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Original Article

Perioperative or intraoperative blood transfusion increases the risk of postoperative pancreatic fistula following pancreaticoduodenectomy

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Abstract

Aim: Postoperative pancreatic fistula (POPF) is one of the most common causes of morbidity following pancreaticoduodenectomy (PD). The optimum way of reducing the prevalence of POPF is to prevent its development. In this study, we attempted to identify the potential perioperative risk factors of POPF and suggestions were made for its.

Material and Methods: In this study, we included patients who had undergone PD from January 2010 to April 2020. POPF was defined as per the International Study Group on Pancreatic Fistula. The patients were followed up for 30 days for POPF.

Results: Fifty-two (52) patients whose medical records were available were enrolled. POPF developed in 19 patients (36.5%). Grade-A POPF developed in six patients (11.5%), Grade-B POPF in eight patients (15.4%), and Grade-C POPF in five patients (9.6%). Percutaneous drainage was performed in a patient with Grade-B POPF, and reoperation was performed for five patients with Grade-C POPF. In univariate analysis, female sex (p=0.03), perioperative blood transfusion (p=0.03), and the number of harvested lymph nodes ≥12 (p=0.008) were related to POPF. In logistic regression analysis, the number of harvested lymph nodes ≥12 (p=0.005) and female sex (p=0.03) were independent risk factors of POPF. Although perioperative blood transfusion increased the POPF risk, the effect was not statistically significant (p=0.10).

Conclusion: POPF was observed to be the most important cause of morbidity following PD in our study. We also found that reduce the POPF risk, it is important to avoid blood transfusion whenever possible.

Keywords: Pancreatic fistula; whipple; risk factor; morbidity; outcome

INTRODUCTION

Pancreaticoduodenectomy (PD) is a standard surgical procedure for malignant or benign diseases of the pancreatic head or the periampullary region. Although the incidence of operative mortality is <5% in patients undergoing PD, postoperative morbidity can be up to 60% (1). Postoperative pancreatic fistula (POPF) is one of the most common causes of morbidity following PD and its prevalence ranges from 6%–25% (2,3). POPF can cause other abdominal complications, such as abdominal abscess, delayed gastric emptying, postoperative delayed bleeding, and pseudoaneurysm, leading to increased morbidity, mortality, hospital stay, and cost (2,4). Many methods have been used to prevent the occurrence of POPF, such as anastomosis techniques, stent use, and somatostatin use (5-9). Although all these approaches can lower the severity of POPF, the optimal method has not been defined yet (10). In this study, perioperative risk factors that may cause POPF were investigated and recommendations have been established for the management of risk factors.

MATERIAL and METHODS

Patients and data collection

The medical records of patients who had undergone PD at the Karadeniz Technical University General Surgery Clinic from January 2010 to April 2020 were scanned. Age; sex; comorbidity; American Society of Anesthesiologists (ASA) score; body mass index (BMI); preoperative interventions, such as percutaneous transhepatic cholangiography (PTC), endoscopic retrograde cholangiopancreatography (ERCP), and biopsy; preoperative bilirubin values; operation duration; the degree of intraoperative hemorrhage; pancreatic anastomosis techniques; diameter of the catheter used in pancreatic anastomosis; perioperative blood transfusion; POPF; other postoperative complications; interventions for postoperative care; length of hospital stay; mortality; and

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results of the pathological examination were examined. The Clavien Dindo classification was used to evaluate the postoperative complications. The patients were followed up for 30 days for POPF and the other complications. This retrospective study was approved by the Ethics Committee of the Karadeniz Technical University (decision number: 2020-167). Informed consent was obtained from all the subjects for study participation.

Surgical approach and technique

Preoperative routine laboratory tests and tumor markers were evaluated examine the organ functions of patients for whom a mass had been detected in the periampullary region following abdominal complaints. Tissue diagnosis was established with ERCP, endoscopic ultrasonography, or percutaneous biopsy in 20 patients. The thorax and abdomen cavity were scanned using tomography to detect local and distant metastases of pancreatic disease. PTC or ERCP was performed in patients who had preoperative jaundice as per the surgeon's preference. Preoperative enteral and/or parenteral nutrition support was provided to patients who had experienced nutritional problems.

In all patients, pancreaticoduodenectomy (PD) was performed. Portal vein (PV) resection was not performed for any patient. The following stages of surgery differed as per the surgeon's preference. Pylor-sparing or distal gastrectomy was performed. Gastrointestinal continuity was achieved with either pancreaticogastrostomy (PG) or pancreaticojejunostomy (PJ). The single-loop technique or dual-loop technique (Roux-en-Y) was used for PJ that was performed in the form of double-layer mucosa-mucosa anastomosis. PG was performed in the form of one layer mucosa-serosa anastomosis. In patients with a suitable pancreatic duct, a catheter was used for anastomosis.

Definition of POPF

POPF was defined as per the definition given by the International Study Group on Pancreatic Fistula as follows (11): a) Grade-A pancreatic fistula (biochemical leak): any measurable volume of drainage fluid output via operatively or postoperatively placed drains on or after postoperative day three with amylase content >3 times the upper normal serum value, b) Grade-B pancreatic fistula: persistent drainage >3 weeks, clinically relevant change in POPF management, percutaneous or endoscopic drainage, angiographic procedures for hemorrhage, and a sign of infections without organ failure, c) Grade-C pancreatic fistula: reoperation, organ failure, and death. The grades were determined only after the fistula was completely healed.

Statistical analyses

The data were statistically analyzed using the SPSS 22 software. The Shapiro–Wilk test was used for testing normality. Measurement data are expressed as the median (range) values. Fisher chi-square and Mann-Whitney U tests were used to compare the categorical and continuous variables of the two groups. All the variables were incorporated into a univariate analysis. Statistically significant variables in the univariate analysis were incorporated into a multivariate logistic regression analysis to identify the independent risk factors. P values <0.05 were considered statistically significant.

RESULTS

A total of 52 patients whose medical records were available were included in the study (Table 1). Of these, 31 were men (59.6%) and 21 were women (40.4%). The mean patient age was 63 (17–79) years. The most common tumor location was the head of the pancreas, and the least common location was the duodenum. No patients had major vascular invasion [superior mesenteric vein (SMV), PV, and superior mesenteric artery] and metastasis. While PD with pylori preservation was performed for 15 patients, and PD with distal gastrectomy was performed in 36 patients. The median operative duration was 310 (220–480) min, and the median amount of intraoperative bleeding was 400 (50–7000) ml. One patient with intraoperative transverse mesocolon invasion underwent simultaneous right hemicolectomy. Less than 90°C tumor invasion in the SMV was detected in four patients. While SMV was seamlessly dissected from the tumor in two patients, primary repair was performed to SMV due to iatrogenic injury in two patients. In one patient with no tumor invasion, primary repair was performed for PV following iatrogenic injury. Right nephrectomy was performed in two patients because they had accompanying renal cell carcinoma, and excision was performed in one patient with an accompanying retroperitoneal mass. PG was performed in 27 patients and PJ was performed in 25 patients for gastrointestinal reconstruction. Catheters were placed in the pancreatic duct in 14 patients who underwent PG and in nine patients who underwent PJ. PJ was performed as a dual-loop technique (Roux-en-Y) in 18 patients and as a single-loop technique in seven patients. Postoperative complications developed in 37 patients (71.6%) (Table 2). The most common complication was POPF (19/52, 36.5%). Grade-A POPF developed in six patients (11.5%), Grade-B POPF developed in eight patients (15.4%), and Grade-C POPF developed in five patients (9.6%). Owing to the development of postoperative complications, eight patients were re-operated, and percutaneous drainage was performed in four patients (Table 3). Percutaneous drainage was performed in a patient who had Grade-B POPF because of an intra-abdominal abscess. One of five patients with Grade-C POPF was re-operated postoperatively on the second day because of upper gastrointestinal bleeding, one on the 9th day due to bile leakage, and one on the 20th day due to POPF. We performed fistula repair in the second postoperative month for one POPF patient and fistulojejunostomy in the seventh postoperative month for another patient. The median length of hospital stay of POPF patients was longer by 10 days. Six (11.5%) patients died during the study period. This included five patients who died because of intra-abdominal bleeding and one who died because of PV bleeding. All patients with mortality had POPF (p=0.001).

Table 1. Demography of patients who underwent pancreaticoduedonectomy

Parameters	n=52
Age (years)	63 (17-79)
Gender (n, %)	
Female	21 (40.4)
Male	31 (59.6)
ASA score (n, %)	
I	11 (19.2)
II	26 (50.0)
III	10 (21.2)
IV	3 (5.8)
Comorbidity (Yes) (n, %)	
Hypertension	17 (32.7)
Diabetes Mellitus type 2	9 (17.3)
Chronic obstructive pulmonary disease	3 (5.8)
Coronary artery disease	2 (3.8)
Chronic kidney failure	1 (1.9)
Cerebrovascular accident	1 (1.9)
Epilepsy	1 (1.9)
Pulmonary embolism	1 (1.9)
Pancytopenia	1 (1.9)
Preoperative total bilirubin (mg/dL)	2.8 (0.3-27.1)
Preoperative Ca 19.9 (U/L)	52.5 (0.6-7590)
Preoperative interventions (n, %)	33 (63.5)
Percutaneous transhepatic cholangiography	10 (19.2)
Endoscopic Retrograde Cholangiopancreatog-raphy	23 (44.2)
Biopsy	20 (38.5)
Preoperative biopsy diagnosis (n, %)	20 (38.5)
Adenocarcinom	11 (21.6)
Dysplasia	4 (7.7)
Adenoma	3 (5.8)
Suspicious cytology	1 (1.9)
Benign	1 (1.9)
Tumor placement (n, %)	
Pancreas head	27 (51.9)
Ampulla of water	21 (40.4)
Distal choledochus	3 (5.8)
Duedonum	1 (1.9)
Operation duration (minute) (n, %)	310 (220-480)
Intropeative hemorrhage (ml) (n, %)	400 (50-7000)
Tumor stage (n, %)	
0	10 (19.2)
1	9 (17.3)
2	20 (38.5)
3	9 (17.3)
na	4 (7.7)
Lenght of stay (day)	16 (1-39)
Mortality (Yes) (n, %)	6 (11.5)

ASA: American Society of Anesthesiologists

Table 2. Postoperative complications in patients who underwent pancreaticoduedoectomys

TPostoperative complications		n=52
I. Abdominal (n, %)		26 (50.0)
	Pancreatic fistula	19 (36.5)
	Grade A	6 (11.5)
	Grade B	8 (15.4)
	Grade C	5 (9.6)
	Surgical site infection	11 (21.2)
	Deep surgical site infection	3 (5.8)
	Organ/space surgical site infection	8 (15.4)
	Biliary leak	6 (11.5)
	Gastrointestinal hemorrhage	5 (9.6)
	Intraabdominal hemorrhage	4 (7.7)
	Lymphatic leak	1 (1.9)
II. Non-abdominal (n, %)		19 (36.5)
	Atelectasis	6 (11.5)
	Acute renal failure	4 (7.7)
	Pneumonia	3 (5.8)
	Hypovolemic shock	3 (5.8)
	Urine tract infection	3 (5.8)
	Septic shock	2 (3.8)
	Multiorgan dysfunction syndrome	1 (1.9)
	Thrombocytopenia	1 (1.9)
	Respiratory failure	1 (1.9)
	Pleural effusion	1 (1.9)
	Pulmonary embolism	1 (1.9)
	Gastric atony	1 (1.9)
	Superior mesenteric artery thrombosis	1 (1.9)
	Portal vein thrombosis	1 (1.9)
	Delirium	1 (1.9)
	Ileus	1 (1.9)

Table 3. Interventions for postoperative complications

Parameters	n=52
Reoperation (n, %)	8 (15.4)
Biliary leak	4 (7.7)
Gastrointestinal hemorrhage	2 (3.8)
Postoperative pancreatic fistula	1 (1.9)
Portal vein hemorrhage	1 (1.9)
Intraabdominal abscess	1 (1.9)
Suspected anastomotic leak+ positive physical examination	1 (1.9)
Percutaneous drainage (n, %)	4 (7.7)
Intrabdominal abscess	2 (3.8)
Lymphatic leak	1 (1.9)
Biliary leak	1 (1.9)

Pathologically, the most common diagnosis was adenocarcinoma (80.8%, 42/52). The other specimen pathologies were as follows: adenoma in four patients (7.7%); chronic pancreatitis in two (3.8%); and solid pseudopapillary tumor, tuberculosis, benign pathology, and intraductal papillary mucinous neoplasm in one (1.9%). The median number of harvested lymph nodes was 14 (2–31).

In one-way analysis, female sex (p=0.01), perioperative blood transfusion (p=0.03), and the number of harvested lymph nodes ≥12 (p=0.002) were related to POPF (Table 4). In logistic regression analysis, the number of harvested lymph nodes ≥12 (OR: 3.290, p=0.005) and female sex (OR: 2.477, p=0.02) were independent variables for POPF risk. Although perioperative blood transfusion increased the risk of POPF, the increase was not significant (OR: 1.411, p=0.10) (Table 5).

Table 4. Risk factors for postoperative pancreatic fistula

Parameters	Pancreatic fistula n=21	No-pancreatic fistula n=31	p
Age (years)	59 (17-75)	60 (36-79)	0.54
Gender (n, %)			0.01
Male	7 (22.6)	24 (77.4)	
Female	12 (57.1)	9 (42.9)	
BMI (kg/m2)	25 (21-33)	23 (19-38)	0.07
Comorbidity (Yes) (n, %)	9 (34.6)	17 (65.4)	0.90
ASA score (n, %)			0.11
III	11 (29.7)	26 (70.3)	
≥III	8 (53.3)	7 (46.7)	
Preoperative total bilirubin (mg/dL)	1.9 (0.3-12.8)	4.7 (0.7-27.1)	0.34
Operation duration (minute)	300 (220-450)	310 (255-460)	0.37
Intraoperative hemorrhage (ml)	400 (50-1300)	350 (50-1100)	0.72
Operation type (n, %)			0.11
Pylor preserving pancreaticoduedonectomy (n, %)	8 (53.3)	7 (46.7)	
Standard pancreaticoduedonectomy	13 (35.1)	24 (64.9)	
Anastomosis type (n, %)			0.62
Pancreaticogastrostomy	9 (33.3)	18 (66.7)	
Pancreaticojejunostomy	10 (40.0)	15 (60.0	
Pancreaticojejunostomy (n, %)			0.66
Isolated Roux loop	8 (44.4)	10 (55.6)	
Conventional	2 (28.6)	5 (71.4)	
Use of catheter (Yes) (n, %)	10 (43.5)	13 (56.5)	0.36
Blood transfusion (Yes) (n, %)	13 (52.0)	2 (48.0)	0.03
Additional surgery (Yes) (n, %)	4 (40.0)	6 (60.0)	0.80
Feeding jejunostomy (Yes) (n, %)	1 (16.7)	5 (66.7)	0.28
Clavien-Dindo classification (n, %)			0.90
≤2	13 (37.1)	22 (62.9)	
>2	6 (35.3)	11 (64.7)	
Harvested number of lymph nodes (n, %)			0.002
12	11 (47.8)	12 (52.2)	
≥12	1 (4.8)	20 (95.2)	
Tumor stage (n, %)			0.22
≤2	13 (33.3)	26 (66.7)	
>2	5 (55.6)	4 (44.4)	
Lenght of hospital stay (day)	26 (9-37)	16 (7-34)	0.001
Mortality (Yes) (n, %)	6 (100.0)	0 (0)	0.001

BMI: Body mass index, ASA: American Society of Anesthesiologists

Table 5. Univariate and multivariate analysis for postoperative pancreatic fistula

Parameters	Univariate analysis				Multivariate analysis			
	OR	%95 C.I.		P	OR	%95 C.I.		p
		Lower	Upper			Lower	Upper	
Female gender	4.571	1.368	15.278	0.01	2.477	1.296	109.460	0.02
Blood transfusion (Yes)	3.792	1.143	12.582	0.03	1.411	0.751	22.391	0.10
Harvested lymph nodes ≥12	6.661	1.673	26.118	0.002	3.290	2.683	268.285	0.005

OR: Odds ratio, C.I.: Confidence imterval

DISCUSSION

POPF is one of the most important and potentially severe complications observed after PD. There is no optimal method to reduce POPF, and research has focused on the evaluation of risk factors (10,12,13). Many risk factors have been reported for POPF, such as age, fat distribution, operation duration, blood loss, perioperative blood transfusion, pathological diagnosis, the diameter of the main pancreatic duct, and texture of pancreatic parenchyma (14,15). Awareness among physicians about the risk factors allows early detection and prevention of POPF. POPF developed in 19 patients (36.5%) who underwent PD in our study. We found that female sex, perioperative blood transfusion, and the number of harvested lymph nodes ≥12 were risk factors for POPF. It has been previously reported that male sex is associated with POPF (54.23% vs. 42.35%, p=0.008) (10). To our knowledge, this is the first study to report that female sex is an independent variable for POPF risk (57.1 vs. 22.6%, p=0.01; respectively). Blood transfusions are performed for about 50% of PD patients (16). Post-bleeding blood transfusion benefits by providing tissue perfusion, oxygen delivery to the tissues, and hemodynamic stability (17). However, perioperative blood transfusion has been associated with an increased risk of POPF (18). In our study, perioperative blood transfusion was an independent variable for POPF risk (52.0% vs. 22.2%, p=0.03).

The most common surgical procedures for pancreatic stump reconstruction following PD are PJ and PG. Both these procedures have a risk of POPF. It is unclear which procedure is better, and the choice is based on the surgeon's personal preference (19). Although the evidence value is low in a Cochrane review, the POPF risk is reportedly lower in patients with PG (21.4% vs. 24.3%; respectively) (19). However, many studies have reported that PG is superior to PJ for the prevention of POPF following PD (1,20-22). In our study, POPF developed in nine patients who underwent PG and 10 patients who underwent PJ. For POPF, there was no difference between PG and PJ (33.3% vs. 40.0%, p=0.62; respectively).

The single-loop technique and dual-loop technique (Roux-en-Y) have been used in PJ reconstruction to reduce POPF after PD. The dual-loop technique is predicted to achieve PJ anastomosis healing and reduce other intra-abdominal complications related to pancreatic leakage. Although several case series have reported convincing results (23,24), the dual-loop technique (Roux-en-Y) for PJ is not associated with a lower prevalence of POPF than the single-loop technique (25,26). In our study, the single-loop technique was used in 18 of the patients with PJ, and the dual-loop technique (Roux-en-Y) was used in seven PJ patients. There was no significant difference between the single-loop technique and the dual-loop technique in terms of POPF occurrence (44.4% vs. 28.6%, p=0.66; respectively).

The most important cause of morbidity and mortality in patients who performed PJ following PD, especially in patients with soft pancreas, is POPF, with a prevalence of 5%–40%. Thus, one study has recommended the insertion of a stent in the pancreatic duct to lower the risk of POPF (27). However, a Cochrane review reported that the use of stents had no significant effect on the occurrence of POPF (28). Winter et al. also reported that the use of stents, although not statistically significant, was associated with a lower prevalence rate of POPF in the hard pancreas and a higher rate in the soft pancreas (8). In our study, we placed internal stents in the pancreatic duct of 23 patients who had undergone PJ. We could not detect a significant effect of stent use on the occurrence of POPF (43.5% vs. 56.5%, p=0.36; respectively).

Standard pancreaticoduodenectomy (SPD) is a complicated surgery that is performed for treating pancreatic malignant tumors. Pylorus-preserving pancreaticoduodenectomy (PPPD) preserves the storage and digestive functions of the stomach and reduces postoperative complications of partial gastrectomy, potentially improving the postoperative life quality of patients (29). The POPF difference between SPD and PPPD remains controversial. Lin et al. reported that the POPF incidence was higher in the SPD group, while Seiler et al. reported that the incidence of POPF was higher in the PPPD group (30,31). Some studies have reported that the POPF incidence is similar to the use of both methods (29,32). In our study, no difference was found between PPPD and SPD in terms of POPF incidence (53.3% vs. 35.1%, p=0.11; respectively).

For optimal pancreatic cancer staging, the lymph node must be removed, containing at least 15 lymph nodes or

approximately 10 negative LNs for curative intent (33). When removing the lymph node in pancreatic cancer surgery, the balance between intraoperative difficulties and postoperative complications should be ensured. Because the effect of removing more lymph nodes on the long-term survival of the patient is limited (34).

Our study has certain limitations: (1) Due to the retrospective nature of the study, information about parameters that could affect the POPF risk, such as pancreatic duct diameter and pancreatic tissue stiffness, could not be obtained, (2) The relatively small sample size may have reduced the effectiveness of some subgroup analyses, and (3) The study was performed at a single center; therefore, POC and their management protocols may differ from that followed in other centers.

CONCLUSION

This study showed that POPF was the most common and most important complication after PD. To reduce the POPF risk, blood transfusion should be avoided when possible.

Conflict of Interest: The author declares that they have no conflict of interest.

Informed consent: Informed consent was not obtained.

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Ethical approval: This study was approved by the Institutional Ethics Committee (decision number: 2020-167) and conducted in compliance with the ethical principles according to the Declaration of Helsinki.

REFERENCES

1. Qin H, Luo L, Zhu Z, et al. Pancreaticogastrostomy has advantages over pancreaticojejunostomy on pancreatic fistula after pancreaticoduodenectomy. A meta-analysis of randomized controlled trials. Int J Surg 2016;36:18-24.
2. Ramacciato G, Mercantini P, Petrucciani N, et al. Risk factors of pancreatic fistula after pancreaticoduodenectomy: a collective review. Am Surg 2011;77:257-69.
3. Chen JS, Liu G, Li TR, et al. Pancreatic fistula after pancreaticoduodenectomy: Risk factors and preventive strategies. J Cancer Res Ther 2019;15:857-63.
4. Ke ZX, Xiong JX, Hu J, et al. Risk Factors and Management of Postoperative Pancreatic Fistula Following Pancreaticoduodenectomy: Single-center Experience. Curr Med Sci 2019;39:1009-18.
5. Bassi C, Falconi M, Molinari E, et al. Reconstruction by pancreaticojejunostomy versus pancreaticogastrostomy following pancreatectomy: results of a comparative study. Ann Surg 2005;242:767-73.
6. Pan SB, Geng W, Zhou DC, et al. One-layer versus two-layer duct-to-mucosa pancreaticojejunostomy after pancreaticoduodenectomy: study protocol for a randomized controlled trial. Trials 2016;17:407.
7. Fujii T, Sugimoto H, Yamada S, et al. Modified Blumgart anastomosis for pancreaticojejunostomy: technical improvement in matched historical control study. J Gastrointest Surg 2014;18:1108-15.
8. Winter JM, Cameron JL, Campbell KA, et al. Does pancreatic duct stenting decrease the rate of pancreatic fistula following pancreaticoduodenectomy? Results of a prospective randomized trial. J Gastrointest Surg 2006;10:1280-90.
9. Shan YS, Sy ED, Lin PW. Role of somatostatin in the prevention of pancreatic stump-related morbidity following elective pancreaticoduodenectomy in highrisk patients and elimination of surgeon-related factors: prospective, randomized, controlled trial. World J Surg 2003;27:709-14.
10. Hu BY, Wan T, Zhang WZ, et al. Risk factors for postoperative pancreatic fistula: Analysis of 539 successive cases of pancreaticoduodenectomy. World J Gastroenterol 2016;22:7797-805.
11. Bassi C, Marchegiani G, Dervenis C, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. Surgery 2017;161:584-91.
12. Xiong JJ, Tan CL, Szatmary P, et al. Metaanalysis of pancreaticogastrostomy versus pancreaticojejunostomy after pancreaticoduodenectomy. Br J Surg 2014;101:1196–208.
13. Allen PJ, Gönen M, Brennan MF, et al: Pasireotide for postoperative pancreatic fistula. N Engl J Med 2014;370:2014–22.
14. Sandini M, Malleo G, Gianotti L. Scores for prediction of fistula after Pancreatoduodenectomy: A Systematic Review. Dig Surg 2016;33:392-400.
15. Polanco PM, Zenati MS, Hogg ME, et al. An analysis of risk factors for pancreatic fistula after robotic pancreaticoduodenectomy: outcomes from a consecutive series of standardized pancreatic reconstructions. Surg Endosc 2016;30:1523-9.
16. Kim Y, Bagante F, Gani F, et al. Nomogram to predict perioperative blood transfusion for hepatopancreaticobiliary and colorectal surgery. Br J Surg 2016;103:1173–83.
17. Yuruk K, Bartels SA, Milstein DM, et al. Red blood cell transfusions and tissue oxygenation in anemic hematology outpatients. Transfusion 2012;52:641-6.
18. Bansal SS, Hodson J, Khalil K, et al. Distinct risk factors for early and late blood transfusion following pancreaticoduodenectomy. Hepatobiliary Pancreat Dis Int 2018;17:349-357.
19. Cheng Y, Briarava M, Lai M, et al. Pancreaticojejunostomy versus pancreaticogastrostomy reconstruction for the prevention of postoperative pancreatic fistula following pancreaticoduodenectomy. Cochrane Database Syst Rev 2017;9:CD012257.
20. Topal B, Fieuws S, Aerts R, et al. Pancreaticojejunostomy versus pancreaticogastrostomy reconstruction after pancreaticoduodenectomy for pancreatic or periampullary tumours: a multicentre randomized trial. Lancet Oncol 2013;14:655-62.
21. Menahem B, Guittet L, Mulliri A, et al. Pancreaticogastrostomy is superior to

pancreaticojejunostomy for prevention of pancreatic fistula after pancreaticoduodenectomy: an updated meta-analysis of randomized controlled trials. Ann Surg 2015;261:882-87.
22. Que W, Fang H, Yan B, et al. Pancreaticogastrostomy versus pancreaticojejunostomy after pancreaticoduodenectomy: a meta-analysis of randomized controlled trials. Am J Surg 2015;209:1074-82.
23. Sutton CD, Garcea G, White SA, et al. Isolated Roux-loop pancreaticojejunostomy: a series of 61 patients with zero postoperative pancreaticoenteric leaks. J Gastrointest Surg 2004;8:701–5.
24. Erdem H, Çetinkünar S, Aziret M, et al. Can isolated pancreaticojejunostomy reduce pancreas fistula after pancreaticoduodenectomy with Roux-en-Y reconstruction? Ulus Cerrahi Derg 2016;32:248-51.
25. Tani M, Kawai M, Hirono S, et al. Randomized clinical trial of isolated Roux-en-Y versus conventional reconstruction after pancreaticoduodenectomy. Br J Surg 2014;101:1084-91.
26. Klaiber U, Probst P, Knebel P, et al. Meta-analysis of complication rates for single-loop versus dual-loop (Roux-en-Y) with isolated pancreaticojejunostomy reconstruction after pancreaticoduodenectomy. Br J Surg 2015;102:331-40.
27. Kamoda Y, Fujino Y, Matsumoto I, et al. Usefulness of performing a pancreaticojejunostomy with an internal stent after a pancreatoduodenectomy. Surg Today 2008;38:524-48.
28. Dong Z, Xu J, Wang Z, et al. Stents for the prevention of pancreatic fistula following pancreaticoduodenectomy. Cochrane Database Syst Rev 2016;5:CD008914.
29. Zhao R, Chang Y, Wang X, et al. Pylorus-preserving pancreaticoduodenectomy versus standard pancreaticoduodenectomy in the treatment of duodenal papilla carcinoma. Oncol Lett 2018;15:6368-76.
30. Lin PWi Lin YJ: Prospective randomized comparison between pylorus-preserving and standard pancreaticoduodenectomy. Br J Surg 1999:86:603-7.
31. Seiler CA, Wagner M, Bachmann T, et al. Randomized clinical trial of pylorus-preserving duodenopancreatectomy versus classical Whipple resection-long term results. Br J Surg. 2005:92:547-56.
32. Tran KT, Smeenk HG, van Eijck CH, et al. Pylorus preserving pancreaticoduodenectomy versus standard Whipple procedure: A prospective, randomized, multicenter analysis of 170 patients with pancreatic and periampullary tumors. Ann Surg 2004:240:738-45.
33. Schwarz RE, Smith DD. Extent of lymph node retrieval and pancreatic cancer survival: information from a large US population database. Ann Surg Oncol 2006;13:1189-2000.
34. Pedrazzoli S. Extent of lymphadenectomy to associate with pancreaticoduodenectomy in patients with pancreatic head cancer for better tumor staging. Cancer Treat Rev 2015;41:577-87.