Chirurgia (2018) 113: 374-384
No. 3, May - June

http://dx.doi.org/10.21614/chirurgia.113.3.374

An Attempt to Build a National Prospective Electronic Database for Pancreaticoduodenectomies in Romania – Preliminary Results of the First Year Enrollment

Adrian Bartos[1], Mihnea Ionescu[2], Cornel Iancu[1], Cezar Stroescu[2,3], Florin Zaharie[1], Vladislav Brasoveanu[2], Nadim Al Hajjar[1], Catalin Vasilescu[2], Florin Graur[1], Ionut Hutanu[4], Lucian Mocan[1], Leonard David[2], Raluca Bodea[1], Dan Cacovean[2], Geza Molnar[1], Luminita Furcea[1], Sorin Alexandrescu[2], Emil Matei[2], Gabriel Mitulescu[2], Constantin Ungureanu[2], Aurel Tonea[2], Radu Zamfir[2], Irinel Popescu[2], Traian Dumitrascu[2]

[1]"Octavian Fodor" Regional Institute of Gastroenterology and Hepatology, 3rd Department of Surgery, Cluj-Napoca, Romania
[2]Fundeni Clinical Institute, "Dan Setlacec" Center of General Surgery and Liver Transplant, Bucharest, Romania
[3]Research and Liver Transplant Department of Surgery, St. Mary Hospital, Bucharest, Romania
[4]Regional Institute of Oncology, 1st Department of Surgery, Iassy, Romania

Corresponding author:
Traian Dumitrascu, MD
"Dan Setlacec" Center of General Surgery and Liver Transplant
Fundeni Clinical Institute
Fundeni Street no 258, 022328
Bucharest, Romania
E-mail: traian.dumitrascu@umfcd.ro

Received: 30.03.2018
Accepted: 28.04.2018

Rezumat

O încercare de a realiza un registru electronic prospectiv la nivel național în România pentru duodenopancreatectomia cefalică – rezultate preliminarii ale primului an de înrolare

Introducere: Constituirea de baze de date naționale pentru duodenopancreatectomiile cefalice (PD) a contribuit la îmbunătățirea rezultatelor postoperatorii după astfel de proceduri chirurgicale complexe deoarece colecția de date la nivel multicentric a permis analize mult mai pertinente, de o mai bună calitate, cu îmbunătățirea unor aspecte legate de tehnica chirurgicală şi îmbunătățirea rezultatelor postoperatorii. Situația actuală privind duodenopancreatectomia cefalică în România este puțin cunoscută deoarece nu exista până de curând o bază de date la nivel național. De aceea, în 2016 a fost creat un registru național electronic pentru PD deschis pentru toate centrele chirurgicale din țara noastră. Studiul îşi propune să prezinte rezultatele preliminarii ale acestui registru de PD la un an de la debut.
Pacienți & Metodă: Baza de date a fost deschisă începând cu data de 1 octombrie 2016. Datele au fost colectate prospectiv cu un formular online ce cuprinde 102 de întrebări pentru fiecare pacient. Registrul a fost deschis pentru toate secțiile de chirurgie din România, fără restricții.

Rezultate: În timpul primului an au fost introduse în registru datele a 181 pacienți cu PD realizate de un număr de 24 de chirurgi în 4 spitale. Vârsta medie a pacienților a fost de 64 de ani (28 – 81 ani), cu o ușoară preponderență a bărbaților (61,3%). Principala investigație imagistică preoperatorie a fost computer tomograful (84,5%). Abordul deschis a fost folosit în toate cazurile. Tehnica Whipple a fost utilizată într-un procent de 53%, iar rezecție venoasă s-a realizat în 14,3% din cazuri. Abordul posterior s-a utilizat în procent de 16,6%. Anastomoza pancreasului s-a realizat cu stomacul într-un procent de 50,1%. Timpul operator a fost de 285 min (110 – 615 min) iar pirderea de sânge (80 – 3000 ml). Rata globală a complicațiilor postoperatorii a fost de 55,8%, cu rata complicațiilor severe (gradul III-IV Dindo-Clavien) de 10% şi mortalitate intraspitalicească de 3,9%. Rata fistulei pancreatice, stazei gastrice şi hemoragiei postoperatorii a fost de 19,9%, 39,8% şi respectiv 15,5%. Principala indicație de PD a fost reprezentată de tumorile maligne periampulare (78,9%), cu neoplasmul pancreatic pe primul loc (48%).
Concluzii: Realizarea unui registru electronic prospectiv la nivel național în România pentru duodenopancreatectomiile cefalice pare să fie un proiect fezabil şi un intrument util în cunoaşterea practicii curente şi a rezultatelor postoperatorii după PD în țara noastră. Totuşi, sunt necesare îmbunătățiri în ceea ce priveşte atragerea mai multor secții de chirurgie în acest proiect.

Cuvinte cheie: duodenopancreatectomie cefalică, registru național, rezultate

Abstract
Introduction: National databases for pancreaticoduodenectomies (PD) have contributed to better postoperative outcomes after such complex surgical procedure because the multicentre collection of data allowed more reliable analyses with quality assessment and further improvement of technical issues and perioperative management. The current practice and outcomes after PD are poorly known in Romania because there was no national database for these patients. Thus, in 2016 a national-intent electronic registry for PD was proposed for all Romanian surgical centers. The study aims to present the preliminary results of this national-intent registry for PD after one-year enrollment.
Patients & Methods: The database was started on October 1st, 2016. Data were prospectively collected with an electronic online form including 102 items for each patient. The registry was opened to all the Departments of Surgery from Romania performing PD, with no restriction.
Results: During the first year of enrollment were collected the data of 181 patients with PD performed by 24 surgeons from four surgical centers. The age of patients was 64 years (28 – 81 years), with slightly male predominance (61.3%). Computed tomography was the main preoperative imaging investigation (84.5%). All the PDs were performed by an open approach. The Whipple technique was used in 53% of patients, and a venous resection was required in 14.3% of cases. A posterior approach PD was considered in 16.6% of patients. The stomach was used to treat the distal remnant pancreas in 50.1% of patients. The operative time was 285 min (110 – 615 min), and the estimated blood loss was 400 ml (80 – 3000 ml). The overall morbidity rate was 55.8%, with severe (i.e., grade III-IV Dindo-Clavien) morbidity rate of 10%, and 3.9% in-hospital mortality rate. The overall pancreatic fistula, delayed gastric emptying and hemorrhage rates were 19.9%, 39.8% and 15.5%. Periampullary malignancies were the main indications for PD (78.9%), with pancreatic cancer on the top (48%).
Conclusions: To build a prospective electronic online database for PD in Romania appears to be a feasible project and a useful tool to know the current practice and outcomes after PD in our country. However, improvements are still required to encourage a larger number of surgical centers to introduce the data of patients with PD.

Key words: pancreaticoduodenectomy, national registry, outcomes

Introduction

Pancreaticoduodenectomy (PD) is a complex surgical procedure used to treat mainly periampullary malignancies (1, 2). It is the merit of Kausch and Whipple to introduce in clinical practice this procedure (3, 4) and, since then, several modifications of the resection or reconstructive technique have been proposed to improve outcomes after PD (2, 5). The very high mortality rates of PD reported in the times of Kausch and Whipple (6) have determined the surgeons to be reluctant to this procedure for a long period. However, mortality rates have dramatically decreased in the early 80's in some surgical centers with high case-load PD (7). Nowadays, in high-volume centers, the mortality rates after PD decreased from more than 25% to around or even less than 5% (7).

National databases for pancreatic resections have contributed to better outcomes after such complex surgical procedure because the multicentre collection of data allowed more reliable analyses with quality assessment and further improvement of technical issues and perioperative management (8-13). In Europe it is worth to mention at least three successful registries for pancreatic resections, assessing the current practice and postoperative outcomes: in Germany (13), Holland (12) and France (8).

The current practice and outcomes after pancreatic resections are poorly known in Romania because there was no national database for these patients. Thus, in 2016 a national-intent electronic registry for PD was proposed for all Romanian surgical centers to better assess the current practice and outcomes of this complex surgical procedure in Romania. Furthermore, the proposed registry of PD was thought to build a larger database for studies and scientific papers. Based on the data provided by this national registry, there is a potential to recommend guidelines for clinical practice. Noteworthy, several Romanian surgical centers have previously reported their technique and outcomes of PD (1, 14-20).

The study aims to present the preliminary results of this national-intent registry for PD after one-year enrollment.

Patients and Methods

Starting with October 1st, 2016 a prospective online electronic database was established for PD at the initiative of "Octavian Fodor" Regional Institute of Gastroenterology and Hepatology, 3rd Department of Surgery, Cluj-Napoca (Cornel Iancu, Adrian Bartos) and Fundeni Clinical Institute, "Dan Setlacec" Center of General Surgery and Liver Transplant, Bucharest (Irinel Popescu, Traian Dumitrascu). Patients with total pancreatectomies were excluded from the present analyses. The registry was opened to all the Departments of Surgery from Romania performing PD, with no restriction.

The online form included pre-, intra- and postoperative data, with a total number of 102 items. Thus, the form included demographics data (12 items), medical history data (12 items), preoperative clinical data (16 items), preoperative bioumoral data (18 items), intraoperative data (26 items), postoperative data (16 items) and pathology data (2 items). The bioumoral data were considered the most recent values close to the time of surgery but no more than one week before pancreatic resection.

The data were prospectively collected and introduced by each operative team at the time of discharge of the patient from the hospital. Thus, the postoperative morbidity and mortality were assessed as in-hospital complications and deaths. The pathological data were collected afterward when available.

The severity of postoperative complications was graded according to Dindo-Clavien classification (21). Furthermore, for specific complications such postoperative pancreatic fistula (22), delayed gastric emptying (23) and postoperative hemorrhage (24) the International Study Group of Pancreatic Surgery definitions and grading system were used.

All data of patients included in the electronic database till October 1st, 2017 was analyzed.

Data are expressed as median (range) or as number (percentage).

Results

During the first year of enrollment, the data of 181 patients with PD were collected. The patients were operated in four surgical centers from Bucharest (2 centers), Cluj-Napoca (1 center) and Iassy (1 center). The PDs were performed by a total number of 24 surgeons.

Demographics and Medical History Data

In the present cohort, the age of patients was 64 years (28 – 81 years), with slightly male predominance (111 patients – 61.3%), and a body mass index of 25.7 kg/m^2 (17.9 – 43.6 kg/ m^2). Smoking was reported in 68 patients (37.6%), while alcohol abuse was observed in 58 patients (32%).

In the present cohort, 10 patients (5.5%) have had previous malignant diseases, 6 patients (3.3%) presented hepatitis B or C viruses, 108 patients (59.7%) have had cardiovascular co-morbidities, and 39 patients (21.5%) have had diabetes mellitus.

Preoperative clinical and bioumoral data

The following clinical signs and symptoms were observed in the present cohort: jaundice at the time of resection (79 patients – 43.6%), cholangitis (27 patients – 14.9%), weight loss (126 patients – 69.6%), upper digestive stenosis (13 patients – 7.2%), abdominal pain (119 patients – 65.7%) and upper digestive hemorrhage (6 patients – 3.3%).

A preoperative biliary drainage was performed in 80 patients (44.2%) by endoscopic (59 patients – 32.6%), surgical approach (20 patients – 11%) or interventional radiology (1 patient – 0.6%).

Preoperative imaging investigations included computed tomography in 153 patients (84.5%), magnetic resonance in 45 patients (24.9%), endoscopic ultrasound examination in 61 patients (33.7%) and endoscopic cholangiopancreato-graphy in 60 patients (33.1%).

The American Society of Anesthesiologists score was 1 in 8 patients (4.4%), 2 in 81 patients (44.8%), 3 in 86 patients (47.5%) and 4 in 6 patients (3.3%).

The following preoperative bioumoral values were observed in the present cohort: hemoglobin serum level – 12.8 g/ dl (5.9 – 16.7 g/ dl), total bilirubin serum level – 1.9 mg/ dl (0.2 – 26 mg/ dl), serum glucose level – 110 mg / dl (63 – 397 mg/ dl), serum amylase level – 65 U/ L (6 – 715 U/ L), serum lipase level – 59 U/ L (6 – 3358 U/ L), serum urea level – 35 mg/ dl (8 – 130 mg/ dl) and CA 19-9 serum level – 65 UI/ ml (0.5 – 5300 UI/ ml).

Operative Data

Most PDs were performed in an elective setting (178 patients – 98.3%). The PDs in an emergency were performed for massive acute upper digestive hemorrhage in 2 patients (1.2%) and for trauma in 1 patient (0.6%). The types of PDs performed in the present series are shown in *Fig. 1.*

Resection of the portal vein/ superior mesenteric vein was performed in 26 patients (14.3%): segmental resection in 13 patients (7.2%) and wedge resection in 13 patients (7.2%). In the group of patients with segmental venous resection, the reconstruction was made by end-to-end direct anastomosis in 9 patients (69.2%), while a graft was used in only 4 patients (30.8%).

Resection of the superior mesenteric artery was performed in 3 patients (1.8%): 2 patients (1.2%) with wedge resection and 1 patient (0.6%) with segmental resection and graft interposition reconstruction.

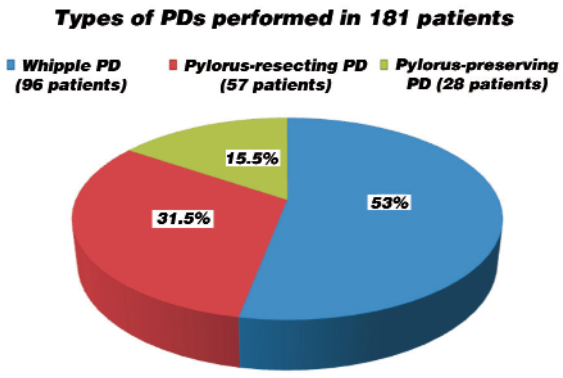

Figure 1. Types of pancreaticoduodenectomies performed in 181 patients

A posterior approach was used in 30 patients (16.6%) with PD (*Fig. 2*) and associated surgical procedures were required in 29 patients (16%).

For treatment of distal remnant pancreatic stump, the jejunum was used in 89 patients (49.1%), while the stomach was used in 91 patients (50.1%), as shown in *Figs. 3* and *4*.

The gastro/duodeno-jejunal anastomosis was performed in the antecolic manner in 104 patients (57.4%) while in 77 patients (42.6%) the transmesocolic approach was preferred.

A stent was used for pancreatico-digestive anastomosis in 59 patients (32.6%): internal lost stent (41 patients – 22.7%) or external stent (18 patients – 9.9%). The diameter of Wirsung duct was 4 mm (1 – 11 mm), and the texture of pancreas was soft in 87 patients (48%).

The operative time was 285 min (110 – 615 min), and the estimated blood loss was 400 ml (80 – 3000 ml). A number of 66 patients (36.5%) required per-operative blood transfusions.

All the PDs were performed by an open approach. Octreotide was administrated at the time of resection and postoperatively for at least 5 days in 106 patients (58.6%).

Postoperative Outcomes and Pathology Data

A number of 101 patients (55.8%) developed complications after PD. Stratification of complications according to the Dindo-Clavien classification is shown in *Fig. 5*.

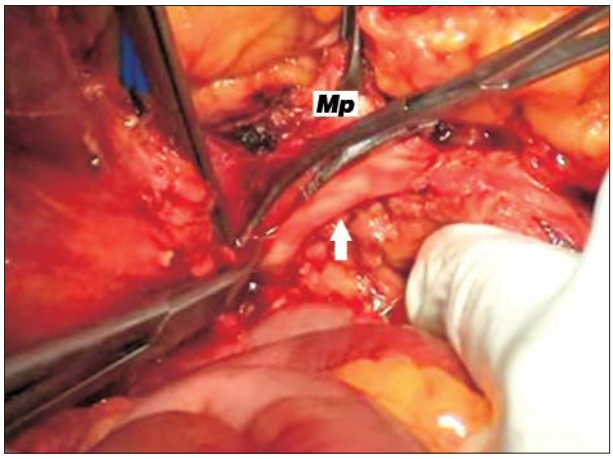

Figure 2. Posterior approach pancreaticoduodenectomy – intraoperative aspects (the white arrow marks the superior mesenteric artery; Mp – mesopancreas)

Specific postpancreatectomy complications rates are shown in *Fig. 6*. Thus, postoperative pancreatic fistulae were assessed as grade A (10 patients – 5.5%), grade B (21 patients – 11.6%) and grade C (5 patients – 2.8%). Postoperative delayed gastric emptying was assessed as grade A (49 patients – 27.1%), grade B (20 patients – 11%) and grade C (3 patients – 1.7%). Postpancreatectomy hemorrhage was assessed as grade A (10 patients – 5.5%), grade B (13 patients – 7.2%) and grade C (5 patients – 2.8%).

Other types of complications were observed in 41 patients (22.7%).

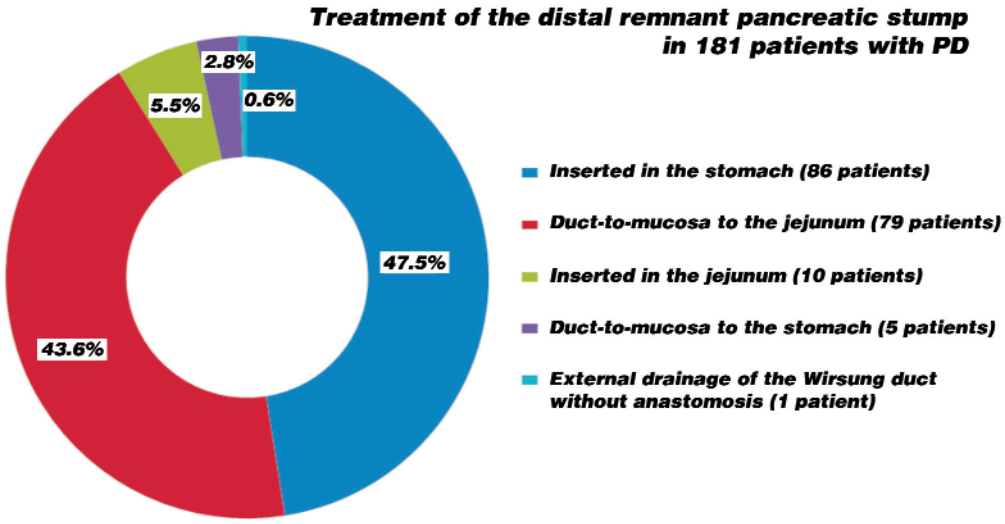

Figure 3. Treatment of the distal remnant pancreatic stump in 181 patients with pancreaticoduodenectomies

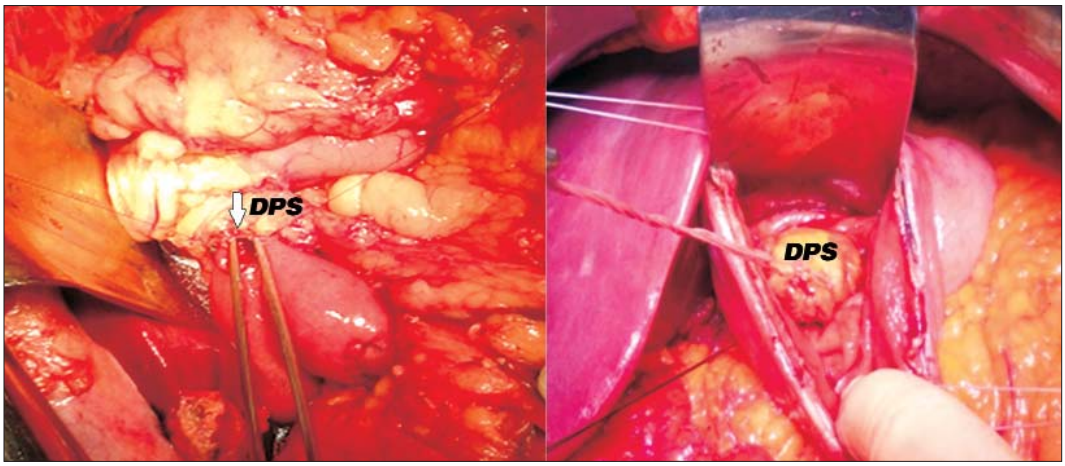

Figure 4. Intraoperative aspects of (a) duct-to-mucosa Wirsungo-jejunostomy (the white arrow marks the Wirsung duct) and (b) insertion of the distal remnant pancreatic stump (DPS) in the stomach

Re-laparotomies for postoperative complications after PD were reported in 13 patients (7.2%).

Grade V complications (i.e., in-hospital postoperative death) were observed in 7 patients (3.9%): 1 death in an emergency PD and 6 deaths in the elective PD group. Thus, the in-hospital mortality for emergency PD was 33.3% while for elective PDs the mortality was 3.4%. The cause of death was multiple organ failures in all patients.

The postoperative hospital stay was 13 days (5 – 123 days). The final pathology examination of the operative specimens is shown in *Fig. 7*.

Discussion

This is the first attempt to assess the current practice and outcomes after PD at a national level in Romania, based on a national-intent prospective online electronic database. It is worth to mention that this database included PDs performed in both low and high-volume centers, by both low and high case-load surgeons and the cohort characteristics (i.e., sex, age, body mass index, co-morbidities, pancreas texture and Wirsung duct size, operative time

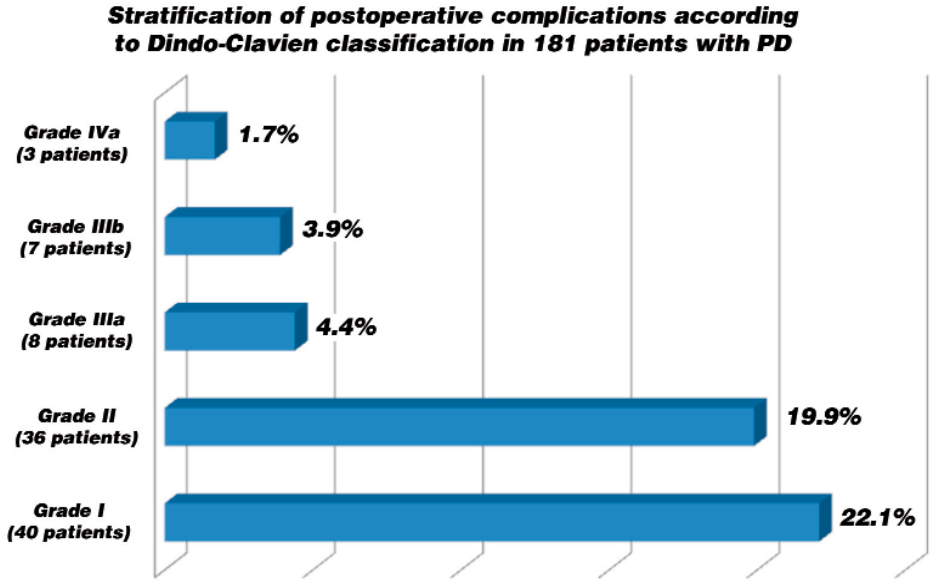

Figure 5. Stratification of postoperative complications according to the Dindo-Clavien classification in 181 patients with pancreaticoduodenectomies

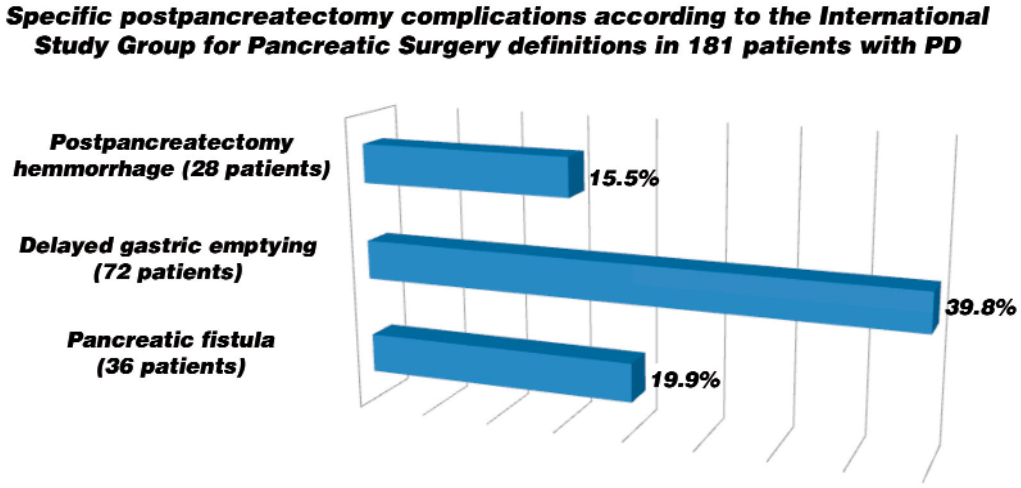

Figure 6. Specific postpancreatectomy complications according to the International Study Group for Pancreatic Surgery definitions in 181 patients with pancreaticoduodenectomies

and blood loss, overall, specific postpancreatectomy and severe morbidity rates, pathology) are quite similar to those reported in other recent large series of PDs (25-27).

Centralization of pancreatic surgery in high-volume centers has been associated with improved outcomes, lower mortality rates, and better survivals, particularly for patients with pancreatic cancer (28, 29). Besides the importance of high-volume centers, the surgeon caseload has a significant impact on postoperative mortality after PD (30, 31). Thus, surgeons with more than 21 PD/ year have reported mortality rates of less than 2% (30). Moreover, it appears that there are no differences of in-hospital mortality for low-volume surgeons at low-volume or high-volume hospitals (31).

Mortality after PD has been traditionally assessed as in-hospital or 30-day mortality. However, recent studies have shown that 90-day mortality reflects more accurately the deaths rates after PD (32). Thus, 90-day mortality rates after PD are double compared with 30-day mortality rates (7.4% vs. 3.7%), being the lowest in hospitals with ≥ 40 PD/ year (32). Thus, the average 90-day mortality rate in

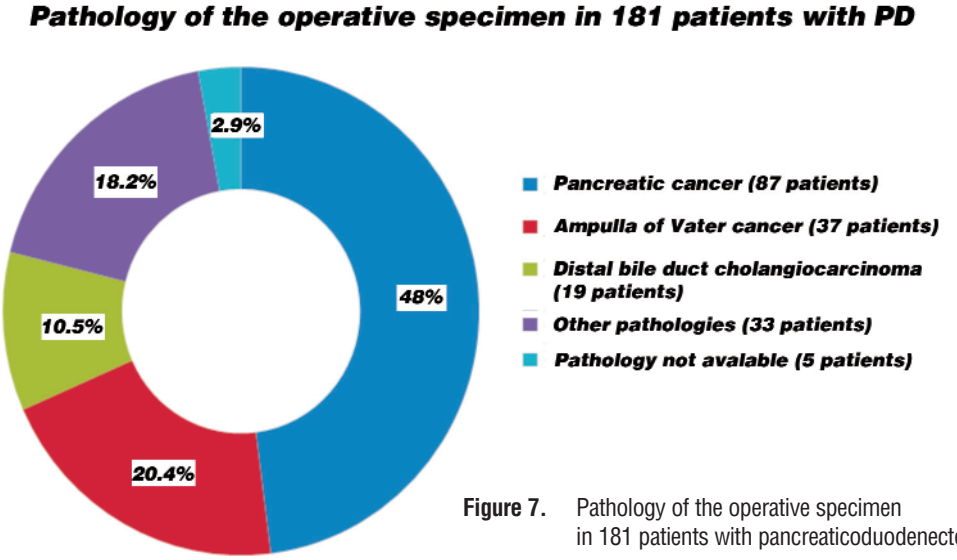

Figure 7. Pathology of the operative specimen in 181 patients with pancreaticoduodenectomies

hospitals with ≥ 40 PD/ year is 8%, compared with 14.2% in hospitals with less than 5 PD/ year (32). In the present cohort, the in-hospital mortality rate was 3.4% for elective PDs.

Several issues about the practice and outcomes in this series of patients with PD should be discussed.

Biliary drainage before PD was performed in an important percentage of patients from the present cohort (44.2%), mainly by endoscopic approach. The indications and benefits of biliary drainage before PD remain controversial because sometimes procedure-related complications might occur and have a detrimental effect on outcomes after PD. Infectious complications after PD appears to be significantly higher when preoperative biliary drainage is performed (25). Recent meta-analyses have suggested that no preoperative drainage may be the best approach for patients with jaundice submitted to PD (33) and, if biliary drainage is however required, it is better to do it by a percutaneous approach (34). Thus, although there are no significant differences of severe morbidity, mortality, postoperative pancreatic fistula and infectious complications rates after PD in patients with percutaneous biliary drainage before PD compared with endoscopic stenting, however, procedure-related and overall post PD complications rates are significantly lower when percutaneous biliary drainage is performed (34). A recent review has shown that routine preoperative biliary drainage in patients submitted for PD should be avoided because it might be harmful, except in a subset of patients (debilitating pruritus, extensive preoperative work-up, signs of cholangitis or systemic infection with impaired renal function or other organ dysfunctions, neoadjuvant therapy, surgery not available in a reasonable period) (35).

Surprisingly in the present cohort of patients with PD, the Whipple procedure was the most frequently used (53% of PDs). The Whipple procedure was the standard approach for PD for many years (2, 36). However, pylorus-preserving PD was introduced to prevent post-antrectomy dumping syndrome and to better preserve on the long-term outcome the nutritional status of these patients, and gained wide acceptance today (36). The main drawback of a pylorus-preserving PD is the increased postoperative delayed gastric emptying rates, which is the most frequently reported complication after PD (36). The results provided by current literature are inconclusive whether delayed gastric emptying rates are significantly different between the Whipple and pylorus-preserving PD (36). Furthermore, to overcome both drawbacks of antrectomy and pylorus preservation, more recently, the pylorus-resecting PD was proposed (36). Initially, the pylorus-resecting PD appears to have significantly reduced delayed gastric emptying rates compared with pylorus-preserving PD; however, more recent data have shown no significant differences between the two surgical techniques (36). In the present cohort, a pylorus-resecting PD was performed in 31.5% of patients while a pylorus-preserving PD was performed in only 15.5% of cases.

A portal vein/ superior mesenteric vein resection can be safely performed with PD. However, our previous studies have shown that portal vein/ superior mesenteric vein resection during PD for pancreatic cancer has been associated with trends of increased mortality and morbidity rates, albeit statistical significance was not reached (17). As expected, both the operative time and blood loss were significantly higher when a venous resection was associated with PD (17). More recent data on larger number of patients have confirmed that increased morbidity and mortality rates should be expected when a venous resection is associated with PD (37). In the present cohort, a portal vein/ superior mesenteric vein resection was performed in 14.3% of PDs. Nevertheless, arterial resections during PD have been demonstrated as safe and feasible (38), but the oncological benefits remains controversial.

Posterior approach PD with total mesopancreas excision has emerged as a technical refinement to better resect periampullary malignancies (5, 39), and the results of this approach have been recently extensively explored (40). Furthermore, several other techniques grouped as "artery-first" PD were proposed (41). A posterior approach with total mesopancreas excision has become the standard approach for PD in some

surgical centers (42), but the survival benefits of this approach in patients with PD for pancreatic cancer remains unclear (39, 43, 44).

Regarding the treatment of distal remnant pancreatic stump, over the years there were proposed a large number of technical solutions, as a recent review has highlighted (45). Studies comparing pancreatico-gastrostomy with pancreatico-jejunostomy reached conflicting results. There is a meta-analysis of the randomized trials that has suggested a slightly superiority of pancreatico-gastrostomy over pancreatico-jejunostomy in the prevention of clinically relevant postoperative pancreatic fistula after PD (46). However, a recent Cochrane review has shown that there is no reliable data to support the use of jejunum instead of the stomach for distal remnant pancreas after PD (47). Recent meta-analyses or randomized trials have shown no significant differences for outcomes after PD between duct-to-mucosa and dunking/invagination techniques for pancreatico-jejunostomy (48, 49). Thus, one might conclude that there is no standard technique to treat the distal remnant pancreatic stump after PD and the approach should be tailored to patients' profile (45).

The use of stents for Wirsung duct during PD remains a matter of debate. A recent meta-analysis did not find any significant differences in pancreatic fistula, delayed gastric emptying, intra-abdominal fluid collections, hemorrhage or overall mortality rates between internal and external stents during PD(50). However, it appears that external stents are associated with significantly reduced rates for clinically relevant postoperative pancreatic fistula and severe morbidity after PD in high-risk patients, compared with patients with no stents (51).

Regarding the gastro/duodenojejunostomy after PD, recent meta-analyses have shown that stapled anastomosis is associated with significantly decreased delayed gastric emptying rates compared with hand-sewn anastomosis at the expense of higher bleeding rates (52), but there are no differences of outcomes between antecolic and retrocolic reconstruction (53).

The present database has collected several particular data. Thus, collection of data about the presence/ absence of hepatitis viruses have been proposed to further explore the potential effect of such viruses on clinical, pathological and outcomes in patients with PD for periampullary malignancies starting from our previous research suggesting that there might be some influences of hepatitis viruses on clinical and pathological features particularly for patients with pancreatic cancer (54) as it was shown for hepatocellular carcinoma (55). Furthermore, the elective or emergency indication for PD was also pointed out because, although a PD in an emergency setting is feasible (56), it is widely accepted to be associated with very high mortality rates (around 34.7%) even in high-volume centers (57). In the present series, there was one postoperative death out of the 3 patients with emergency PD (mortality rate of 33.3%), but the cause of death was not related to pancreatic surgery complications.

Future perspectives for the Romanian national registry of PD are to collect more patients with PD, involving other surgical centers, to develop infrastructure and gain financial support, along with strong cooperation with national and international surgical societies. The timely analysis of the collected data has the potential to improve outcomes after PD with better selection of patients who would fit for this complex surgical procedure.

The present study has some limitations. The accuracy of information provided in the database is based on the honesty of surgeons who introduce the data. Thus, it might be a tendency to underestimate particularly the postoperative complications rates and severity. Furthermore, the introduction of data for all consecutive PD performed in the analyzed period was verified in only two out of four surgical centers. Thus, both mortality and morbidity rates might not reflect the reality since some surgeons might be reluctant to introduce in the database the patients with unfavorable postoperative outcomes.

Conclusions

To build a prospective electronic online database for PD in Romania appears to be a feasible project and a useful tool to know the current practice and outcomes after PD in our country.

However, improvements are still required to encourage a larger number of surgical centers to introduce the data of patients with PD.

Funding and conflict of interests: none

Acknowledgments

Several data from the present manuscript were presented at the Romanian National Conference of Surgery (October 4th - 7th, 2017, Iassy, Romania).

References

1. Bartos A, Bartos D, Al-Hajjar N, Puia C, Munteanu D, Bodea R, et al. Risk factors for complications after duodenopancreatectomy. Initial results after implementing a standardized perioperative protocol. Chirurgia (Bucur) 2014;109(3):318-24.
2. Popescu I, Dumitrascu T. [Pancreatoduodenectomy-past, present and future]. Chirurgia (Bucur) 2011;106(3):287-96.
3. Rosenberg R. Partielle Duodenopankreatektomie. Chirurg 2004;75: 828-9.
4. Whipple AO, Parsons WB, Mullins CR. Tratment of carcinoma of the ampulla of Vater. Ann Surg 1935;102(4):763-79.
5. Popescu I, Dumitrascu T. Total meso-pancreas excision: key point of resection in pancreatic head adenocarcinoma. Hepatogastroenterology 2011;58(105):202-7.
6. Whipple AO. The rationale of radical surgery for cancer of the pancreas and ampullary region. Ann Surg 1941;114(4):612-5.
7. Garcea G, Dennison AR, Pattenden CJ, Neal CP, Sutton CD, Berry DP. Survival following curative resection for pancreatic ductal adenocarcinoma. A systematic review of the literature. JOP 2008; 9(2):99-132.
8. Farges O, Bendersky N, Truant S, Delpero JR, Pruvot FR, Sauvanet A. The Theory and Practice of Pancreatic Surgery in France. Ann Surg 2017;266(5):797-804.
9. Hallet J, Mahar AL, Tsang ME, Lin Y, Callum J, Coburn NG, et al. The impact of peri-operative blood transfusions on post-pancreatectomy short-term outcomes: an analysis from the American College of Surgeons National Surgical Quality Improvement Program. HPB (Oxford) 2015;17(11):975-82.
10. Healy MA, Krell RW, Abdelsattar ZM, McCahill LE, Kwon D, Frankel TL, et al. Pancreatic Resection Results in a Statewide Surgical Collaborative. Ann Surg Oncol 2015;22(8):2468-74.
11. Nayar P, Chandak A, Gupta N, Yu F, Qiu F, Ganti AK, et al. Postoperative mortality following multi-modality therapy for pancreatic cancer: Analysis of the SEER-Medicare data. J Surg Oncol 2017;115(2):158-63.
12. van Rijssen LB, Koerkamp BG, Zwart MJ, Bonsing BA, Bosscha K, van Dam RM, et al. Nationwide prospective audit of pancreatic surgery: design, accuracy, and outcomes of the Dutch Pancreatic Cancer Audit. HPB (Oxford) 2017;19(10):919-26.
13. Wellner UF, Klinger C, Lehmann K, Buhr H, Neugebauer E, Keck T. The pancreatic surgery registry (StuDoQ|Pancreas) of the German Society for General and Visceral Surgery (DGAV) - presentation and systematic quality evaluation. Trials 2017;18(1):163.
14. Bud V, Copotoiu C, Coros F, Budisca O, Serba N. [Pancreatic fistula after cephalic duodenopancreatectomy. Its incidence, significance and therapeutic characteristics]. Chirurgia (Bucur) 1998;93(1):23-6.
15. Costea I, Glod M, Terinte R, Chiriac R, Bulimar V, Grigorovici M, et al. [Pancreaticoduodenectomy in surgical treatment of malignant tumors of Vater's region]. Chirurgia (Bucur) 2011;106(6):815-24.
16. Cretu OM, Hut EF, Dan RG, Sima LV, Blidisel CIA, Lighezan DF, et al. Modified Whipple-Child pancreaticoduodenectomy with anastomosis on jejunal loop in continuity. Presentation of surgical technique and preliminary observations on 45 patients. Rom J Morphol Embryol 2017;58(4):1295-9.
17. Dumitrascu T, Dima S, Brasoveanu V, Stroescu C, Herlea V, Moldovan S, et al. Impact of a portal/superior mesenteric vein resection during pancreatico-duodenectomy for pancreatic head adenocarcinoma. Minerva Chir 2014;69(6):301-13.
18. Georgescu S, Ursulescu C, Grigorean VT, Lupascu C. Hind right approach pancreaticoduodenectomy: from skill to indications. Gastroenterol Res Pract 2014;2014:210835.
19. Moldovanu R, Grecu F, Tarcoveanu E, Georgescu S, Scripcariu V, Niculescu D, et al. [Pancreaticoduodenectomy for pancreatic head cancer, 54 cases]. Rev Med Chir Soc Med Nat Iasi 2007;111(2): 402-15.
20. Valcea S, Beuran M, Vartic M. Intraluminal Postpancreatoduodenectomy Hemorrhage - Last 5 Years Experience. Chirurgia (Bucur) 2017;112(1): 39-45.
21. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240(2):205-13.
22. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery 2005;138(1):8-13.
23. Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR, et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery 2007;142(5):761-8.
24. Wente MN, Veit JA, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, et al. Postpancreatectomy hemorrhage (PPH): an International Study Group of Pancreatic Surgery (ISGPS) definition. Surgery 2007; 142(1):20-5.
25. De Pastena M, Paiella S, Marchegiani G, Malleo G, Ciprani D, Gasparini C, et al. Postoperative infections represent a major determinant of outcome after pancreaticoduodenectomy: Results from a high-volume center. Surgery 2017;162(4):792-801.
26. El Nakeeb A, Askar W, Atef E, Hanafy EE, Sultan AM, Salah T, et al. Trends and outcomes of pancreaticoduodenectomy for periampullary tumors: A 25-year single-center study of 1000 consecutive cases. World J Gastroenterol 2017;23(38):7025-36.
27. Kowalsky SJ, Zenati MS, Steve J, Lee KK, Hogg ME, Zeh HJ, III, et al. Ketorolac use may increase risk of postoperative pancreatic fistula after pancreaticoduodenectomy. J Surg Res 2018;221:43-8.
28. Gooiker GA, van GW, Wouters MW, Post PN, van de Velde CJ, Tollenaar RA. Systematic review and meta-analysis of the volume-outcome relationship in pancreatic surgery. Br J Surg 2011;98(4): 485-94.
29. Gooiker GA, Lemmens VE, Besselink MG, Busch OR, Bonsing BA, Molenaar IQ, et al. Impact of centralization of pancreatic cancer surgery on resection rates and survival. Br J Surg 2014;101(8): 1000-5.
30. Eppsteiner RW, Csikesz NG, McPhee JT, Tseng JF, Shah SA. Surgeon volume impacts hospital mortality for pancreatic resection. Ann Surg 2009;249(4):635-40.
31. Mathur A, Luberice K, Ross S, Choung E, Rosemurgy A. Pancreaticoduodenectomy at High-volume Centers: Surgeon Volume Goes Beyond the Leapfrog Criteria. Ann Surg 2015; 262(2):e37-e39.
32. Swanson RS, Pezzi CM, Mallin K, Loomis AM, Winchester DP. The 90-day mortality after pancreatectomy for cancer is double the 30-day mortality: more than 20,000 resections from the national cancer data base. Ann Surg Oncol 2014;21(13):4059-67.
33. Lee PJ, Podugu A, Wu D, Lee AC, Stevens T, Windsor JA. Preoperative biliary drainage in resectable pancreatic cancer: a systematic review and network meta-analysis. HPB (Oxford) 2018 Mar 8. pii: S1365-

182X(17)31194-2. doi: 10.1016/j.hpb.2017.12.007
34. Dorcaratto D, Hogan NM, Munoz E, Garces M, Limongelli P, Sabater L, et al. Is Percutaneous Transhepatic Biliary Drainage Better than Endoscopic Drainage in the Management of Jaundiced Patients Awaiting Pancreaticoduodenectomy? A Systematic Review and Meta-analysis. J Vasc Interv Radiol 2018 Mar 13. pii: S1051-0443(18)30766-8. doi: 10.1016/j.jvir.2017.12.027
35. Gholami S, Brennan MF. Preoperative Stenting for Benign and Malignant Periampullary Diseases: Unnecessary if Not Harmful. Surg Clin North Am 2018;98(1):37-47.
36. Klaiber U, Probst P, Buchler MW, Hackert T. Pylorus preservation pancreatectomy or not. Transl Gastroenterol Hepatol 2017;2:100.
37. Kantor O, Talamonti MS, Wang CH, Roggin KK, Bentrem DJ, Winchester DJ, et al. The extent of vascular resection is associated with perioperative outcome in patients undergoing pancreaticoduodenectomy. HPB (Oxford) 2018;20(2):140-6.
38. Brasoveanu V, Dumitrascu T, Bacalbasa N, Zamfir R. Splenic artery used for replaced common hepatic artery reconstruction during pancreatoduodenectomy--a case report. Chirurgia (Bucur) 2009; 104(4):499-504.
39. Dumitrascu T, David L, Popescu I. Posterior versus standard approach in pancreatoduodenectomy: a case-match study. Langenbecks Arch Surg 2010;395(6):677-84.
40. Negoi I, Hostiuc S, Runcanu A, Negoi RI, Beuran M. Superior mesenteric artery first approach versus standard pancreaticoduodenectomy: a systematic review and meta-analysis. Hepatobiliary Pancreat Dis Int 2017;16(2):127-38.
41. Sanjay P, Takaori K, Govil S, Shrikhande SV, Windsor JA. 'Artery-first' approaches to pancreatoduodenectomy. Br J Surg 2012;99(8): 1027-35.
42. Adham M, Singhirunnusorn J. Surgical technique and results of total mesopancreas excision (TMpE) in pancreatic tumors. Eur J Surg Oncol 2012;38(4):340-5.
43. Dumitrascu T, Popescu I. Posterior approach pancreaticoduodenectomy: does it really improve long-term survival in pancreatic head cancer? JOP 2011;12(5):491-2.
44. Dumitrascu T, Popescu I. Total mesopancreas excision in pancreatic head adenocarcinoma: The same impact as total mesorectal excision in rectal carcinoma? Comment on article "surgical technique and results of total mesopancreas excision in pancreatic tumours" by Adham M and Singhirunnusorn J, Eur J Surg Oncol, 2012. Eur J Surg Oncol 2012;38(8):725.
45. Xu J, Ji SR, Zhang B, Ni QX, Yu XJ. Strategies for pancreatic anastomosis after pancreaticoduodenectomy: What really matters? Hepatobiliary Pancreat Dis Int 2018;17(1):22-6.
46. Ricci C, Casadei R, Taffurelli G, Pacilio CA, Beltrami D, Minni F. Is pancreaticogastrostomy safer than pancreaticojejunostomy after pancreaticoduodenectomy? A meta-regression analysis of randomized clinical trials. Pancreatology 2017;17(5):805-13.
47. Cheng Y, Briarava M, Lai M, Wang X, Tu B, Cheng N, et al. Pancreaticojejunostomy versus pancreaticogastrostomy reconstruction for the prevention of postoperative pancreatic fistula following pancreaticoduodenectomy. Cochrane Database Syst Rev 2017;9:CD012257.
48. Singh AN, Pal S, Mangla V, Kilambi R, George J, Dash NR, et al. Pancreaticojejunostomy: Does the technique matter? A randomized trial. J Surg Oncol 2018;117(3):389-96.
49. Zhang S, Lan Z, Zhang J, Chen Y, Xu Q, Jiang Q, et al. Duct-to-mucosa versus invagination pancreaticojejunostomy after pancreaticoduodenectomy: a meta-analysis. Oncotarget 2017;8(28): 46449-60.
50. Zhao Y, Zhang J, Lan Z, Jiang Q, Zhang S, Chu Y, et al. Are Internal or External Pancreatic Duct Stents the Preferred Choice for Patients Undergoing Pancreaticoduodenectomy? A Meta-Analysis. Biomed Res Int 2017;2017:1367238.
51. McMillan MT, Ecker BL, Behrman SW, Callery MP, Christein JD, Drebin JA, et al. Externalized Stents for Pancreatoduodenectomy Provide Value Only in High-Risk Scenarios. J Gastrointest Surg 2016;20(12):2052-62.
52. Hajibandeh S, Hajibandeh S, Khan RMA, Malik S, Mansour M, Kausar A, et al. Stapled anastomosis versus hand-sewn anastomosis of gastro/duodenojejunostomy in pancreaticoduodenectomy: A systematic review and meta-analysis. Int J Surg 2017;48:1-8.
53. Huttner FJ, Klotz R, Ulrich A, Buchler MW, Diener MK. Antecolic versus retrocolic reconstruction after partial pancreaticoduodenectomy. Cochrane Database Syst Rev 2016 Sep 30;9:CD011862.
54. Dumitrascu T, Pineau P, Dima S, Stroescu C, Brasoveanu V, Herlea V, et al. Impact of Hepatitis B Virus on Clinicopathological Features and Outcomes After Resection for Pancreatic Adenocarcinoma. Anticancer Res 2015;35(9):5123-8.
55. Tanase AM, Dumitrascu T, Dima S, Grigorie R, Marchio A, Pineau P, et al. Influence of hepatitis viruses on clinicopathological profiles and long-term outcome in patients undergoing surgery for hepatocellular carcinoma. Hepatobiliary Pancreat Dis Int 2014; 13(2):162-72.
56. Dumitrascu T, Ionescu MI, David L, Popescu I. Emergency pancreaticoduodenectomy in a patient with an ampullary adenocarcinoma associated with severe acute pancreatitis: a case report. Chirurgia (Bucur) 2011;106(3):409-13.
57. Strobel O, Schneider L, Philipp S, Fritz S, Buchler MW, Hackert T. Emergency pancreatic surgery--demanding and dangerous. Langenbecks Arch Surg 2015;400(7):837-41.