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Research Article

Analysis of the main complications following pancreaticoduodenectomy in a specialized Romanian surgery department

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Abstract. Aim: The aim of this study is to identify the risk factors for the main complications (pancreatic fistula-POPF, delay gastric emptying-DGE, pancreatic stump bleeding) following pancreaticoduodenectomy (PD) in a specialized surgery department. Material and method: Between January 2009-December 2015, 298 pancreaticoduodenectomies (PD) were performed in our department. 168 (56.19%) of cases were males and 131 (43.81%) were females, ages between 22-84 (61±10.4). Their data were introduced in a prospective database, also including co-morbid conditions, clinical characteristics and intraoperative aspects. Results: There were 27 (9.06%) cases of POPF, 61 (20.47%) of DGE and 20 (6.71%) of pancreatic stump bleeding. Pancreatico-jejunostomy (p=0.02) and the soft texture of the pancreas (p=0.05) significantly have favored POPF. The pancreatico-gastrostomy (p=0.05), the classical Whipple resection (p=0.03) and the need for intraoperative transfusion (p=0.016) were identified as risk factors for DGE. For pancreatic stump bleeding, significant risk factors were the soft texture of the gland (p=0.0007) and the intraoperative blood loss (p=0.016). The average length of hospital stay was 13.9+/-8.86 days. Reoperation rate was 12.08%. We had a 6.04% mortality rate relating to surgical complication. Conclusion: We can improve our results following PD by correcting some intraoperative risk factors: pancreatico-gastroanastomosis should be the choice for pancreatic stump treatment and we must care more for intraoperative blood loss and consecutively need for transfusion. The soft texture of the pancreas should warn us about a possible incidental postoperative outcome.

Key Words: Postoperative pancreatic fistula, delay gastric emptying, pancreatic stump bleeding, pancreaticoduodenectomy protocol

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Introduction

Pancreaticoduodenectomy (PD), the operation required by periampullary location of some tumors, is considered high-risk surgery. Although the morbidity rate is still high, 30-70% (Hsu et al 2012), and it hasn't decrease in the last decades, the mortality rate in specialized centers, 1-5%, is improving due to better management of these patients (Hata et al 2016). This means more accurate diagnosis, preoperative correction of anemia, hypoalbuminemia, liver function, but also reduce intraoperative blood loss and need for transfusion, correct treatment of pancreatic stump and lower operative time. Even more important is the postoperative management, which involves homeostasis maintenance, nutritional support, early mobilization and oral feeding, and much vigilance in early recognition and therapeutic intervention in case of complications.

To accomplish all these requirements, a multidisciplinary team is needed, including gastroenterologist, radiologist, surgeon and anesthesiologist. We co-opt also a pathologist, who inspect the specimen immediately after operation and try to identify elements in the peritumoral pancreatic tissue, which can lead to pancreatic fistula (grades of fibrosis, lipomatous atrophy, inflammatory infiltrate and necrosis; the presence of microscopic tumoral tissue or intravascular thrombosis).

In order to ameliorate our results after pancreaticoduodenectomy, we elaborated a management protocol in 2009, including a diagnosis pathway and a preparation one. The present study is one necessary step in the evaluation process of this protocol.

Material and methods

In January 2009, we prepared a management protocol for patient with periampullary cancer, including two parallel pathways, a diagnosis one and a preparation one. As for diagnosis, the golden standard was, and still is, the computer-tomography exam (CECT), which offers information on the local development of the tumor, mostly the involvement of the portal vein (PV), superior mesenteric vessels (SMA, SMV), inferior cava vein (ICV) or common hepatic artery (CHA), and the presence of the metastases (hepatic, peritoneal or pulmonary). In cases of doubt regarding vascular invasion, we perform an endoscopic ultrasound (EUS) exam. We consider a periampullary tumor to be unresectable if it invades arteries, if there are signs of venous thrombosis or if there are metastases.

In parallel, we prepare the patient for major surgery, correcting anemia (by blood transfusion until the hemoglobin levels exceeds 10 g/dl), hypoalbuminemia and liver status (if transaminases levels are more than five times normal, or bilirubin levels

are more than ten times normal, we perform a preoperative biliary shunt, either endoscopic, or laparoscopic). We use oral nutritional supplements as preoperative preparation, at least for 7 days if the total proteins or albumin serum levels are under 6 g/dl or 3.5 g/dl, respectively. During surgery, the most controversial topic was the pancreatic stump treatment, as the two most experienced surgeons treat it differently: pancreatico-gastro, respectively pancreatico-jejunostomy. It was decided to let the surgeon choose the modality, according to each case, as long as the stump is not simply closed (mostly, the surgeon preference and the local anatomy were the factors influencing this choice, not the consistence of the pancreas or the Wirsung diameter). We didn't use main pancreatic duct drainage, neither internal or external, to any patient. After surgery, the patient is admitted in ICU. Early mobilization and early oral feeding are encouraged. Enteral nutrition via jejunostomy is mandatory until nutritional status is satisfying and the patient can feed himself orally. Parenteral nutrition is use only if the enteral route is insufficient or cannot be utilize.

Between January 2009-December 2015, 298 PD were performed in Surgical Department of Regional Institute of Gastroenterology and Hepatology, University of Medicine and Pharmacy Cluj-Napoca, Romania. 168 (56.19%) of the patients were males and 131 (43.81%) were females, with ages between 22-84 (61±10.4). The data from all these patients were introduced in a prospective database, which also include the presence of co-morbid conditions (chronic obstructive pulmonary disease, hypertension, ischemic coronary disease, diabetes mellitus, renal insufficiency, obesity) and clinical characteristics (presenting symptoms, specific laboratory values). Postoperatively, the database was completed with ASA score, pancreatic texture, pancreatic duct size, pancreatic stump anastomosis, operative time, intraoperative blood loss, intraoperative transfusion needs.

For postoperative pancreatic fistula (POPF) we use the international study group (ISGPF) definition: a drain output of any measurable volume of fluid on or after postoperative day 3 with an amylase content greater than 3 times the serum amylase activity (Bassi et al 2005). A grade A fistula is considered when it has no clinical impact and implies no deviation in the normal postoperative pathway. A grade B POPF is associated with increased amylase level in the fluid from any drain and clinically relevant condition. The drains are left in place for more than 3 weeks or there may be a need to reposition the drains through imagistic ultrasound guided, or endoscopic means, in order to evacuate an intra-abdominal fluid collection. Grade C POPF involves organ failure or clinical instability leading to reoperation (Bassi et al 2005).

Delayed gastric emptying (DGE) represents the inability to return to a standard diet by the end of the first postoperative week and includes prolonged nasogastric intubation of the patient (Wente et al 2007).

Pancreatic stump bleeding is defined by two/parameters: onset and severity. The onset is either early (≤24 hours after the end of the operation; it is the consequence of a suboptimal hemostasis) or late (>24 hours). The severity of bleeding may be mild or severe (Wente et al 2007).

We consider two categories of risk factors for developing postoperative complications: preoperative ones (serum levels of hemoglobin, leucocytes, total proteins and albumin) and intraoperative ones (main pancreatic duct diameter, pancreatic texture, pancreatic stump treatment, blood loss, transfusion and surgical team experience).

The data were collected using Excel 2013 and for the statistical analysis we utilized R v3.2.4 statistical software. The Kolomogorov-Smirnov test was the first step in the process. Continuous data are presented as means ± standard deviation and were analyzed using the T-tests. Categorical data are presented as frequencies and were analyzed using the chi-square test. P values < 0.05 were considered statistically significant.

This study was approved by the Ethics Committee of the Regional Institute of Gastroenterology and Hepatology Cluj-Napoca. We have no conflict-of-interest to declare. All enrolled patients signed a typified informed consent paper.

Results

There were 168 men and 131 women, aged 61 ± 10.4 (range 22–84) years old. Malignant tumors accounted for 91.95% (274/298) of the cases and benign diseases accounted for 8.05% (24/298). Pathological examinations confirmed 139 periampullary tumors (ampullary carcinoma, distal common bile duct cancer and duodenal papillary carcinoma), 112 pancreatic ductal adenocarcinomas, 9 duodenal adenocarcinomas, 8 pancreatic neuroendocrine tumors, 6 malignant stromal tumors, 15 chronic pancreatitis, 3 pancreatic cystadenomas, 3 pancreatic solid pseudopapillary neoplasms, 3 islet cell adenomas. According to the AJCC 6th Edition TNM Staging System for pancreatic cancer (Bilimoria et al 2007), the cases were classified as: IA (7-6.25%), IB (10-9.82%), IIA (33-29.46%) and II B (62-55.36%). As for the non-pancreatic periampullary tumors, the seventh edition of the AJCC cancer staging manual (Edge 2010) was used. For ampullary carcinoma cases, 12.6% (11 patients) were in stage I, 52.8% (46 patients) in stage II and 34.6% (30 patients) in stage III. For distal cholangiocarcinoma cases, 12.8% (5 cases) were in stage I, 30.8% (12 cases) were in stage II, 20.5% (8 cases) were in stage III and 35.8% (14 cases) were in stage IVA.

The average length of hospital stay was 139±8.86 days.

According to Clavien-Dindo classification of surgical complications (Clavien et al 2009), there were 111grade I-II cases (43 wound infections, 34 DGE, 10 POPF, 10 biliary fistulas, 8 pancreatic stump bleeding, 5 intraperitoneal bleeding, one digestive fistula), 27 grade III-IV cases (12 pancreatic stump bleeding, 6 intraperitoneal bleeding, 5 POPF, 4biliary fistula) and 18 grade V cases (multiple system organ failure-MSOF following fistulas-12 pancreatic, 5 gastro-jejunotomy, one biliary). Also, there were 44 cases of general complications (pulmonary, cardiac, renal, hepatic).

Reoperation rate was 12.08% (10 bleeding cases, 26 cases of intraperitoneal abscesses or peritonitis following fistulas: 16 POPF, 5 biliary, 5 gastro-jejunostomy).

Of the 298 consecutive patients undergoing PD during the study period, 27 (9.06%) developed POPF, 61 (20.47%) presented DGE and 20 (6.71%) have been diagnosed with pancreatic stump bleeding. For each complication, the patients were classified into two groups: the group who experienced it and the group who did not.

There were 18 cases of MSOF following sepsis (12 POPF, 5 gastro-jejunostomy fistulas, one biliary fistula). We had a 6.04%

Table 1. Risk factors for POPF

	POPF group (n=27)	No POPF group (n=271)	P
Preop hemoglobin			
<12 g/dl (n=100)	7 (2.35%)	93 (31.21%)	0.38
>12 g/dl (n=198)	20 (6.71%)	178 (59.73%)	
Preop leucocytes			
<11.000 uL (n=44)	9 (3.02%)	35 (11.74%)	0.06
>11.000 uL (n=254)	18 (6.04%)	236 (79.19%)	
Preop total proteins			
<6 g/dL (n=43)	2 (0.67%)	41 (13.76%)	0.22
>6 g/dL (n=255)	25 (8.39%)	230 (77.18%)	
Preop albumin			
<3.5 g/dL (n=118)	13 (4.3%)	105 (35.23%)	0.34
>3.5 g/dL (n=180)	14 (4.7%)	166 (55.7%)	
Pancreatic stump			
Pancreatico-gastrostomy (PG) (n=250)	18 (6.04%)	232 (77.85%)	0.02
Pancreato-jejunostomy (PJ) (n=48)	9 (3.02%)	39 (13.09%)	
Pancreatic duct size			
<3mm (n=135)	12 (4.03%)	123 (41.28%)	0.93
>3mm (n=163)	15 (5.3%)	148 (49.66%)	
Pancreatic texture			
Soft (n=88)	9 (3.02%)	79 (26.51%)	0.05
Normal (n=99)	13 (4.3%)	86 (28.86%)	
Firm (n=111)	5 (1.68%)	106 (35.57%)	
Intraoperative blood loss (ml)	524.08 ±87.3	412 ±68.6	0.34
Intraoperative transfusions			
Yes (n=61)	8 (2.68%)	53 (17.79%)	0.14
No (n=237)	19 (6.38%)	218 (73.15%)	
Surgical experience			
16-50 PD (4 surgeons) (n=125)	8 (2.68%)	117 (39.26%)	0.72
>50 PD (2 surgeons) (n=173)	19 (6.38%)	154 (51.68%)	

mortality rate following surgical complications and a 4.03% POPF related mortality.

As for comparison, Bartos (2014) published a study including results after duodenopancreatectomies performed in the same surgical clinic between 1993-2008. It shows a progressive increasing number of PD, from 6.6/year (1993-1998) to 14.8/year (1998-2002) and 25.6/year (2003-2008), with a decreasing morbidity rate, from 53.1% (1993-1998) to 43.1% (1998-2002) and 33.9% (2003-2008). During 1993-2008, the incidence of POPF was 10%, 43% for delayed gastric emptying and 2% for bleeding from the pancreatic stump. The POPF related mortality rate was 9.1%.

Postoperative pancreatic fistula

As for POPF,10 cases were grade A, one was grade B and 16 cases were grade C. The grade A fistula did not influence the normal recovery pathway, being diagnosed mainly on day 4-5 after surgery, based on a high level amylase activity on an increasing drain output. All these patients benefit from somatostatin, added to their treatment. During the time they had the fistula, we re-inserted the nasogastric tube, we stopped the oral feeding, but we used the jejunostomy for enteral feeding and, in six cases with low albumin and protein profile, we associated parenteral nutrition. As soon as possible, these patients have resumed the oral nutrition. The grade A POPF did not significantly influence the hospital length of stay (15.2 days, p=0.1).

The patient with grade B fistula had an pancreatico-jejunal anastomosis and prolonged (more than 4 weeks) maintenance of a drainage tube. The drained liquid decreased after 10 days of somatostatin treatment, but re-increased during the following 10 days, so the somatostatin treatment was resumed for another 10 days. During this time, he was allowed to feed normally. The length of hospital duration for grade B POPF patient grew (34 days).

The patients with grade C fistula developed either a retro-gastric collection, or multiple intraperitoneal abscesses, or peritonitis. If the collection was retro-gastric, under 6 cm diameter and the pancreatic stump was viable, the endoscopic drainage was

Table 2: Risk factors for DGE

	DGE group (n=34)	No DGE group (n=264)	p
Preop hemoglobin			
<12 g/dl (n=100)	12 (4.02%)	88 (29.53%)	0.81
>12 g/dl (n=198)	22 (7.38%)	176 (59.06%)	
Preop leucocytes			
<11.000 uL (n=44)	27 (9.06%)	227(76.17%)	0.31
>11.000 uL (n=254)	7(2.34%)	37 (12.41%)	
Preop total proteins			
<6 g/dL (n=43)	8(2.68%)	35(11.74%)	0.11
>6 g/dL (n=255)	26 (8.72%)	229 (76.85%)	
Preop albumin			
<3.5 g/dL (n=118)	14 (4.7%)	104 (34.9%)	0.84
>3.5 g/dL (n=180)	20 (6.71%)	160 (53.69%)	
Pancreatic stump			
Pancreatico-gastrostomy (PG) (n=250)	29 (9.73%)	221 (74.16%)	0.05
Pancreato-jejunostomy (PJ) (n=48)	5 (1.68%)	43 (14.43%)	
Digestive anastomosis			
Duodeno-jejunoanastomy (n=38)	1(0.33%)	37 (12.42%)	0.03
Hoffmeister-Finsterer gastro-jejunostomy (n=201)	19 (6.38%)	182 (61.1%)	
Reichel-Polya gastro-jejunostomy (n=59)	10 (3.36%)	49 (16.44%)	
Antecolic/retrocolic assembly			
Antecolic gastro-jejunostomy (n=138)	16(5.37%)	122 (40.94%)	0.07
Retrocolic gastro-jejunostomy (n=160)	22 (7.38%)	138 (46.31%)	
Intraoperative blood loss (ml)	448.5 (±74.7)	418.8 (±69.8)	0.43
Intraoperative transfusions			
Yes (n=61)	10 (3.35%)	40 (13.42%)	0.016
No (n=237)	19 (6.38%)	229 (76.85%)	
Surgical time (minutes)	262.45 ±43.7	250.7 ±41.8	0.21
Surgical experience			
16-50 PD (4 surgeons) (n=125)	18 (6.04%)	107 (35.9%)	0.73
>50 PD (2 surgeons) (n=173)	24 (8.05%)	149 (50%)	

successfully performed (two cases). For the other 14 patients, re-laparotomy was needed. In 10 cases, total pancreatectomy was performed and for the other 4 patients, drainage of the infected collections was the choice. All grade C fistula patients were admitted in ICU. Due to septic shock, 12 (75%) of them died during hospitalization.

The risk factors for POPF considered in this study were statistically analyzed (see Table 1). Pancreatico-jejunostomy as the choice for pancreatic stump treatment and the soft texture of the pancreas significantly have favored the POPF.

Delay gastric emptying

Delay gastric emptying rate in our study was 20.47%. Almost half of the cases (27/61) developed the complication as a result of a fistula (21 POPF, 6 gastro-jejunostomy fistula).

For the rest of 34 cases, all of them grade I-II Clavien-Dindo complications, the pancreatico-gastrostomy, the gastro-jejunostomy following Whipple PD and the need for intraoperative transfusion were identified as risk factors (see Table 2).

Of all patients, pylorul-preserving pancreaticoduodenectomy (PPPD) was perform in 38 cases (12.75%), with only one patient (2.63%) developing DGE. Hoffmeister–Finsterer gastro-jejunal anastomosis was the choice for 201 patients, 19 (9.45%) presenting DGE and Reichel-Polya gastro-jejunostomy was preferred in 59 cases, 10 (16.95%) developing DGE. We found a significant difference between duodeno-jejunostomy and gastro-jejunostomy regarding DGE appearance (p=0.03).

Antecolic assembly was chosen for 138 (46.3%) patients, 16 (5,37%) presenting DGE, while for the rest of 160 cases with retrocolic gastro-jejunostomy, the rate of DGE was 13.75% (22 cases) (p=0.07).

In this group, DGE was a self-limiting complication, but involving prolonged hospital stay (up to 35 days), increased hospital costs (also due to prolonged enteral and parenteral nutrition), and low quality of life (most of them needing psychological

Table 3. Risk factors for pancreatic stump bleeding

	Pancreatic stump bleeding group (n=20)	No pancreatic stump bleeding group (n=278)	p
Preop hemoglobin			
<12 g/dl (n=100)	5 (1.68%)	95 (31.88%)	0.81
>12 g/dl (n=198)	15 (5.03%)	183 (61.41%)	
Preop leucocytes			
<11.000 uL (n=44)	2 (0.67%)	42 (14.09%)	0.41
>11.000 uL (n=254)	18 (6.04%)	236 (79.19%)	
Preop total proteins			
<6 g/dL (n=43)	2 (0.67%)	41 (13.76%)	0.42
>6 g/dL (n=255)	18 (6.04%)	237 (79.53%)	
Preop albumin			
<3.5 g/dL (n=118)	6 (2.01%)	112 (37.58%)	0.36
>3.5 g/dL (n=180)	14 (4.7%)	166 (55.7%)	
Pancreatic stump			
Pancreatico-gastrostomy (PG) (n=250)	18 (6.04%)	232 (77.85%)	0.34
Pancreato-jejunostomy (PJ) (n=48)	2 (0.67%)	46 (15.44%)	
Pancreatic duct size			
<3mm (n=135)	9 (3.02%)	126 (42.28%)	0.98
>3mm (n=163)	11 (3.69%)	152 (51.01%)	
Pancreatic texture			
Soft (n=88)	13 (4.36%)	75 (25.17%)	
Normal (n=99)	1 (0.34%)	98 (32.89%)	0.001
Firm (n=111)	6 (2.01%)	105 (35.23%)	
Intraoperative blood loss (ml)	462.5±77.1	419.24±69.9	0.37
Intraoperative transfusions			
Yes (n=61)	10 (3.36%)	40 (13.42%)	0.016
No (n=237)	10 (3.36%)	238 (79.87%)	
Surgical experience			
16-50 PD (4 surgeons) (n=125)	14 (4.7%)	111 (37.25%)	0.73
>50 PD (2 surgeons) (n=173)	14 (4.7%)	159 (53.36%)	

support or anxiolytics). As treatment we used intravenous prokinetics, serotonin antagonists (ondansetron) or motilin agonists (Erythromycin).

Pancreatic stump bleeding

Pancreatic stump bleeding occurred in 20 cases (6.71%). Eight of them were self-limiting, manifesting without hemodynamic consequence, being diagnosed based on the aspect of the nasogastric tube liquid (containing digested blood) and low decrease of hemoglobin level (less than 3 g/dl). For these patients, if the hemoglobin level dropped under 9 mg/dl, blood transfusion was indicated. The other 12 cases of pancreatic stump bleeding were classified as grade III-IV Clavien-Dindo complications. For 8 of them the hemorrhage was stopped by endoscopic approach, but 4 patients needed reoperation, due to endoscopic methods failure or profound hemodynamic instability. None of the patients with pancreatic stump bleeding died because of the hemorrhage. In our study, the soft texture of the pancreas and the intraoperative need for transfusion were identified as risk factors for this complication (see Table 3).

Discussion

Postoperative pancreatic fistula

Postoperative pancreatic fistula (POPF) involves extravasation of pancreatic enzymes outside the glandular ductal system into abdominal cavity, leading to peritonitis, abscesses, sepsis and even death. The reported rate of this complication varies between 10-32 % (Vin et al 2008; Faccioli et al 2012), without significant changes in the last two decades, despite numerous attempts: changes in surgical technique and modification of postoperative management. As technical modifications from Whipple operation, the most important were the pancreatico-jejunostomy using an isolated "Roux-en-Y" loop, the "duct-to-mucosa" alternative and the pancreatico-gastrostomy. None of them reduce the incidence of POPF, but neither increase it (Klaiber et al 2015; Hua et al 2015; Guerrini et al 2016; Javed et al 2015).

Also, some authors reported postoperative approaches aimed to reduce POPF. While the use of somatostatin (Sarr 2003; Wang et al 2013; Fernandez-Cruz et al 2013; Allen et al 2014) shows no benefit, Allen (2014) obtained a significant reduction in the rate of high grade POPF in 300 patients who received perioperative pasireotide (9 % vs. 21 %; p=0.006). In our Institute, we use somatostatin if there is a certified POPF.

The POPF rate in the present study was 9.06% (27 cases). Of them, 9 entailed only pancreatic juice, being pancreatico-jejunostomy fistulas, and 18 were complex fistula, with extravasation of pancreatic enzymes, bile and gastric juice, following pancreatico-gastrostomy. Although the fistula was more frequent after pancreatico-jejunostomy (9/48 versus 18/250, p=0.02), these cases had a much more favorable outcome. In this group, we have recorded 6 grade A fistula, one grade B and 2 grade C. The patients with grade C fistula needed re-laparotomy but for only one of them total pancreatectomy was decided. This patient died from septic shock.

In pancreatico-gastrostomy fistula group (18/250), there were 4 grade A and 14 grade C fistula. Two grade C fistulas were drained via endoscopic approach and 12 needed re-laparotomy (9 total pancreatectomy and 3 abscess drainage). Two patients with total pancreatectomy and one with abscess drainage survive the severe condition they were in.

In our study, the experience of the main surgeon did not favor POPF because all surgeons involved performed more than 40 PD during their career, being off the learning curve. The increased number of POPF in the most experienced surgeons group (>50 PD) is related to the preference of one of this surgeons for the pancreatico-jejunal anastomosis, a significant risk factor (p=0.02) for POPF.

The POPF related mortality rate in the study was 4.03% (12/298), without deaths in POPF grade A or B groups, but with a very high mortality in grade C POPF group, due to sepsis. POPF was the most common reason for reoperation and the most common cause for mortality following septic shock.

Delay gastric emptying

The incidence of DGE following PD in the literature rise up to 45% (Welsch et al 2010). In our study it was 20.47%, but almost half cases appeared after fistula, so their treatment was directly dependent by the treatment of the main complication. The same connection between DGE and POPF can be find in many literature reports (Malleo et al 2010; Parmar et al 2013; Hu et al 2014; Robinson et al 2015; Qu et al 2013).

We tried different methods to avoid DGE, like antecolic duodeno or antecolic gastro-jejunoanastomosis, and this complication rate decreased (from 43% to 13.3%) (Bartos et al 2014). In our study, the option for antecolic or retrocolic gastro/duodeno-jejunostomy did not influence the appearance of DGE (p=0.07). In a 2016 meta-analysis including 10 studies and 1067 patients undergoing pylorus-preserving pancreaticoduodenectomy (PPPD), Hanna (2016) demonstrated that antecolic duodeno-jejunostomy is significantly less associated with DGE. The same result can be found in Bell (2015) and Su (2012) reports. Regarding subtotal stomach-preserving PD (SSSPD), the most recent meta-analysis found no difference between antecolic and retrocolic gastro-jejunostomy as risk factor for developing DEG (Joliat et al 2016; Qian et al 2016). Imamura (2016) published a meta-analysis involving fourteen studies and 1969 patients undergoing either PPPD or SSSPD and concluded that antecolic reconstruction does not provide an advantage over retrocolic reconstruction regarding DGE.

We used the pancreatico-gastrostomy in 83.89% of all cases, due to the safety it offers regarding POPF, the most feared complication, but our analysis showed that it significantly raises the risk of DGE.

In our study, performing a PPPD significantly reduces the rate of DGE (p=0.03).

Statistically, DGE was the most frequent complication, and also the complication that constantly increased hospitalization duration and costs and had a very strong impact on the quality of life, because of the prolonged nasogastric tube usage. Also, it causes a delay of further important treatment, as it is the adjuvant chemotherapy. None of the patients included in our study who had experienced DGE without any other complication died.

Pancreatic stump bleeding

Pancreatic stump bleeding is part of so called "postpancreatectomy hemorrhage-PPH" complication, which also includes postoperative intra-abdominal bleeding, more often analyzed due to its connection to fistulas and intra-abdominal abscesses. Pancreatic stump bleeding is an independently complication, manifesting as an upper digestive hemorrhage.

Clerveus (2014), analyzing 1121 pancreaticoduodenectomies, found this complication to be more frequent in the pancreatico-gastrostomy group (562 cases). Wellner (2014) also reported pancreatico-gastrostomy as risk factor for postoperative intraluminal hemorrhage. Kapoor (2016) indicates the superior and inferior pancreatic arteries running along the superior and inferior borders of the pancreas as the main sources for this kind of hemorrhage.

In our study, the pancreatic stump bleeding depended a lot on the texture of the gland (the soft texture of the pancreas is significantly related to the postoperative hemorrhage) and intraoperative blood loss. To avoid the complication, we tried to knot the vessels from the pancreatic cutting line, instead of coagulating them. But it is difficult to knot these arteries localized in soft tissue, because when they are cut, they retract immediately in the parenchyma. Attempting to intercept them, we were forced to use sutures, which produced new lesions, augmenting the blood loss. But knotting is the best solution and also allows better protection for the main pancreatic duct. When during dissection we confront difficulties leading to important blood loss (usually by portal or SM veins injuries), we are forced to cut the pancreas in order to obtain access for correct hemostasis, without the same concern for pancreatic stump bleeding, much less important. After few minutes needed for vein suture, apparent pancreatic stump hemostasis is obtain by compression, not allowing to identify all bleeding sources, which can manifest postoperatively. The most frequent cause of pancreatic stump bleeding, seen on emergency upper digestive endoscopy, was the detachment of a small necrotic coagulated fragment including a vessel, mostly a small artery which was not properly knot during surgery. This situation occurred after a few days (more than 4 days), on a patient with a good outcome so far. Upper digestive endoscopy was the standard approach for hemostasis, using either clips, argon or constrictive agents. The success

rate of this method was 66.67% (8 cases). We do not found a connection between the presence of the pancreatic stump in the stomach and the bleeding, suggesting that the acid environment can lead to hemorrhage (PJ versus PG, p=0.34). None of the pancreatic stump bleeding group patients died.

This internal audit revealed some other important aspects. So, we consider the mandatory jejunostomy as one of the most important measures included in the protocol, especially because it allows enteral nutrition during fistula management. Also, because the texture of the pancreas can influence both the POPF and the pancreatic stump bleeding, we introduce the early pathological exam of the non-tumor pancreatic tissue as an important step in the postoperative management, impartially indicating the risk patients for developing these complications. The exam offers data about the normal pancreatic tissue on the cutting pancreatic line, assuming that the same morphological characteristics can be found on the pancreatic stump: grades of fibrosis, lipomatous atrophy, inflammatory infiltrate and necrosis; the presence of microscopic tumoral tissue or intravascular thrombosis). We try to adopt the ERAS principles for pancreatic surgery (Coolsen et al 2013), without compromising patient safety and outcomes: epidurals, early mobilization and oral intake, specific instructions for the use of surgical drains and nasogastric tubes (Porter et al 2000; Abu Hilal 2013).

Conclusion

By introducing the management protocol which includes preoperative measures regarding liver function, infections and nutritional status, we ameliorated the POPF rate (from 10% to 9.06%) and its mortality rate (from 9.1% to 4.03%). Thus, the statistical analysis reveals that preoperative hemoglobin, leucocytes, serum proteins and albumin, which had been corrected before surgery according to our protocol, are no longer statistically significant risk factors. Secondly, it shows that we are an homogeneous team, the experience of the main surgeon being no longer risk factor for any analyzed complications. Neither operating time influenced the patient outcome. There were six surgeons performing all these operations, each conducting more than 16 pancreaticoduodenectomies during 2009-2015. Thirdly, it points out where we still have problems to solve: the mortality rate following sepsis. The solutions might be earlier diagnosis and treatment of fistulas, including more often minimally invasive approach methods as imagistic or endoscopic drainage.

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