocolic region, the only possible obstacle being at the passage of the small bowel through the mesocolon.

Despite the fact that early enteral feeding provides the most physiological and functional nutrition route and it prevents the morphological alteration of the gut, this method was demonstrated to be, based on previous studies, a risk factor for postoperative complications, including DGE(13). We believe that that the advantages of early enteral feeding, especially immunonutrition surpasses the potential complications induced and that this should be demonstrated by further randomized trials. In all the patients in our series a jejunostomy feeding tube was inserted at the end of the intervention and early enteral nutrition was used.

One of the most difficult key points during PD is the treatment of the pancreatic stump. The end result is the reduction of PF that can itself cause serious second-degree complications, such as: sepsis, hemorrhage, wound infection, prolonged hospitalization, the need for reintervention and death. The risk factors for this complication are: the consistency of pancreas, a small pancreatic duct with a posterior localization, a decreased blood supply and surgeon experience (14). In order to give evidence based recommendations several randomized trials have been conducted in order to find the best anastomotic technique (invagination vs. duct-to-mucosa, pancreticojejunostomy vs. PG, pancreatic duct stenting, fibrin glue). Up to date there is no sufficient data to promote the superiority of either technique. There are several techniques for pancreaticojejunostomy (end-to-side, invagination, duct-to-mucosa, binding technique, using a single or double layer) (15). The results of several studies suggested that duct-to-mucosa is the safest technique in term of fistula formation (less than 20%) (16). PG was considered to be an alternative to pancreaticojejunostomy,

the rationale for this technique is: the lack of activation of pancreatic enzymes in the acidic gastric environment, the anatomic proximity of the two organs (less anastomotic tension) and high vascularization of the stomach wall, and also it might be technically easier to perform. Despite those advantages, the long-term consequence of this technique is the exocrine insufficiency, which can develop in up to 62% of cases (17), the predictive factors for this technique are the hard consistency of the parenchyma, duct dilatation due to anastomotic stricture and previous impaired pancreatic function (18, 19). Currently there a 9 randomized trials published that investigated the superiority of each anastomosis. In 5 trials there were no statistical significant differences regarding the incidence of PF(20-24), the other 4 trials showed lower rates of fistulas following PG (25-27). Due to the lack of homogeneity between those studies there were published 17 meta-analysis. In one of the recent one, that included 1121 patients, the incidence of PF is lower after PG (11.2% vs. 18.7%; OR 0.53, p=0.0003) (6). In our series the use of pancreaticojejunostomy was based on experience with acceptable morbidity rates and the rationale for this type of anastomosis were enounced previously. We believe that the anatomic proximity of the two organs and the rich vascularization of the stomach are the two main reasons in order to perform this type of anastomosis.

In our series preoperative biliary stenting was limited to two cases due to the lack of this maneuver in the first 3 years of our study, and it was limited to patients with severe cholestasis and impaired liver functional tests. Both patients developed cholangitis prior to surgery that required antibiotics. Preoperative biliary stenting has the role of improving liver function, nutritional status and cell mediated immunity (28). Although the intention is to reduce postoperative morbidity, this procedure was demonstrated to prolong the duration of surgery, to increase the risk of sepsis and overall higher postoperative complication rates (29). Current recommendations are that preoperative stenting should be avoided and restricted to patients with cholangitis and elevated bilirubin levels, and if the surgery can be performed within a week the drainage should be avoided (30).

There are major drawbacks of our study: it is not a comparative study, the number of cases in which pancreaticojejunostomy was used is lower in order to perform adequate statistical analysis andthe relatively lower number of cases limits. The advantages are that is a continuous series of patients, the same surgical technique with the same postoperative protocol.

## Conclusion

Currently, all over the world there is a large heterogeneity regarding the extent of resection (with or without distal gastric resection) and the reconstruction method and yet no best practice has emerged as the ideal surgical technique. Moreover, there is no standardization regarding the use of stent, somatostatin analogues and other means to reduce PF. The most common sense rule is that the performance and the refinement of a single technique can lead to lesser rates of complications.

### *Conflict of interest*

The authors declare no conflicts of interests.

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