# Is Sutureless Pancreaticogastrostomy More Effective than Single-Layer Duct-to-Mucosa Pancreaticojejunostomy in Pancreaticoduodenectomy?

Pankreatikoduodenektomide Dikişsiz Pankreatikogastrostomi Tek Katlı Duct-To-Mukozal Pankreatikojejunostomiden Daha mı Etkilidir?

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#### **ABSTRACT**

Objective: The present study aimed to assess the safety of pancreatic anastomosis after pancreaticoduodenectomy (PD) and to compare the results of sutureless pancreatogastrostomy (PG) with those of single-layer duct-to-mucosa pancreatojejunostomy (PJ) after PD in patients with malignant disease of the pancreatic head and of the periampullary region.

Materials and Methods: The study included 173 consecutive patients undergoing PD from May 2009 to December 2015 at a single surgical center: Single-layer duct-to-mucosa PI was performed in 52 patients and sutureless PG in the remaining 123. The primary endpoint was the safety of the procedures, which was assessed as the occurrence of complications during hospitalization. Postoperative pancreatic fistula (POPF) was classified as grade A, B, or C according to the International Study Group of Pancreatic Fistula classification.

Results: We found that the incidence of POPF was 11.52%. With regard to POPF, the present study showed no significant difference in the two groups (p=0.043). The incidence of Grade C POPF was significantly higher in the PJ group than in the PG group (p=0.001), which was been reflected in the form of a higher rate of postoperative hemorrhage (p=0.001), intra-abdominal abscess (p=0.012), and septic shock (p=0.012) events in the PJ group.

Conclusion: The evaluation of short-term outcomes demonstrates that suturelessPG is a feasible and safe technique, associated with lower life-threatening complications than single-layer duct-to-mucosa PJ. If longterm functional outcomes confirm similar results, sutureless PG could become a valid alternative for pancreatic anastomosis after PD in patients with soft pancreas and high morbidity.

Keywords: Pancreaticogastrostomy, pancreaticojejunostomy, pancreaticoduodenectomy, pancreatic fistula

#### ÖZ

Amaç: Bu çalışmanın amacı pankreatikoduodenektomi (PD) sonrası pankreatik anastomozun güvenliğini değerlendirmek ve malign pankreas başı ve periampuller bölge hastalığı olan hastalarda PD sonrası dikişsiz pankreatikogastrostomi (PG) ile tek katlı duct-to-mukozal pankreatikojejunostomiyi (PJ) karşılaştırmaktır.

Gereç ve Yöntem: Çalışma tek bir cerrahi merkezde Mayıs 2009 ile Aralık 2015 tarihleri arasında PD uygulanan 173 ardışık hastayı kapsamıştır. Tek katlı duct-to-mukozal PJ 52 hastaya, dikişsiz PG kalan 123 hastaya uygulandı. Primer sonlanım noktası işlemlerin güvenliği olarak düşünüldü ve hastane yatışı süresince komplikasyonların gelişimi olarak değerlendirildi. Postoperatif pankreatik fistül (POPF) Uluslararası Pankreatik Fistül Çalışma Grubunun sınıflandırma kriterlerine göre A, B ve C evresi olarak sınıflandırıldı.

Bulgular: Çalışmamızda POPF oranı %11,52 olarak bulundu. İki grup arasında anlamlı bir farklılık görülmedi (p=0,043). Evre C POPF insidansı PJ'de PG grubuna göre anlamlı ölçüde daha yüksekti (p=0,001), Ayrıca PJ grubunda postoperatif hemoraji (p=0,001), intraabdominal apse (p=0,012) ve septik şok (p=0,012) vakalarının oranları da daha yüksek bulundu.

Sonuç: Kısa dönem sonuçların değerlendirilmesine göre, tek katlı duct-to-mukozal PJ ile kıyaslandığında dikişsiz PG daha düşük oranda yaşamı tehdit eden komplikasyonlarından dolayı uygulanabilir ve güvenli bir tekniktir. Uzun dönem fonksiyonel sonuçlarla benzer bulgular doğrulandığı takdırde dikişsiz PG, yumuşak yapılı pankreası ve yüksek morbiditesi olan hastalarda PD sonrası pankreatik anastomoz için geçerli bir alternatif olabilir.

Anahtar Kelimeler: Pankreatikogastrostomi, pankreatikojejunostomi, pankreatikoduodenektomi, pankreatik fistül

#### Introduction

Pancreaticoduodenectomy (PD) (Whipple's procedure) is the standard surgical procedure for different malignant and benign diseases of the pancreas, distal choledochus, and ampulla of Vater. Nevertheless, the operative morbidity after PD remains high, occasionally approaching 30%-40%, and it most often involves pancreatic and biliary fistulas, intra-abdominal bleeding or collection, and abdominal wall abscesses [1]. Pancreatic anastomosis leakage and fistula for-

mation after PD are some frequent complications. Lack of a timely diagnosis and improper management are associated with high morbidity and mortality. The magnitude of postoperative pancreatic fistula (POPF) is not insignificant; a worldwide literature search revealed that the incidence of pancreatic fistula after PD is at 16% and at 13% after distal pancreatectomy [2]. Other reports have revealed that fistula rates reach up to 31% for distal pancreatectomies [3]. Recent series have reported POPF rates between 20% and 30% after PD [4]. The principal risk factor for the development of POPF is healthy, nonfibrotic pancreas with a standard exocrine function, described as "soft" during intraoperative palpation [5]. Pancreatic surgeons have attempted to determine the optimal technique for reconstruction after PD in order to decrease the frequency and seriousness of postoperative complications, mainly pancreatic anastomosis leakage. Many different methods of anastomosis, which are directed at reducing the incidence of POPF, have been described. However, which is the best technique for pancreatic anastomosis after PD remains debatable. Nowadays there are two main techniques: pancreatojejunostomy (PI) and pancreatogastrostomy (PG). For each technique, several subtypes have been developed [6, 7].

The primary aim of the study was to compare the results of two different methods of pancreatic anastomosis after PD in patients with pancreatic head adenocarcinoma or malignant periampullary tumor: sutureless PG and single-layer duct-to-mucosa Pl.

## Materials and Methods

The present study was conducted at Division of Surgery, Naval Hospital, Military Medical Academy, Varna, Bulgaria rom May 2009 to December 2015 to allow for a 12 month follow-up period for the last patient who underwent surgery.

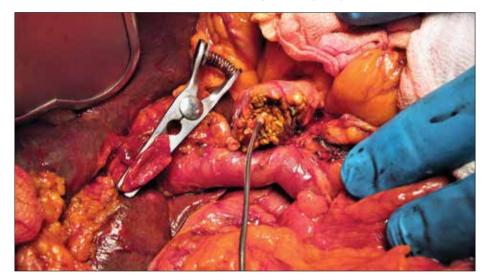
## **Patients**

In total, 173 consecutive patients were included in this retrospective study (78 women and 95 men; average age 65.9 years); all the patients underwent PD during a 6-year period (between May 2009 and December 2015) in the Division of Surgery Naval Hospital, Military Medical Academy, Varna, Bulgaria. PD with standard lymph node dissection was performed in each patient. The execution of a classical Whipple's procedure or pyloruspreserving resection was decided by the surgeon. Single-layer duct-to-mucosa PJ using our technique had been the procedure of choice

for pancreatic reconstruction after PD at our hospital since 2009. In 2012, this was replaced with sutureless PG. All operations were performed by the same surgeon. Single-layer ductto-mucosa PI was performed in 52 patients and sutureless PG in the remaining 123. Preoperative staging included blood analyses (including analysis of serum concentration of carbohydrate antigen 19-9), endoscopic ultrasound to specify operability, and thoracic and abdominal computed tomography (CT) and magnetic resonance imaging (MRI) in selected patients. Endoscopic biliary stenting was implemented to treat biliary obstruction preoperatively. The intra-abdominal drains were removed if the amylase concentration in the drain contents had not increased after the third postoperative day (POD).

## Surgical technique

The trial was approved by the Institutional Review Board of Naval Hospital, Military Medical Academy, Varna, Bulgaria and was conducted in accordance with the principles of good clinical practice. All the participants in the study gave their informed consent prior to commencement of the research. The operation began with median laparotomy. The abdominal cavity was completely explored to rule out peritoneal or liver metastasis. The single-layer duct-to-mucosa PJ technique was detailed in 2014, and the operative method is briefly presented in Figure 1-7 [8]. Sutureless PG was first introduced in 2015; the technical execution involves five stages, as shown in Figure 8-12 [9, 10].



**Figure 1.** The ductal wall of the main pancreatic duct is liberated from the pancreatic tissue at 2-3 mm caudally to the cut end.



**Figure 2.** Three PDS 5-0 must traverse the full thickness of the pancreatic parenchyma from the dorsal pancreatic surface until the needle comes out from the posterior ductal wall 2-3 mm caudally to the cut end.

PDS: polydiaxone sutures



**Figure 3.** Two interrupted sutures traverse the full thickness of the pancreatic parenchyma from the anterior wall of the duct until the needle comes out from the anterior pancreatic surface. The sutures pass through the ductal wall 2-3 mm caudally to the cut end.



**Figure 4.** The posterior layer is a series of three to four horizontal mattress sutures using PDS 4/0 between the whole pancreatic remnant to the seromuscular layer of the jejunum. PDS: polydiaxone sutures



**Figure 5.** The posterior ductal sutures are also used to ensure that the posterior wall of the main pancreatic duct is anastomosed to that of the open jejunum.

## **Terminology**

The International Study Group on Pancreatic Fistula (ISGPF) defines POPF as a drain output of any gaugeable volume of fluid on or after the third POD with an amylase concentration three times greater than the serum amylase activity [11]. ISGPS has put forward a classification system for postpancreatectomy hemorrhage (PPH), which distinguishes between an early hemorrhage occurring within 24 h after operation and a late hemorrhage occurring after the first 24 h [12]. We examined delayed PPH occurring after the first 24 h after operation. Grade A delayed PPH does not necessitate therapeutic intervention. Grade B PPH is a mild, late intra- or extraluminal hemorrhage that requires blood transfusion, endoscopy, or embolization. Grade C PPH is severe intra- or extraluminal bleeding that requires embolization, endoscopy, or laparotomy. Biliary fistula was identified by the presence of biliary leakage beyond POD 5, confirmed by a contrast examination of the bile ducts [13]. Delayed gastric emptying (DGE) was defined as the inability to tolerate solid peroral intake by POD 7 as the patient needed continuous decompression of the stomach by nasogastric intubation [14]. The texture of the pancreas was defined as "hard" or "soft" according to the criteria suggested by Reid-Lombardo et al. [15]. The incidence of postoperative death was determined by the mortality rate within the first 30 days AFTER the operation. Postoperative complications were categorized according to the classification of Clavien-Dindo [16].

## Statistical analysis

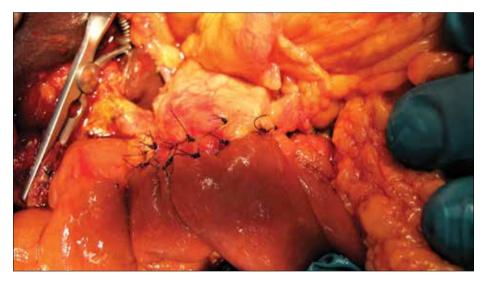
Statistical analyses were conducted by implementing the Statistical Package for Social Sciences software version 21.0 (IBM Corp.; Armonk, NY, USA). All continuous data are presented as the median (range) and mean±standard deviation (SD). All continuous data are presented as the median (range) and mean±SD. Mean values of continuous variables are benchmarked against a two-tailed Student's t test. Nonparametric statistical tests were performed in cases where the variables did not follow normal distribution. Categorical variables were assessed and compared using Pearson's χ2 test or Fisher's exact test contingency tables. A p value < 0.05 was considered statistically significant.

#### Results

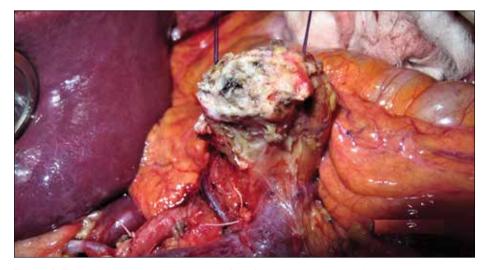
We performed PD in 173 patients; in 30 (17.34%) of these, PD was performed for cholangiocarcinoma of the distal choledochus and carcinoma of the Ampulla of Vater, while in the remaining 143 (82.65%), PD was not



**Figure 6.** Similar to the posterior ductal sutures, the anterior ones are used to ensure that the anterior wall of the main pancreatic duct is anteriorly anastomosed to the open jejunum.

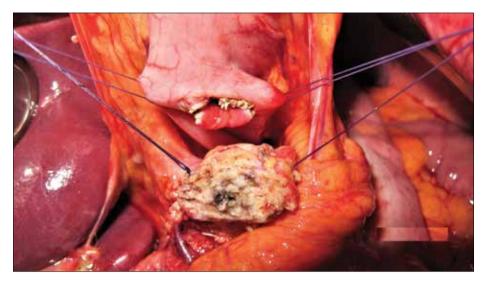


**Figure 7.** Anteriorly interrupted sutures apposing the seromuscular layer of the jejunum to the pancreas are performed using 4/0 PDS sutures, thus completing PJ. PDS: polydiaxone sutures PI: pancreaticojejunostomy

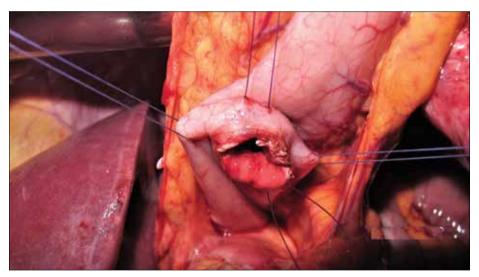


**Figure 8.** The pancreatic remnant is mobilized 3 cm from the splenic vein and the surrounding tissues.

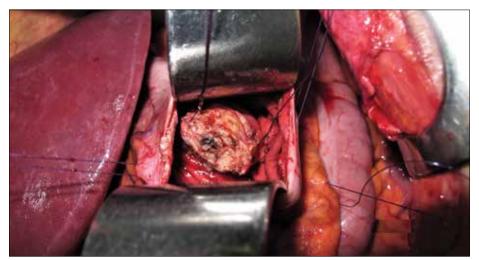
performed for pancreatic head adenocarcinoma. Demographics are shown in Table 1. Intraoperative variables, pancreatic texture, pancreatic leak, and postoperative outcomes of the pancreatic reconstruction technique are shown in Table 2. The rate of soft pancreatic parenchyma (p=0.375) and nondilated (<2 mm) pancreatic duct (p=0.497) did not differ significantly between the two groups. The overall mortality rate in the study population was 2.89%. The incidence of postoperative mortality was significantly lower in patients with PG (p=0.021). The postoperative morbidity rate of all the patients was 30.05%. The number of patients who experienced postoperative complications within 30 days of the operation was higher in the PI group than in the PG group, although this difference was considered to be statistically insignificant (p=0.037). There were no significant differences in the surgical time in both the groups (p=0.042). The median postoperative stay was identical in both the groups, with a median duration of 12 days (p=0.025). Pancreatic leak was diagnosed in a total of 20 (11.05%) patients. The incidence of POPF was 8.26% after PG and 19.23% after PJ (p=0.043). The patient group with Grade B POPF was treated conservatively, that with Grade C POPF required surgery. The rate of patients with Grade C POPF and PI was significantly higher compared to that observed in patients with PG (p=0.001). The average duration between the primary operation and relaparotomy was 7 days (range: 6-9 days). In this series, the cause of relaparotomy was pancreatic fistula combined with intraabdominal fluid collection and subsequent health-threatening complications. The rate of reoperations necessitated by the presence of POPF was 2.31%. All reoperations were performed in an emergency setting. Patients with Grade C POPF were reoperated for intra-abdominal abscess and late extraluminal bleeding classified as Grade C (three patients). The clinical presentation of these patients involved blood loss through intra-abdominal drains with an accompanying drop in the hemoglobin level to >3 mg/dL (compared with the first postoperative value). However, due to obstruction the drains with blood clots, patients with PPH may also experience abdominal pain or distension and low drain output. Patients with Grade C PPH were hemodynamically unstable, requiring treatment with vasopressors in conjunction with fluid therapy. In fact, these patients underwent emergency surgery to control bleeding and to complete pancreatectomy. Extraluminal PPH was managed by suture ligation. The locus, which was the origin of bleeding, was at the level of the proper



**Figure 9.** A transversal full-thickness incision is made on the posterior gastric wall with a mzximum length of 2 cm to ensure tight adherence to the posterior wall of the stomach and the pancreatic stump.



**Figure 10.** A continuous seromuscular circular suture (3-0 PDS) is placed around the gastric incision I cm away from the cut edge. PDS: polydiaxone sutures

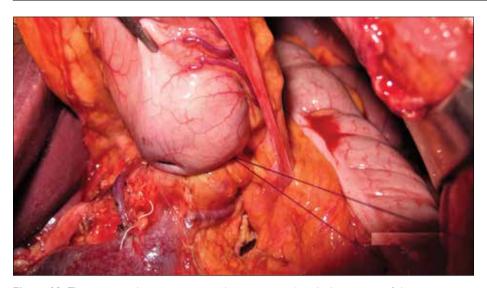


**Figure 11.** The pancreatic remnant is pulled with slide tension on the holding sutures through the incision on the posterior gastric wall into the stomach.

hepatic artery (one patient), at the level of the stump of the gastroduodenal artery (one patient), and at the level of the superior mesenteric artery (one patient). In severe cases, there may be instances of organ/multiorgan failure and hypovolemic shock. Four patients were diagnosed with complications of PPH: single-organ failure of Grade IVa (one patient) and multiorgan failure of Grade IVb (three patients). Delayed extraluminal bleeding did not occur without pancreatic fistula. The median estimated late blood loss was 1020 mL (range: 800-2000 mL). The median quantity of blood transfused was 5.3 units (range: 4-9 units). Patients with extraluminal PPH died of multiorgan failure caused by septic shock on the third POD. The mortality rate in patients with POPF was 25%. The number of patients with extraluminal hemorrhage (p=0.001), intraabdominal abscess (p=0.012), septic shock (p=0.012), and PJ was significantly higher than that of patients with PG. There was late intraluminal bleeding of Grade A/B in the PG group and not in the PJ group (p=0.001). The point where bleeding began was a cut surface of the pancreatic remnant. There was no difference existed between the groups with respect to DGE, chyle leakage, and bile leakage (p=0.023, p=0.021, p=0.035).

#### Discussion

Pancreatic anastomotic disruption is perhaps the most dreaded complication following Whipple's procedure. The incidence of POPF is still high at 10%-22% after PD and at 30% after distal pancreatectomies, even in highvolume centers [17-20]. In the present study, the rate of POPF was 11.52%. There was no statistically significant difference in POPF rates between the groups (p=0.043). Intriguingly, when causes of postoperative complications were analyzed on an individual basis, the proportion of patients with POPF of grade C was considerably higher in the PJ group, i.e., this latter approach was characterized by a higher incidence of postoperative hemorrhage (p=0.001), intra-abdominal abscess (p=0.012), and septic shock (p=0.012). Extraluminal PPH occurred only in patients with POPF and intra-abdominal abscess (p=0.001). while intraluminal PPH occurred in patients with PG (p=0.001). PJ was associated with a higher rate of extraluminal bleeding as a consequence of damage to the vascular wall by activated proteolytic enzymes, which enter the abdominal cavity through POPF [21]. Throughout the years, multiple studies of different operative techniques for the creation of pancreatic anastomosis and pharmacological prophylactic approaches have been proposed



**Figure 12.** The seromuscular continuous circular suture is tied to the lowest part of the pancreatic stump and a gastric decompression tube is placed.

W. T.L.	Total	Single-layer duct-to-mucosa	Sutureless	
Variable	(%)	PJ (%)	PG (%)	Р
N	173 (100)	52 (30.05)	121 (69.94)	0.932
Gender				
male	95 (54.91)	28 (28.47)	67 (70.52)	
female	78 (45.08)	24 (30.76)	54 (69.23)	0.792
Age years				
median	65	63	66	
mean±SD	65±44	63±82	66±13	0156
Pancreatic head adenocarcinoma	143 (82.65)	46 (32.16)	97 (67.83)	0.895
Cholangiocarcinoma of the distal choledochus				
Carcinoma of the Ampulla of Vater	30 (17.34)	6 (20.00)	24 (80.00)	0.964
Jaundice	165 (95.37)	50 (30.30)	115 (69.69)	0.445
Epigastric pain	43 (24.85)	13 (30.23)	30 (69.76)	0.843
Body weight loss	134 (77.45)	50 (30.30)	84 (62.68)	0.745
Diabetes mellitus	84 (48.55)	41 (48.80)	43 (51.19)	0.122

[22-27]. However, to date, no technique for pancreatic anastomosis has been proven to be the most effective in decreasing rates of pancreatic leakage. Which method is optimal to restore pancreatic digestive continuity remains controversial. It has been claimed that PG is a better pancreatic reconstruction method because it reduces the incidence and severity of POPF. Four recent meta-analyses based on eight randomized control trials have concluded that the POPF rate is significantly lower in PG than in PJ [28-30]. We recommended sutureless PG as an alternative to PJ because of the following advantages: (i) there is an absence of trans-pancreatic sutures because the trans-parenchymal sutures cause

damage to the pancreatic tissues and leakage; (ii) PG is performed for a short time because of the proximity of the stomach to the pancreas; (iii) the stomach wall is well-vascularized and thick; (iv) there is early detection of intraluminal bleeding from the pancreatic remnant; (v) the pancreatic enzymes are inactive due to the high acidity in the stomach and a lack of enterokinase, which prevents a digestive damage to the PG; (vi) PG is isolated and is spaced apart from a. mesenterica superior, a. hepatica propria, v. portae and v. mesenterica superior; (vii) gastric decompression by a nasogastric tube eliminates gastric and pancreatic secretions, exerts less tension on PG, and can be used as a drainage if fistula occurs; and (viii)

PG decreases the number of anastomoses in a single loop of jejunum, reducing the probability of loop kinking. However, four functional flaws are inherent to PG: (i) PG is burdened with a high incidence of DGE; (ii) exocrine pancreatic secretion is reduced after PG due to atrophy of the remnant pancreas; (iii) pancreatic enzymes are activated by intestinal enterokinase and bile, which are lacking in the gastric secretion; (iv) the main pancreatic duct is clogged over time because of overgrowth of the gastric mucosa. In the present study. there were no differences in the incidence of DGE between the two groups (p=0.023). Retrocolic gastroenteric anastomosis, located to the left of the middle colic artery, is associated with a lower incidence of DGE. Patients in both the groups had an equal need of pancreatic enzyme (Kreon 25000 UI; AB-BOTT) replacement therapy for a period of 6 months. After this period, pancreatic enzyme replacement therapy was necessary in individual cases from both the groups. The preventive gastroscopies performed over a period of 6 months revealed a functionally active main pancreatic duct in patients with PG, without overgrowth of the gastric mucosa. Hence, sutureless PG appears useful in situations where high morbidity is expected after PD. The typical situation in which this technique should be utilized is when the pancreatic parenchyma is soft and the main pancreatic duct has a diameter of less than 2 mm. Another typical situation arises when Whipple's procedures are performed in low-volume centers.

As any study, the present study has some limitations. In particular, the retrospective nature of the study and a potential for era bias can be considered limitations. Additionally, all patients were treated in a high-volume center after being evaluated by a multidisciplinary team, which may introduce a selection bias. Despite this, we found the clinical audit to be helpful for evaluating our subjective impressions in terms of whether the outcomes had improved after we introduced the standard use of sutureless PG.

In conclusion, the evaluation of short-term outcomes indicated that sutureless PG is a feasible technique that is safe, i.e., it is associated with lower rates of life-threatening complications than single-layer duct-to-mucosa PJ. If long-term functional results confirm similar outcomes, sutureless PG could become a valid alternative for pancreatic anastomosis after PD in patients with soft pancreas and high morbidity. However, it should not be forgotten that successful management of pancreatic anastomosis depends to

		Single-layer duct-to-mucosa	Sutureless	
Variable	Total	PJ	PG	Р
N	173 (100)	52 (30.05)	121 (69.94)	0.93
Pancreatic parenchyma				
firm	30 (17.34)	-	30 (29.41)	0.00
soft	124 (71.67)	52 (30.05)	72 (70.58)	0.04
Pancreatic duct diameter (mm)				
<2 mm	113 (65.31)	-	60 (49.58)	0.00
>2 mm	60 (34.68)	52 (30.05)	61 (50.41)	0.49
Duration of operation (h)				
Median	4.0	4.4	4.1	
mean±SD	4±4	4±1	4±1	0.04
Blood loss (mL) during elective surgery				
<500	144 (83.23)	42 (80.76)	102 (84.29)	0.03
500-1000	24 (13.87)	8 (15.38)	16 (13.22)	0.35
>1000	5 (2.89)	2 (3.84)	3 (2.47)	0.42
Hospital stay (day)				
median	12 (6-64)	14 (6-68)	13 (6-62)	
mean±SD	12±14	13±22	11±18	0.02
Surgical mortality	5 (2.89)	4 (7.69)	I (0.82)	0.02
Surgical morbidity	52 (30.05)	14 (26.92)	38 (31.40)	
Grade I	8 (4.62)	3 (5.76)	5 (4.13)	
Grade II	26 (15.02)	2 (3.84)	24 (19.83)	
Grade Illa/b	8 (4.62)	I (I.92)	7 (5.78)	
Grade IVa/b	5 (2.89)	4 (7.69)	I (0.82)	
Grade 5	5 (2.89)	4 (7.69)	I (0.82)	0.03
POPF	20 (11.52)	10 (19.23)	10 (8.26)	0.04
Grade A	7 (4.06)	2 (3.84)	5 (4.13)	0.02
Grade B	9 (5.20)	4 (4.69)	5 (4.13)	0.04
Grade C	4 (2.31)	4 (7.69)	-	0.00
Late extraluminal PPH	-	-	-	
Grade A	-	-	-	
Grade B	I (0.57)	I (I.92)	-	
Grade C	3 (1.73)	3 (5.76)	-	0.00
Late intraluminal PPH		•		
Grade A	I (0.57)	-	I (0.82)	
Grade B	3 (1.73)	-	3 (2.47)	
Grade C	-	-	-	0.00
Intra-abdominal abscess	5 (2.89)	4 (7.69)	I (0.82)	0.01
Septic shock	5 (2.31)	4(7.69)	1(0.82)	0.01
Pancreatic enzyme replacement therapy	( )	` /	` /	
6 months postoperatively	41 (23.69)	13(25.00)	28 (23.14)	0.53

a greater extent on a rigorous surgical technique combined with experience that is pertinent to

my hemorrhage; PD: pancreaticoduodenectomy

the procedure at hand rather than on the type of technique by itself.

Ethics Committee Approval: This study was approved by the Ethics Committee of the Naval Hospital, Varna 9010 (Decision No: 2016-29).

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author contributions: Concept - D.K., G.K.; Design - D.K., G.K.; Supervision - D.K.; Resource - D.K., G.K.; Materials - D.K., G.K.; Data Collection and/or Processing - D.K., G.K.; Analysis and/or Interpretation - D.K.; Literature Search - D.K.; Writing - D.K, G.K.; Critical Reviews - D.K.

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**Conflict of Interest:** No conflict of interest was declared by the authors.

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