

## Open and Minimally Invasive Pancreatoduodenectomy: Short-Term Results from a Single Center

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### **ABSTRACT**

#### **BACKGROUND**

Minimally invasive pancreatoduodenectomy (MIPD) is the complex operation available to certain patients in the institutions that have extensive experience with this procedure. However, it is not clear whether MIPD enhances patient recovery and reduces postoperative complications, compared to open pancreatoduodenectomy (OPD).

#### **METHODS**

This prospective study includes 262 patients with malignant neoplasm (MN) or pseudotumoral chronic pancreatitis (PCP) who underwent elective MIPD (laparoscopic (LPD) or robotic (RPD) or "open" approach in our surgical center from January 1, 2013 to January 30, 2021.

#### **RESULTS**

There were 101 postoperative complications recorded in 69 patients (26.33%). 233 out of the 262 patients were discharged from hospital (88.93%) and 29 patients died (11.07%). After OPD, in the group of patients with pancreaticogastric anastomosis complications were detected in 27 cases (41.53%) and 4 patients (6.15%) had a fatal outcome, whereas in the group of patients with pancreatico-enteric anastomosis complications were reported in 54 patients (37.50%) and 19 patients died (13.19%).

The total number of complications after "open" approach was significantly lower compared to MIPD ( $p < 0.05$ ). There were no statistically significant differences in the total number of complications between minimally invasive variants (LPD and RPD). No statistically significant correlation was observed between type of pancreatoduodenectomy and mortality.

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## CONCLUSIONS

This study showed that LPD and RPD are feasible and technically safe for the management of malignant neoplasm pancreaticobiliary area and chronic pancreatitis. MIPD may have acceptable oncological outcomes and postoperative hospital survival comparable with open approach

## KEYWORDS

Pancreatoduodenectomy; Minimally invasive; Laparoscopic; Robotic; Complication

## INTRODUCTION

Minimally invasive surgery is undoubtedly the method of choice for multiple gastrointestinal surgical procedures because of its minimally invasive nature and number of benefits such as reducing postoperative pain, shorter hospital stays, and earlier return to work [1-3]. Current advances in technological innovation and surgical strategies have made surgical procedures on the pancreas a routine practice [2,4]. However, the use of new surgical techniques in pancreatic surgery has been slow due to the complexity of the operations and the steep learning curve required for their use [5,6]. For example, minimally invasive pancreatoduodenectomies (MIPD) have not yet become widespread [3,5]. Due to these interventions have a complex reconstructive stage MIPD are still performed in a very few centers by specialized surgeons [5-7].

Although laparoscopic PD was first described in 1994 and the robotic approach in 2003, MIPD still account for less than 14% of all DPE cases [6-8]. The multicenter randomized controlled trial (LEOPARD-2) for the first time compared laparoscopic and open pancreatoduodenectomy for pancreatic or periampullary tumors [9,10]. The study that involved 99 patients did not reveal the superiority of laparoscopic PD (LPD) and provided an estimated mortality of 6%; 5 patients died in the laparoscopy group and 1 patient died in the group open PD. The trial was stopped early due to high mortality in the migratory invasive interventions group. Therefore, advantages of minimally invasive procedures for removal of pancreato-biliary zone tumors remain controversial [3,11,12].

In our study, we analyzed perioperative surgical outcomes and short-term survival outcomes in patients undergoing MIPD, including LPD and robotic PD (RPD), as well as “open” proximal pancreatoduodenectomy (OPD).

## MATERIAL AND METHODS

### *Study design*

This prospective study includes 262 patients with malignant neoplasm (MN) of the pancreatic head or large papilla of the duodenum (LPofD) or distal common bile duct (DCBD) and/or pseudotumoral chronic pancreatitis (PCP) who underwent elective MIPD (LPD or RPD approach) or OPD in our center from January 2013 to January 2021.

An oncological diagnosis was based on laboratory examination (CA19-9 level, computed tomography (CT), abdominal ultrasound), with morphological verification in 201 cases (82.71%). The PD procedure in patients with chronic pancreatitis was selected because of low prognostic effectiveness of resection interventions (due to the possibility of damage to the pancreatic uncinate process). All patients were assessed using the American Society of Anesthesiology (ASA) Physical Status Classification System.

### *Patient Selection*

Inclusion criteria were as follows: clinically/histologically established diagnosis of MN (for patients with pancreatic tumors/LPofD/DCBD) or the presence of the main (Wirsung) pancreatic duct dilatation, ultrasound- and CT-

signs of the portal vein compression or its branch (in PCP patients) and age over 18-years.

Patients over 80-years-old were excluded from the study. Other exclusion criteria were as follows: instrumental findings of the tumor process prevalence; general somatic status on the ASA III-V scale; presence of ultrasound and CT signs of acute pancreatitis; hyperbilirubinemia above 60  $\mu\text{mol/L}$  (3.51 mg/dl) ((normal range, 4  $\mu\text{mol/L}$  - 20  $\mu\text{mol/L}$ )). Additionally, patients with intraoperative positive express-histological presence of tumor growth along the border of the pancreas resection were also excluded from the study.

During the preoperative stage, all patients with obstructive jaundice, who underwent antegrade transdermal transhepatic drainage of the biliary tract, were referred to a local community hospital for further hyperbilirubinemia reduction to  $\leq 3.51$  mg/dl. Later, the patients were re-hospitalized in our hospital for radical surgery. All operations were performed by the same team of surgeons, using the “no-touch” technique with expanded lymphatic dissection. The choice of the type of pancreatodigestive anastomosis during open interventions was determined by the state (structure) of the pancreatic tissue and the diameter of the Wirsung duct: in the case with the “soft” gland and “thin” duct (with a diameter of less than 4 mm), preference was given to invaginating pancreatogastro-anastomosis, which was performed by a continuous double-row suture. In the presence of a dilated Wirsung duct and / or “dense” gland, a double-row pancreatoenteroanastomosis “duct to mucosa” was applied.

Perioperative management of patients was carried out according to the enhanced recovery after surgery (ERAS) and fast-track protocols, suggesting a unified approach to preoperative preparation, surgical intervention technique, postoperative management of patients and minimal intervention in physiological processes [13]. Mechanical

methods of bowel cleansing before surgery were not used. The first administration of anticoagulants was carried out 12 hours prior to the operation, and intravenous infusion of 10% glucose solution 2 hours prior to operation. The surgical operation was performed in accordance with standard techniques for mobilizing and reconstructing organs; prophylaxis of pancreatitis had been carried out; patients were verticalized on the first day after surgery; the nasogastric tube was removed in the absence of gastrostasis; abdominal cavity drainage was performed on the first or second postoperative day.

Thirty-day perioperative outcomes included mortality, return to the operating room, length of stay, operative time and overall complications. A major complication was defined as having one of the following: deep surgical site infection, organ space surgical site infection, dehiscence, pneumonia, bleeding, sepsis and/or septic shock, renal failure, or postoperative pancreatic fistula (POPF). While evaluating the postoperative results, the duration of the intervention and the amount of intraoperative blood loss were taken into account; the occurrence of pancreatic fistula evaluated according to the classification of the International Study Group of Pancreatic Fistula [14-16].

#### *Statistical analysis*

Chi-square tests were used for categorized data using frequency distributions and percentages. We used student t-tests to compare outcomes between two groups, and one-way analysis of variance to compare results among all three groups. Descriptive statistics were expressed as means  $\pm$  standard deviations. The 95% confidence interval for differences in proportions were estimated, and P-values were two-sided, with statistical significance set at  $<0.05$ .

This study was approved by S.V. Ochapovsky Regional Clinical Hospital №1 and Institutional Review Board; ethics approval was granted by the Human Research

Ethics Committee of the Kuban State Medical University (Ethics Approval Ref. No. 12/217).

**RESULTS**

The mean age of the patients (n = 262) was 67.2 ± 3,4 years at the time of presentation to the hospital; 64.1% of the patients were females (n=168) and 35,9% (n=94) were males. The patients were divided into several groups depending on the cause of the PD and tumor localization: malignant neoplasm (MN) of the pancreatic head - 184 patients (70.2%), with MN of the LPofD - 42 (16.0%), with MN of the DCBD - 18 (6.9%), with PCP - 18 (6.9%).

Out of 262 patients, 209 (79.8%) underwent open PD, 30 (11.5%) patients - laparoscopic PD (LPD) and 23 (8.8%) - robotic PD (RPD). In the group, where open PD was used, 24 patients (11.5%) required portal vein resection, 8 patients (3.8%) had right-sided hemicolectomy simultaneously performed (n = 4), right-sided adrenalectomy (n = 2) and gastrectomy / distal gastrectomy with splenectomy (n = 2). (Table 1).

Diagnosis	OPD n (%)	LPD n (%)	RPD n (%)	All Patients n (%)
Malignant tumor of pancreatic head	150 (57,3)	19 (7,3)	15 (5,9)	184 (70,2)
Malignant tumor of major duodenal papilla	30 (11,3)	9 (3,4)	3 (1,2)	42 (16,04)
Malignant tumor of common bile duct	14 (5,0)	1 (0,4)	4 (1,5)	19 (6,9)
Chronic pseudotumor pancreatitis	15 (5,7)	1 (0,4)	1 (0,4)	17 (6,5)
Total	209 (79,5)	30 (11,5)	23 (9,0)	262 (100,0)

**Table 1:** Dispersion of nosological forms for performing pancreatoduodenectomy. **Note:** In this table and other tables: OPD – open pancreatoduodenectomy, LPD - laparoscopic pancreatoduodenectomy, RPD – robot-assisted pancreatoduodenectomy.

Conversion from MIPD to open PD was performed in 8 patients: in 6 while attempting to perform LPD and 2 in RPD, in 5 cases due to the “soft” gland consistency and/or lack of visualization of the main pancreatic duct, in 3 cases due to bleeding that occurred at the stage mobilization of the organocomplex.

Histological differentiation, tumor size and involved regional lymph nodes are shown in Table 1.

Pancreatico-enteric anastomosis was created in 177 (67.6%) cases, pancreatico-gastric anastomosis in 85 (32.4%). In all cases, where gastropancreatoduodenectomy was performed, anastomoses were applied on one loop. Patients with LPD had the longest operation (420 ± 60.2 minutes), patients with RPD had the shortest procedure (370 ± 106.7 minutes). Intraoperative blood loss was higher in patients with OPD (190 ± 60 ml) compared to patients with LPD (120 ± 40 ml) or RPD (130 ± 30 ml). A similar pattern was observed when we administered narcotic analgesics in the postoperative period: PD - 209 (100%) patients - 4.8 days, LPD - 26 (86.7%) - 2.8 days and RPD - 20 (87.0%) patients - 2.6 days. The length of hospital stay was higher in the open PD group (16.4 ± 4.0 days), RPD (13.6 ± 3.2 days), and the shortest hospital stay was in patients with LPD (11.2 ± 4.2 days) (p < 0.05). The quality of the performed lymph node dissection was conventional in all groups. Differences in the histological assessment of the “purity” of the pancreatic resection margin were found only in patients with OPD in 5 (2.4%) cases (Table 2).

Criterion	OPD n (%)	LPD n (%)	RPD n (%)	All Patients n (%)
<b>Tumor Grade</b>				
G1	0	0	0	0
G2	38 (15,6)	10 (4,1)	6 (2,5)	54 (22,1)
G3	97 (39,8)	13 (5,3)	12 (4,9)	122 (50,0)
G4	57 (23,4)	7 (2,9)	4 (1,6)	68 (27,9)
Total in subgroup	192 (78,7)	30 (12,3)	22 (9,0)	244 (100,0)
<b>Tumor Size</b>				
T1	12 (4,9)	6 (2,5)	7 (2,9)	25 (10,2)
T2	109 (44,7)	22 (9,0)	15 (6,1)	146 (59,8)
T3	71 (29,2)	2 (0,8)	0	73 (30,0)
Total in subgroup	192 (78,7)	30 (12,3)	22 (9,0)	244 (100,0)
<b>Regional Lymph Nodes</b>				
N0	108 (44,3)	18 (7,4)	18 (7,4)	144 (59,0)
N1	84 (34,4)	12 (4,9)	4 (1,6)	100 (41,0)
Total in subgroup	192 (78,7)	30 (12,3)	22 (9,0)	244 (100,0)

**Table 2:** Prevalence and differentiation degree of tumors.

A total of 101 postoperative complications were recorded in 69 (26.3%) patients. The postoperative period was uneventful in 193 (73.7%) patients. Most often, complications were observed in patients with OPD - 81

patients (80.2%), less often with LPD - 11 patients (10.89%) and with RPD - 9 patients (9.9%). The most common complications were pancreonecrosis - or postoperative pancreatic fistula (POPF): local, subtotal, general - in 49 (71.0%) patients and the suppuration of postoperative wound - 15 (21.7%) (Table 3). Different forms POPF (as erosive abdominal bleeding, bleeding from the stump of the pancreas (including gastric bleeding), peritoneal seroma and eventration) we observed in patients with OPD - 55 (72.6%), less often in patients with LPD - 11 (15.1%), and quite rarely this problem occurred in patients with RPD - 9 (12.3%) (Table 3).

Index	OPD	LPD	RPD
Operative time (min)	390.2 ± 44.2	420 ± 60.2	370 ± 106.7
Intraoperative blood loss (ml)	190 ± 60	120 ± 40	130 ± 30
Postoperative hospital staying *	16.4 ± 4.0	11.2 ± 4.2	13.6 ± 3.2
Frequency of narcotic analgesics use	209 (100%)	26 (86.66%)	20 (86.96%)
Narcotic analgesics used (days)	4.8	2.8	2.6
Lymph nodes removed	19.2 ± 3.5	18.0 ± 2.3	18.1 ± 1.6
Number of patients with R0 resection margin:			
express test:	209	30	23
final conclusion:	204	30	23

**Table 3:** Features of surgical intervention and perioperative management of patients. **Note:** \* - in case of uncomplicated postoperative period.

Suppuration of the postoperative wound was found in 8 patients (7.9%) who underwent combined PD with resection of the portal vein and/or splenic-superior mesenteric confluence, which led to an extension of operative time duration.

The analysis  $\chi^2$  criteria Pearson's showed the total  $\chi^2$  for complications after applying variants of PD turned out to be  $6.09 > \chi^2_{st} = 5.99$  (df = 2,  $p < 0.05$ ); for mortality. -  $0.29 < \chi^2_{st} = 5.99$  (df = 2,  $p > 0.05$ ). When assessing the correlation between the options for the implementation of the PD and the occurrence of complications, the value of criterion V Cramer and the Chuprov criterion was 0.36 and 0.51, respectively. Thus, the correlation between the type of operation performed and the number of complications turned out to be reliable and average in strength.

The analysis  $\chi^2$  (Pearson criterion) showed that the number of complications after surgery performed by OPD was significantly lower comparing to LPD: the corresponding

$\chi^2$  empirical was  $5.99 > \chi^2_{st} = 3.84$  (df = 1,  $p < 0.05$ ). There were no statistically significant differences in the number of complications between the remaining PD options.

Complications	OPD		LPD		RPD		Total	
	Abs. val.	%	Abs. val.	%	Abs. val.	%	Abs. val.	%
Pancreatic necrosis	33	32.67*	10	9.90	6	5.94	49	48.51
Thrombosis	2	1.98*					2	1.98
Eventration	2	1.98*					2	1.98
Pancreatic stump hemorrhage / anastomosis	10	9.90*	1	0.99	2	1.98	13	12.87
Surgical site infections	15	14.85*					15	14.85
Pneumonia	2	1.98*					2	1.98
Acute intestinal obstruction	2	1.98*					2	1.98
Sepsis	3	2.97*					3	2.97
Abdominal bleeding	2	1.98*					2	1.98
Hepatic artery hemorrhage	1	0.99*					1	0.99
Anastomosis failure	8	7.92*			1	0.99	9	8.91
External purulent fistula formation	1	0.99*					1	0.99
Total	81	80.20*	11	10.89	9	8.91	101/69	26.33
Mortality	23	11.00	4	13.33	2	8.69	29	11.07

**Table 4:** Distribution of postoperative complications and mortality. **Note:** \* was significantly different (p Value <0.05; as Student's t-test).

A total of 233 patients (88.9%) were discharged from the hospital; a fatal outcome was recorded in 29 (11.07%) cases (Table 3). The Pearson's test showed that there was no statistically significant correlation between the PD option and mortality; the value of the Cramer V criterion and the Chuprov criterion was 0.09 and 0.12, respectively.

	PD	LPD	RPD
PD	-	5.99*	0.05
LPD	0.14	-	1.68
RPD	0.12	0.28	-

**Table 5:** The empirical values of the Pearson criterion  $\chi^2$  obtained by comparing the frequencies of patients with complications / deaths and the ratio of different variants of PD implementation. **Note:** \* after the empirical value of  $\chi^2$  Pearson means the presence of statistically significant differences between the distributions. Above the main diagonal, the values of the empirical criterion  $\chi^2$  Pearson obtained by comparing the frequency distribution of patients with complications and without after applying different types of PDD, ( $\chi^2_{st} = 3.84$  at df = 1), below - when comparing mortality with different anastomoses ( $\chi^2_{st} = 9.49$  with df = 4).

Analysis of complications rates depending on the type of pancreatic anastomosis showed that in the group of patients with OPD who underwent PGA 27 patients (41.5%) had complications. The lethal outcome occurred in 4 (6.2%) cases due to sepsis resulted from POPF (2 cases), bleeding from the pancreatic stump into the

stomach (2 cases). In patients with PEA, there were 54 (37.5%) complications and 19 (13.2%) deaths. The most common complication was also POPF. Analysis of LPD results revealed that only 10 complications (33.3%) were observed in patients with PGA - 2 (15.4%) with fatal outcomes in 2 patients (15.4%), whereas after PEA complications were recorded in 8 cases (47.1%) and fatal outcome occurred in 4 patients (23.5%). After RPD, only 8 complications (34.8%) were noted: in patients with PEA - 6(46.2%), fatal outcome was in 2(15.4%) patients; after PGA application, complications were recorded in 2 (20.0%) patients. In most cases the use of minimally invasive drainage interventions allowed to avoid fatal outcome.

There was no statistically significant correlation between the type of pancreatic anastomosis and mortality/ complications (for complications  $0.042 < \chi^2_{st=5,99} (df=2, p > 0,05)$ ; for mortality:  $2.606 < \chi^2_{st=5,99} (df=2, p > 0,05)$ ).

## **DISCUSSION**

Pancreatoduodenectomy is a challenging operation for many surgeons [1,3,17]. This approach to pancreatobiliary zone requires complex resection of the pancreatic head, bile duct and intestines. Additionally, it entails complex reconstruction, in which serious complications and mortality can be caused by anastomotic failure or bleeding [2,6,18]. Despite significant advances in patient selection, surgical technique, and postoperative care, morbidity occurs in up to 40% of patients undergoing pancreatoduodenectomy. Minimally invasive interventions are expected to reduce morbidity after pancreatectomy through typical benefits such as reduced blood loss, pain, wound-related morbidity, shorter hospital stays, and time to recovery [4,5,19]. Still some surgeons prefer to perform OPD in patients with a large tumors, vascular involvement, a thin duct, a “soft” gland [11,13]. There are no randomized controlled studies of MIPD

versus open pancreaticoduodenectomy in the management of pancreatobiliary diseases. After Gagner and Pomp, who first described LPD in 1994 [20], and Giulianotti, who reported the first robotic PD in 2003 [21], the most important was the study of Kendrick with co-authors, which was presented at IHPBA State of the Art Conference on Minimally Invasive Pancreatic Resection, Sao Paulo, Brazil [22]. In their work, the authors demonstrated that MIPD is feasible and safe and reproduces all stages of open surgery. MIPD has its own challenges: increased operative time, steep learning curve, limited supervised training opportunities, reduced tactile feedback. Additionally, MIPD may be more expensive compared to other type of surgeries, described in this manuscript. Finally, Kendrick and co-authors agree with other surgeons that MIPD is a newer approach requiring additional investigation and so far, the total number of published LPD and RPD cases is insufficient to make a definitive conclusion whether MIPD provides significant benefits [22-25].

Since some MIPD stages are challenging (pancreas exposing, bleeding control, and the reconstruction of the gastrointestinal tract), LPD and RPD are time-consuming [8,13]. Ke Chen and co-authors in their meta-analysis reported that the operative time for LPD ranged from 287 to 510 min and for RPD from 340 to 660 min according to published studies that included more than 10 patients [26]. In this study, our data showed an average surgery time of 420 minutes for LPD and 370 minutes for RPD, which is a little less than the previously reported values. However, for laparoscopic the operative time was reduced from 582.5 min (interquartile range 504.6-664.8 min) for the first 15 cases to 410 min (interquartile range 361.5-484.2 min) for the last 15 cases; and for robotic the operative time was reduced from 502.5 min (interquartile range 484.5-552.5 min) for the first 10 cases to 330 min (interquartile range 341.5-466.5 min) for the last 10 cases. There is also one study that compared totally minimally

invasive and open approaches and did not find any significant difference in duration [27]. Our findings were consistent with the trend described by Kendrick and Zureikat: increased experience with MIPD, the standardization of the operative procedures, and the cooperation in the surgical team likely contribute to shortened operative time in the most last cases [22,28,29].

The most frequent specific major complication after pancreatic resection is POPF, which is potentially life-threatening and leads to a longer hospital stay and increased cost. CR-POPF, especially Grade C POPF, is strongly associated with postoperative recovery. CR-POPF, with a prevalence of 5% to 45% after PD remains a clinically relevant problem [25]. The incidence of pancreatic fistulas after open pancreaticoduodenectomy ranges from 2.0 to 36.0 %, while the reported incidence after MIPD ranges from 0 to 35.0 % [9,16,26]. In the present study, POPF after OPD occurred in 33 patients (25.8 %), after LPD occurred in 11 patients (15.1%), after RPD occurred in 9 patients (12.3%). The present analysis revealed no significant difference in CR-POPF rates between LPD and RPD groups. In our study, patients with grade B pancreatic fistulas were treated conservatively, however, the one grade C pancreatic fistula patient required peritoneal lavage, placement of drainage tubes, enhanced nutritional support, antibiotics, and somatostatin. Similar results have also been observed in previous studies.

In the present study the criteria of the ISGPF were used to define POPF, but were ignored pancreatic texture and pancreatic duct diameter. These two factors are closely related to the occurrence of POPF.

Our results indicate that MIPD had advantage over OPD in avoiding postpancreatectomy hemorrhage (PPH): we had higher severity of abdominal bleeding and pancreatic stump hemorrhage in OPD - 12 cases (10,8%) and over MIPD - 3 cases (2,8%). PPH data are variable in previous

studies [6,27]. Possible reasons for this variability include differences in the MIPD procedure and in the definition of MIPD. Our results suggest that MIPD has some degree of safety in terms of POPF, delayed gastric emptying (DGE) and PPH.

Some authors speculate that conversions to the open pancreaticoduodenectomy should not be regarded as failures if they did not increase surgical risk. So, the overall conversion rate previously reported was 9.1 % (ranging from 0 to 40.0 %), and most of conversions were performed due to tumor adherence, positive margins, uncontrollable bleeding, limited operative space, and other unexpected events/observations [24,29]. In our data, conversion from MIPD to open PD was performed in 8 patients (3.1%): in 3 cases (1.2%) due to bleeding that occurred at the stage mobilization of the organocomplex and, in 5 cases (1,9%) due to the “soft” gland consistency and / or lack of visualization of the main pancreatic duct. We suppose that the conversion rate of MIPD wouldn't decrease with increased laparoscopic experience because more difficult cases will be encountered with the increased willingness of surgeons and patients to consider minimally invasive approach.

Given that pancreaticoduodenectomy is often performed in patients with malignancy, it is important to compare oncological outcomes between minimally invasive and open procedures. However, whether minimally invasive pancreaticoduodenectomy is superior to OPD (open pancreaticoduodenectomy) with respect to the amounts of lymph nodes collected and the R0 ratio remains unclear.

Lai et al. [29] compared 20 patients undergoing robot-assisted laparoscopic pancreaticoduodenectomy with 67 patients undergoing OPD and demonstrated that the R0 resection rates and harvested lymph node numbers were comparable between the two groups. Chalikonda et al. [30] compared 30 patients undergoing a minimally invasive procedure with 30 patients undergoing OPD and

found that the number of harvested lymph nodes was similar between the two groups, but that a higher rate of positive margins was observed in the OPD group (0 vs. 13.0 %,  $P = 0.02$ ).

The results of a comparative study with a large sample size (180 patients) showed a similar R0 resection rate and a higher number of harvested lymph nodes in the minimally invasive group compared with the OPD group ( $23.44 \pm 10.1$  vs.  $16.84 \pm 10.6$ ,  $P < 0.001$ ) [28].

In our study there were no significant differences regarding resection margins and R0 resection. The median number of harvested lymph nodes was  $19.2 \pm 3.5$  for OPD,  $18.0 \pm 2.3$  for LPD and  $18.1 \pm 1.6$  for RPD, which was within the recommended range (11-17 lymph nodes) for the minimum number of collected lymph nodes necessary to provide optimal staging and to serve as a quality indicator [18,19,24]. We speculate that resection margin was clear in more cases for two reasons: 1) intraoperatively resected material was sent for express-histological examination; which made it necessary to perform re-resection or pancreatectomy in the case of extended growth along the edge of the resection; 2) as mentioned above, not only in our work, but also in other authors, there is a subjective component in the selection of patients for minimally invasive procedures: more "simple" cases.

Some systematic reviews and meta-analyses also revealed that the incidence of POPF was not significantly different between minimally invasive PD (laparoscopic and robotic PD) and open PD [1,11,12]. Boggi et al [31] reported the results of an RCT comparing the laparoscopic approach for PD with the open approach. The results showed no significant difference in the overall complications rates, including POPF, after laparoscopic PD. Ioannis D Kostakis et al. in the systematic review and meta-analysis found no significant difference between robotic and laparoscopic pancreaticoduodenectomy in regards to

pancreatic leak or bile leak [2]. Similarly, no significant difference was detected between robotic and open pancreaticoduodenectomy in regards to pancreatic leak.

Another study using multi-institutional data from the American College of Surgeons National Surgical Quality Improvement Program compared pancreas-specific outcomes of minimally invasive PD and open PD, with a focus on clinically relevant POPF [12,19]. The rates of POPF were slightly greater in MIPD compared to OPD (15.3% vs 13.0%, respectively,  $p = 0.03$ ); however, MIPD was not an independent factor associated with POPF in the adjusted multivariable analysis.

In our study rates of postoperative complications was significantly different between minimally invasive PD (laparoscopic and robotic PD) and open PD (Table 4). This was especially true for POPF (pancreatic necrosis, pancreatic stump hemorrhage/anastomosis, external purulent fistula formation, abdominal bleeding) -  $p < 0.05$ . However, the hospital mortality rate did not differ significantly between the groups ( $p > 0.05$ ). As mentioned above, in our opinion, this is because the patients for this study were selected based on the condition (structure) of the pancreatic tissue and the diameter of the Wirsung duct (not randomized study); in addition, subjective surgeon's opinion was taken in account.

The advantage of MIPD over open PD concerning POPF remains unclear. However, MIS-PD has a shorter exposure time in the abdominal cavity, and a smaller surgical wound than open-PD. This may reduce the potential infection during surgery. As a result, there is a possibility of reducing the occurrences of septic POPF because surgery is performed under conditions where infection is less likely to occur.

Our study has a few limitations. We did not compare long-term survival rates of our patients with other studies, due to a potential bias that would have been generated by a



small sample size of our study different different types of tumors.

## **CONCLUSIONS**

Pancreatoduodenectomy still remains a technically difficult operation, which should be performed in well-equipped specialized surgical departments of multidisciplinary medical centers. The experience gained by a team of surgeons in the "open" surgical treatment of patients with tumors in the periampicular area allows starting using minimally invasive technologies. An analysis of the complications developed during the early postoperative period and the immediate results of treatment in patients undergoing LPD and RPD shows the absence of statistically significant correlations between it, but the number of complications after surgery performed by OPD was significantly lower comparing to MIPD ( $p < 0.05$ ). There was no statistically significant correlation between the PD option and mortality.

Evaluation of the technical features for performing "open" and MIPD made it possible to formulate the following criteria in selected patients for "minimal access" surgery: tumor size  $< 3.5$  cm; absence of invasion into the main vessels; the diameter of the Wirsung duct  $> 0.4$  cm. Admittedly, this study is limited by its small sample size, the enrollment of patients with tumors of different origins, and the short follow-up time. Therefore, randomized,

comparative studies with large sample sizes are necessary to draw definitive conclusions regarding the role of MIPD.

## **DECLARATIONS**

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### ***Conflict of Interest***

All the authors declare that they have no conflict of interest.

### ***Ethical approval***

All procedures performed in studies involving human participants were in accordance with the ethical standards and with the 1964 Helsinki declaration and its later amendments.

### ***Informed consent***

Informed consent was obtained from all individual participants included in the study.

### ***Consent for publication***

All authors consented for the publication.

### ***Availability of data and material***

The data that support the findings of this study are available from the corresponding author upon request.

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