Surgical techniques and postoperative management to prevent postoperative pancreatic fistula after pancreatic surgery

Hiromichi Kawaida, Hiroshi Kono, Naohiro Hosomura, Hidetake Amemiya, Jun Itakura, Hideki Fujii, Daisuke Ichikawa

ORCID number: Hiromichi Kawaida (0000-0003-3507-0167); Hiroshi Kono (0000-0001-6843-0814); Naohiro Hosomura (0000-0003-0483-3635); Hidetake Amemiya (0000-0002-4520-755X); Jun Itakura (0000-0001-9070-9133); Fujii Hideki (0000-0002-5247-4844); Daisuke Ichikawa (0000-0003-0093-2206).

Author contributions: All authors contributed equally to this paper regarding the conception and design of the study, literature review and analysis, drafting and clinical revision and editing, and final approval of the final version.

Conflict-of-interest statement: No potential conflict of interest. No financial support.

Open-Access: This is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

Manuscript source: Invited manuscript

Received: March 20, 2019
Peer-review started: March 20, 2019
First decision: June 10, 2019
Revised: June 20, 2019

Abstract

Postoperative pancreatic fistula (POPF) is one of the most severe complications after pancreatic surgeries. POPF develops as a consequence of pancreatic juice leakage from a surgically exfoliated surface and/or anastomotic stump, which sometimes cause intraperitoneal abscesses and subsequent lethal hemorrhage. In recent years, various surgical and perioperative attempts have been examined to reduce the incidence of POPF. We reviewed several well-designed studies addressing POPF-related factors, such as reconstruction methods, anastomotic techniques, stent usage, prophylactic intra-abdominal drainage, and somatostatin analogs, after pancreaticoduodenectomy and distal pancreatectomy, and we assessed the current status of POPF. In addition, we also discussed the current status of POPF in minimally invasive surgeries, laparoscopic surgeries, and robotic surgeries.

Key words: Postoperative pancreatic fistula; Pancreaticoduodenectomy; Pancreateojejunostomy; Pancreatogastrostomy; Distal pancreatectomy; Prophylactic drainage; Somatostatin analogs

©The Author(s) 2019. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: We reviewed recent reports concerning postoperative pancreatic fistula (POPF)-related factors, such as reconstruction methods, anastomotic techniques, stent usage, prophylactic intra-abdominal drainage, and somatostatin analogs, after pancreaticoduodenectomy and distal pancreatectomy, and we assessed the current status of POPF.
INTRODUCTION

The incidence of pancreatic cancer has increased in both Asian and Western countries. Surgical resection is the cornerstone of treatment for this aggressive disease. With advances in surgical techniques and perioperative management, the operative mortality of pancreaticoduodenectomy (PD) in high-volume centers has decreased to less than 3% [1-3]. Postoperative pancreatic fistula (POPF), however, develops frequently, and previous prospective studies have reported an incidence of more than 10% [4-7]; therefore, POPF is the most frequent lethal complication after pancreatectomy, regardless of the type of procedure.

POPF is believed to be primarily caused by the leakage of pancreatic juice into the abdomen; it can lead to intraperitoneal abscesses and also occasional hemorrhage, which cause life-threatening conditions with mortality rates of up to 40% [4,6,7-11]. In clinical practice, various ingenuities have been attempted to prevent the development of POPF, and some randomized controlled trials (RCTs) have been conducted to compare different optional procedures.

In this review, we aimed to summarize the current status of POPF in pancreatic surgery and to present the recent findings of the reconstruction methods of PD, stump closure methods of distal pancreatectomy (DP) and evidence for the risk factors and preventive treatment for the development of POPF.

DEFINITION AND INCIDENCE

Pancreatic fistula was defined by the International Study Group on Pancreatic Fistula (ISGPF) in 2005 [12] and was revised in 2016 [4]. The ISGPF’s definition divides pancreatic fistula into biochemical fistula and clinically significant POPF.

A grade A POPF is called a biochemical fistula and is defined as measurable fluid output on or after postoperative day 3, with an amylase content higher than three times the upper normal serum level; a grade A POPF has no clinical impact on the normal postoperative pathway. Clinically significant POPFs are classified as grades B and C. A grade B POPF requires one of the following conditions: an endoscopic or radiological intervention, a drain in situ for > 3 wk, clinical symptoms without organ failure, or clinically relevant change in POPF management. Whenever a major change in clinical management or deviation from the normal clinical pathway is required or organ failure occurs, the fistula shifts to a grade C POPF [4,6].

Following this definition, the incidence of clinically significant POPF has been reported to vary from approximately 1% to 36% [6,21-27]. There are different causes related to the development of POPF in the PD and distal pancreatectomy (DP) [28] procedures, and the incidence is generally recognized to be relatively higher in DP than in PD. Therefore, we discuss recent findings and evidence of POPF in PD and DP separately as described later in this review.

PANCREATICODUODENECTOMY

PD remains the only curative treatment option for malignant and some borderline/benign tumors of the pancreatic head and peripancreatic region even though the excessive invasive procedure is associated with high morbidity and mortality rates. One of the most important factors of morbidity and mortality following PD is the incidence of POPF. Many previous studies have reported several risk factors in PD, such as gender (male) [19], BMI > 25 kg/m [20], anastomotic method [6,21], external stent [22], fasting blood glucose level < 108.0 mg/dL [23], etc. However, the most reliable consensus risk factors for POPF after PD are small pancreatic duct (≤ 3 mm) and soft pancreas [6,21-27], which reflect the possibility that adequate anastomosis of the pancreatic duct and active exocrine function are deeply involved in the development of POPF. Therefore, various surgical techniques have been attempted to prevent
POPF.

**Reconstruction methods**

Identifying the best anastomosis technique for pancreatic surgery has remained controversial thus far. Of the several available techniques, pancreatogastrostomy (PG) and pancreatojejunostomy (PJ) are the most commonly performed. Some RCTs\(^{36-40}\) and meta-analyses\(^{36-44}\) have compared PG and PJ. Topal et al\(^{32}\) reported comparative results of the occurrences of POPFs (grade B or C) in an RCT with 329 patients. They stratified the randomization according to the pancreatic duct diameter, and the results clearly demonstrated that the occurrence of POPF was significantly lower after PG than after PJ (OR = 2.86; 95% CI: 1.38-6.17; \(P = 0.02\)). Conversely, a recent German multicenter RCT\(^{31}\) demonstrated that there was no significant difference in the rate of grade B/C fistulas after PG vs PJ (20% vs 22%, respectively, \(P = 0.617\)). Each RCT has variable eligibility criteria for patients with diseases and suture methods for reconstruction; therefore, their conclusions should be interpreted with caution.

Several meta-analysis results on this issue have been reported and demonstrated the apparent superiority of PG in the risk for POPF despite the slight difference in the included studies\(^{36-44}\). However, PJ was found to have physiological advantages compared to PG although the follow-up periods were relatively short\(^{36-40}\).

In recent retrospective studies, a significantly higher postoperative atrophic change of the pancreatic parenchyma and frequent severe steatorrhea were reported in the PG group during long-term follow-up periods\(^{45-49}\). Additionally, a higher frequency of impaired glucose tolerance after PG has been reported compared to PJ during the follow-up period. Considering the function of the remnant pancreas, the use of only short-term results is not sufficient for comparison\(^{44,49}\).

Reconstruction after pancreatic surgery remains under debate, and it is impossible to confidently conclude which method is better after PD. Therefore, the reconstruction method should be determined based on the patient and tumor characteristics, such as pancreatic duct diameter, consistency of pancreas, and oncological prognosis (Table 1).

**Anastomotic techniques**

In recent years, several simple and facilitating surgical anastomotic techniques have been reported. A transpancreatic U-suture technique was devised by Blumgart et al\(^{40}\), and the ratio of clinically relevant PFs was reported to be only 6.9% in the original report. Other researchers have conducted confirmatory studies and reported that the occurrence rates of POPFs were less than 5%\(^{41,42}\). Furthermore, favorable short-term outcomes have been achieved by some modifications of the novel technique. Fujii et al\(^{39}\) reported on the modified Blumgart’s method. The differences between the original and modified method are described below. The original Blumgart’s method used four to six transpancreatic jejunal seromuscular U-shaped sutures to approximate the pancreas and the jejunum\(^{40}\), whereas the modified Blumgart’s method used only one to three sutures. In the original method, the sutures were tied at the pancreatic wall, whereas the sutures were tied at the ventral wall of the jejunum in the modified method. The results showed that the ratio of clinically relevant POPFs was significantly lower after the modified Blumgart’s method than after Kakita’s method (2.5% vs 36%, respectively)\(^{43}\). However, other studies did not confirm the superiority of the Blumgart or modified Blumgart’s methods in preventing POPFs compared to Kakita’s method or conventional interrupted sutures\(^{44,45}\).

The most beneficial feature of duct-to-mucosa PJ is the secure drainage of pancreatic juice into the intestinal lumen. The anastomatic procedure, however, is not always easy, particularly with narrow pancreatic ducts. An invagination method in which the cross-sectional surface was inserted into the intestinal lumen might be a substitutive option of duct-to-mucosa PJ as an easier reconstruction method.

Nearly a decade ago, two types of invagination methods were examined to reduce POPF after PD in large-scale RCTs\(^{46-48}\) (Table 2). Peng et al\(^{46}\) performed binding PJ, in which the stump of the jejunum was everted and the remnant of the pancreas and the everted jejunum were anastomosed in a circular fashion; finally, the everted jejunum was restored to wrap over the pancreatic stump. Conversely, Berger et al\(^{48}\) performed invagination PJ in endo-to-side anastomosis. Both RCTs clearly revealed significantly decreases in POPF rates in invagination PJ compared to conventional duct-to-mucosa PJ; likewise, the tendency was more remarkable in soft pancreases compared to hard pancreases. Recently, however, several RCTs were unable to confirm the superiority in POPF rates with invagination PJ. Although RCTs are recognized to provide the most reliable results suggesting future evidence-based medicine, the results could be affected by many factors, including patient-related, tumor-related, and surgeon-
Table 1 Characteristics and intraoperative data of 7 randomized controlled trials included studies comparing pancreatogastrostomy vs pancreatojejunostomy

| First author | Country    | Publication year | Setting                  | n (PG/PJ) | PG group | PJ group | Technique                        |
|--------------|------------|------------------|--------------------------|-----------|----------|----------|----------------------------------|
| Fernandez-Cruz et al \[30\] | Spain     | 2008             | Single center            | 108 (53/55) | 24/29    | 25/30    | Double layer with stent           |
| Wellner et al \[31\] | Germany   | 2012             | Single center            | 116 (59/57) | 36/23    | 29/28    | Invagination                     |
| Topal et al \[32\] | Belgium   | 2013             | Multiple centers         | 329 (162/167) | N/A      | N/A      | Double or single layer           |
| Figueras et al \[33\] | Spain     | 2013             | Multiple centers         | 123 (65/58) | 34/31    | 33/58    | Double or single layer           |
| El Nakeeb et al \[34\] | Egypt     | 2014             | Single center            | 90 (45/45) | 26/19    | 22/23    | Double layer                     |
| Greendar et al \[35\] | Canada    | 2015             | Single center            | 98 (48/50) | 25/23    | 38/32    | Double layer with or without stent |
| Keck et al \[5\] | Germany   | 2016             | Multiple centers         | 320 (171/149) | 95/66    | 83/62    | Invagination                     |

PG: Pancreatogastrostomy; PJ: Pancreateojejunostomy; N/A: Not applicable.

related factors. In fact, for patient-related factors, Senda et al \[57\] indicated the possibility of reducing POPFs in invagination PJ for high risk patients with a soft pancreas although they revealed the non-superiority of invagination over duct-to-mucosa PJ with the risk of POPF as their primary endpoint. To overcome surgeon-related factors, Bai et al \[59\] conducted a similar RCT in which all procedures were performed by the same surgeon. They demonstrated that the overall POPF and morbidity rates were similar between invagination and duct-to-mucosa PJ; however, clinically relevant POPFs and severe complications were more frequent in the invagination PJ group.

Some meta-analyses were conducted concerning the superiority of invagination PJ on the rate of POPFs and demonstrated that invagination PJ did not reduce POPF rates and other adverse events compared to duct-to-mucosa PJ \[63,64\]; however, many of the analyzed studies were heterogeneous in several respects. The duct-to-mucosa PJ was performed by the conventional anastomotic technique, and therefore, invagination PJ does not appear significantly better than the current duct-to-mucosa PJ with respect to the incidence of POPF for low risk patients at least.

Stent or no-stent

Another concern is the necessity of stent placement for PJ anastomosis, whether a stent should be used, and whether the stent should be external or internal stent. Non-stent PJ anastomosis is the ideal and physiologically favorable procedure because stenting is sometimes associated with tube-related complications, digestive fluid loss, and subsequently impaired digestive and absorptive functions with external stents. Several previous studies, however, have reported that draining the pancreatic juice from the pancreaticojejunal anastomosis with a stent placed in the main pancreatic duct is an effective method to promote the healing of the anastomotic site by preventing pancreatic trypsin from corroding the anastomotic site during the early period after surgery, thereby reducing the rate of POPFs after PD \[65,66\].

Several RCTs have been conducted to examine the short-term outcomes of patients with external or internal stents compared to those without stents after PJ \[65-69\]. However, there were no differences in the incidence of POPFs or other morbidities between the stent (external or internal) and the no-stent groups. One meta-analysis reported that an external stent for PJ decreased the rates of POPFs \[65\]; however, another recent comprehensive systematic review with a meta-analysis reported that there was no significant difference in the rates of POPFs, in-hospital mortality, re-operation, delayed gastric emptying, wound infection, and intra-abdominal abscesses between the stent and no-stent groups. They only found that the postoperative overall morbidity was lower and the total hospital stay was shorter in the external stent group compared to the no-stent group \[71\].
Table 2 Characteristics and intraoperative data of 7 randomized controlled trials included studies comparing invagination vs duct-to-mucosa

| First author       | Country | year | D to M | Inv | Pancreatic parenchyma (soft/hard) | stents | Use of smatostatin analogs | Result                      |
|--------------------|---------|------|--------|-----|---------------------------------|--------|---------------------------|-----------------------------|
| Peng et al[56]      | China   | 2007 | 111    | 106 | 39/72                           | NA     | No                        | No                          | Invagination significantly reduced POPF |
| Berger et al[57]    | United States | 2008 | 97     | 100 | 50/47                           | NA     | No                        | No                          | Invagination significantly reduced POPF |
| Senda et al[58]     | Japan   | 2018 | 61     | 59  | 31/30                           | Yes    | Yes                       | NA                          | NS                          |
| Bai et al[59]       | China   | 2016 | 64     | 68  | 36/28                           | 47 used | 52 used                   | 2 used                      | 12 used                     | D to M significantly reduced POPF |
| El Nakeeb et al[60] | Egypt   | 2018 | 53     | 54  | 25/28                           | Intraoperative temporary | Intraoperative temporary | NA                          | NS                          |
| Singh et al[61]     | India   | 2017 | 97     | 96  | 42/55                           | 15 used | 26 used                   | 38 used                     | 31 used                     | NS                          |
| Maggiori et al[62]  | France  | 2010 | 25     | 22  | 11/14                           | NA     | NA                        | 11 used                     | 10 used                     | NS                          |

D to M: Duct to mucosa; Inv: Invagination; NA: Not available; NS: Not significant.

Other studies have reported comparable results in POPFs between external and internal stents for PJ anastomosis. Compared to an internal stent, an external stent has the advantage of more complete diversion of pancreatic juice from the PJ anastomosis and the prevention of activation of pancreatic enzymes by bile juice[66]. However, there are shortcomings of more surgical procedures, liquid loss, and the risk of local peritonitis after removal of the stent tube[72]. Moreover, an external stent may develop tube-related complications, kinks, and obstructions[73]. Wang et al[74] reported that the length of pancreas juice in the stent tube was the predicting factor for clinical POPF. Internal drainage with a stent is considered one of the optimal methods to avoid exposing pancreatic juice to the PJ anastomosis without digestive fluid loss and impaired digestive and absorptive function[72,73,75]. However, the real-time drainage status of pancreatic juice cannot be monitored, and the stent rarely migrates into the bile duct with internal stents. Several RCTs have reported that internal stents tend to reduce the POPF ratio compared to external stents; however, no difference was observed in the incidence of POPF between the two stent methods[76-78]. This is also reported in past RCTs that internal stents did not reduce the POPF ratio compared to non-stents[79,80].

Almost all of the previous studies were conducted in single centers. Therefore, additional multicenter RCTs comparing the efficacy of external pancreatic duct stenting versus internal pancreatic duct stenting versus non-stenting must be performed, particularly for cases with a soft pancreas.

The use of surgical tissue adhesives

Several studies evaluated the effect of topical application of fibrin glue applied to the pancreatic anastomosis[81-85]. When a pancreatic tissue tearing occurred, it was expected to be covered by the fibrin sealant. Although there was also a report that evaluated the effect[81], most reports concluded that fibrin sealants might have no effect on POPF in patients undergoing pancreatoduodenectomy[82-85].

Also, omental wrapping was expected to reduce the incidence of the POPF and intra-abdominal hemorrhage[86,87]. Although there have been reports of reduced intra-abdominal complications, this method did not significantly reduce POPF[86-89].
DISTAL PANCREATECTOMY

The primary indications for DP include both benign and malignant tumors of the pancreatic body and tail. Although the mortality associated with DP has decreased in recent decades because of improvements in operative techniques and perioperative managements, morbidity remains high. The most ominous complication is POPF, which may cause life-threatening conditions. The incidence of clinical POPF (Grade B or C) after DP ranged from 5% to 40%[20,21,90-98], this rate is higher than that after PD. However, POPFs that occur after DP are usually clinically less severe compared to those that occur after PD[99,100]. Various surgical techniques that involve transecting the pancreatic parenchyma have been attempted to reduce the incidence of POPF after DP. In recent years, these techniques include hand-sewn closure and stapler closure.

Numerous risk factors for POPF after DP have been previously reported, particularly pancreatic thickness[90,93,100,101], age[90,93], and BMI[90,93,96,99]. In patients with a thick pancreas, the stapler method may crush the pancreas parenchyma, which leads to the breakage of small pancreatic ducts and causes the development of POPF[99]. BMI may influence the physiological condition of the pancreas because fibrosis or fatty changes may occur[90,93]. In any case, the most important factor to reduce the incidence of POPF is to close the stump of the remnant pancreas completely at the time of surgery.

Stump closure methods

Recently, the most commonly used techniques for stump closure are hand-sewn closure or stapler closure. Hand-sewn closure is a common technique that involves suturing the pancreas stump in a fish-mouth fashion after ligating the main pancreatic duct. Conversely, the stapler method has become a widely used technique for pancreatic stump closure in recent years because of its convenience. Zhou et al.[102] performed a meta-analysis comparing stapler versus hand-sewn closure of the pancreatic stump; they described that indicate the superiority of the stapler method (22.1% vs 31.2%) although it did not reach statistical significance. However, in a multicenter randomized Dispatch trial that was conducted among 21 centers in Europe in 450 randomized patients (of whom 296 were analyzed), the stapler closure method did not reduce the incidence of POPF compared to hand-sewn closure for DP (stapler closure, 32% vs hand-sewn closure, 28%)[103]. Although the occluded areas of the stapler develop local necrotizing pancreatitis and may cause POPF[104], the stapler method is used as the standard technique. However, this technique experiences difficulties when the cutting line of the pancreas is on the right side of the portal vein.

To reinforce the staple line, RCTs assessing the use of several different materials have been reported. Three RCTs and one meta-analysis attempted to demonstrate the effect of reinforcement with an absorbable fibrin sealant patch (TachoSil®) over the pancreatic stump[102-106]. This technique was unable to reduce POPFs compared to conventional methods of the stapler only. However, Montorsi et al. reported that the amylase level of the drainage fluid was significantly lower in the TachoSil® group on day 1[106]. This result suggests that TachoSil® may be useful in sealing the cutting line of the pancreas. However, many reports described that fibrin sealants might lead no difference in POPF[107].

The DISCOVER trial was conducted to investigate the technique of remnant pancreatic reinforcement by use of a teres ligament patch to prevent POPF. Although this clinical trial was unable to significantly reduce the rate of POPFs (P = 0.1468), the rates of clinically relevant POPFs with coverage and without coverage were 22.4% and 32.9%, respectively, resulting in a 10% reduction in clinical POPF[108].

A reinforced stapler (REINF) with bioabsorbable materials is used with the expectation of further effects. Kawaida et al.[109] clarified the safety of the REINF for pancreatic stump closure during DP. A 2013 meta-analysis including five retrospective and five prospective studies compared staplers without reinforcement (STPL) vs REINF. Although the incidence of POPF was 24% and 17%, respectively, and tended to be lower in REINF, the superiority of reinforcement was not proven[109]. Additionally, a recent RCT reported that REINF significantly reduced POPF to a clinically relevant degree compared to STPL (11.4%, and 28.3%, respectively)[109]. Conversely, Kondo et al. reported that REINF for pancreatic stump closure during DP does not reduce the incidence of clinically relevant PF compared to STPL. However, in patients with a pancreatic transection line thickness of less than 14 mm, a significant difference was shown in the incidence of clinically POPF (4.5% vs 21.0% in the reinforced stapler vs. bare stapler groups, respectively, P =0.01)[109]. Jensen et al[108] reported that polyglycolic acid mesh induces an inflammatory reaction immediately after insertion, and this may promote adhesion and prevent leakage of pancreatic juice from the cutting line of the remnant pancreas. As described above, although the efficacy of REINF has not been sufficiently proven, the incidence of POPF tends to
decrease compared to previous techniques.

Pancreatoenteral anastomosis

Three retrospective studies have demonstrated that pancreatoenteral anastomosis (PE) of the pancreatic stump significantly reduced POPFs compared to stump closure only\(^{[111-113]}\). In these reports, the main pancreatic duct was ligated in both groups, and the anastomosis of the PE was performed by the invagination method. Octreotide was administered in two of these studies\(^{[107,109]}\), and in the other study, PJ and PG were both performed in the PE group and hand-sewn closure and stapler closure were both performed in the stump closure group\(^{[112]}\). Additionally, the rate of postoperative hemorrhage was high in all reports. However, the statistical power of these studies was limited because of the small sample size of patients.

Two recent RCTs have been reported. Kawai \textit{et al}\(^{[114]}\) compared PJ of the pancreatic stump with the stapler without reinforcement method. In this study, anastomosis was performed in a non-stented duct-to-mucosa fashion using a single layer of interrupted absorbable suture and the addition of a seromuscular-pancreatic anastomosis. However, the ratio of POPFs in PJ tends to be lower than that in stapler closure, but the difference is not significant. Furthermore, Uemura \textit{et al} investigated whether PG of the pancreatic stump reduced clinical POPFs compared to hand-sewn closure\(^{[115]}\). In this RCT, PG was performed as described below. Interrupted 5-0 absorbable monofilament sutures were placed between the gastric mucosa and the main pancreatic duct, and interrupted sutures were placed between the wall of the pancreatic parenchyma and the gastric seromuscular layer. Additionally, an internal stenting tube was inserted for internal drainage of the pancreatic juice into the stomach. Hand-sewn closure was performed so that the main pancreatic duct was ligated and the cutting line of the remnant pancreas was closed using the fish-mouth technique. The incidence of intra-abdominal fluid collection was significantly lower in the PG group than in the hand-sewn group. However, PG did not reduce the incidence of clinical POPF and other complications compared to hand-sewn closure. Thus, the efficacy of PE has not yet been demonstrated.

However, the above two RCTs have a problem: even if the main pancreatic duct is reconstructed, small branches remain always present and may be a source of pancreatic leakage. Additionally, PE may cause the activation of pancreatic enzymes by enterokinase. Furthermore, in recent years, there has been a tendency to perform this operation with a laparoscopic procedure. It seems that adaptation should be carefully selected.

LESS INVASIVE SURGERIES

Less invasive surgeries have recently become more popular worldwide in pancreatic resection. In laparoscopic DP, a linear stapler is commonly used for stump closure of the pancreas. Therefore, the incidence of POPF from the pancreatic stump is thought to be generally similar between laparoscopic and open DP. In fact, some retrospective well-designed studies using a propensity score-matching analysis and systematic review with non-randomized trials have suggested that there was no significant difference in clinically relevant POPF although an RCT has never been conducted to examine this issue\(^{[116-120]}\). More recently, a robotic approach has been attempted for DP and compared with the laparoscopic approach concerning perioperative outcomes. The study demonstrated that there was no significant difference in the rate of the occurrence of POPF although spleen-preserving DP was performed more frequently in the robot-assisted approach\(^{[119-121]}\).

Palanivelu \textit{et al}\(^{[117]}\) reported the results of an RCT comparing the laparoscopic approach for PD with the open approach. In this study, 64 of 268 patients were randomized to each group and assessed for eligibility. The results suggested that laparoscopic PD offered significant benefits in terms of hospital stay although there was no significant difference in the overall complication rates including POPF. Other 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\(^{[122]}\).

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 (MIS-PD), including open assistance and open PD (OPD), with a focus on clinically relevant POPF\(^{[124]}\). In this study, 16% of patients underwent MIS-PD, of whom 15% converted to unplanned conversion. The rates of POPF were slightly greater in MIS-PD compared to OPD (15.3% vs 13.0%, respectively, \(P = 0.03\)); however, MIS-PD was not an independent factor associated
with POPF in the adjusted multivariable analysis. Other studies compared the rates of postoperative 30-d overall complications between laparoscopic PD and robotic PD [125,126]. This type of approach was not correlated with the overall complication rates.

The advantage of MIS-PD 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. Some surgeons have recently developed more suitable techniques for laparoscopic or robotic PJ [125,126], and additional experiences and the development of new devices may improve perioperative outcomes.

**PERIOPERATIVE MANAGEMENT**

**Intraperitoneal drainage**

Drains are frequently placed at the time of pancreatic surgery. However, adaptation and drain insertion and the time of removal have not yet been clarified. Drains allow for the evacuation of blood, pancreatic juice, bile, and lymphatic fluid. However, drains may increase the chances of retrograde infection. Moreover, there is a possibility that the indication may differ depending on whether the operation to be performed is PD or DP.

One of the issues concerning intraperitoneal drainage is the need for prophylactic intraperitoneal drainage. There was no significant difference in the incidence of POPFs in a comparison between DP with and without a drain [127,128]. However, Van Buren et al. [129] and Fisher et al. [130] reported that elimination of routine intraoperative drain placement was associated with a statistically significant decrease in the length of hospital stay. In these reports, the incidence of clinical POPF tended to decrease in DP without drainage [129-132].

Two RCTs on PD with different results have been reported. In one RCT, the PANDRA trial, 395 patients were analyzed, and comparisons were made between patients with routine prophylactic intraperitoneal drains or those without drains. In the group with drains inserted, the drains were removed on the second postoperative day or later, whenever the amylase and lipase values of the drain fluid were lower than three times the serum amylase activity and there was less than 150 ml of fluid. Otherwise, the drains were not removed until the criteria were fulfilled. This trial concluded that prophylactic drainage was not necessary because clinical POPF was significantly reduced in the patients without drainage although there was no significant difference in the overall morbidity [133]. Another RCT was interrupted prematurely because the PD without prophylactic intraperitoneal drainage had a higher mortality compared to PD with drainage, although the criteria for drain removal were similar [134]. A subsequent meta-analysis reported that patients without prophylactic drainage had a significantly higher mortality despite fewer overall major complications and readmissions [135]. Patients who had a low risk of POPF may have benefits from avoiding routine intraperitoneal drainage [136]. The need for drainage after pancreatic resection continues to be controversial, particularly following PD.

Another issue is the timing of drain removal. First, the criteria for early drain removal are not defined. Kawai et al. [136] reported improved outcomes with early drain removal after pancreatoduodenectomy. In this prospective cohort study, early drain removal was defined as removal on POD4 and as late as or after POD8. Adachi et al. [137] demonstrated the improvement of POPF after DP with early drain removal. The authors defined early drain removal as POD1 and late removal as POD5; there was a 0% incidence of CR-POPF in the early group compared to 16% in the late removal group. However, in this study, gabexate mesilate, octreotide, and antibiotics were administered to patients with a high drain amylase level. Bassi et al. [138] randomized 114 patients who underwent either PD or DP with early removal on POD3 or late removal on or after POD4. They concluded that early drain removal was associated with a decreased rate of POPF. However, in this study, Penrose drains were used, and patients whose amylase value in the drain was greater than 5000 U/mL were excluded. Although the best time to remove the drain remains unclear, prolonged placement of a drain might be a major cause of POPF because retrograde intra-abdominal infection may occur [133,136,139].

**Somatostatin analogs**

Octreotide and octreotide analogs are well known to inhibit the effects of pancreatic exocrine secretion [140], and they have been used as prophylactic agents to prevent POPF after pancreatic surgery. Therefore, the efficacy of octreotide after pancreatic
surgery in the prevention of POPF was expected. Two RCTs reported the efficacy of a prophylactic somatostatin analog for the prevention of POPF following PD\cite{145,142}; however, these RCTs were reported before the definition given by ISGPF in 2005. Conversely, a recent RCT and meta-analysis evaluating somatostatin analogs did not demonstrate the reduction in the incidence of POPF after pancreatic surgery\cite{143-151}. In particular, Nakeeb et al\cite{152} evaluated the effect of the postoperative use of octreotide on the postoperative outcomes of PD in patients with soft pancreas and nondilated pancreatic duct. In this study, pancreatogastrostomy was used for pancreatic reconstruction. The results showed that octreotide did not affect the incidence of POPF and other complications.

Recently, the efficacy of pasireotide, which displays a broader affinity to somatostatin receptor subtypes and acts than octreotide, was noted. Allen et al\cite{153} investigated whether pasireotide can be used to prevent POPFs in both PD and DP. In this RCT, patients received subcutaneous pasireotide or a placebo twice daily beginning preoperatively on the morning of the operation and continuing for seven days. P) was typically performed by a duct-to-mucosa anastomosis, and pancreatic transection during DP was performed either with the use of a stapler with or without reinforcement or with hand-sewn closure. The RCT on pasireotide demonstrated the significant reduction of POPF after PD and DP. Furthermore, this drug reduced the rate of POPFs in patients who had nondilated pancreatic duct (normal pancreas).

Although there have also been reports that the use of pasireotide after pancreatic surgery does not decrease clinical POPF\cite{154,155}, a therapeutic effect by pasireotide is expected. Unfortunately, a key problem of pasireotide is cost-effectiveness because it is expensive. However, some studies have reported that pasireotide appears to be a cost-saving treatment following PD\cite{156-158}. Indeed, the efficacy of pasireotide in reducing the incidence of POPF or other complications remains unclear, and it may be cost-effective in patients with a high risk of POPF.

**CONCLUSION**

POPF is still regarded as the most relevant and severe complication of pancreatic surgery, and it might develop intra-abdominal infection, hemorrhage, shock, and consequently death in some cases. Furthermore, POPF leads to increased health care costs and prolonged hospital stay. Several attempts to reduce the incidence of POPF have been made in recent years several RCTs described about methods of the reconstruction and anastomotic techniques in PD, stump closure in DP and need for stents; however, standard methods with which to minimize the incidence of POPF have not yet been established for both PD and DP. The perioperative management of POPF also remains controversial including the best time to remove the drain and the need of somatostatin analogs. Therefore, innovative attempts and further further RCTs should be performed to standardize surgical techniques and perioperative management.

**REFERENCES**

1. Büchler MW, Wagner M, Schmied BM, Uhl W, Friess H, Zgraggen K. Changes in morbidity after pancreatic resection: toward the end of completion pancreatectomy. *Arch Surg* 2003; 138: 1310-1314; discussion 1315 [PMID: 14662530]
2. Kimura W, Miyata H, Gotoh M, Hira I, Kenjo A, Kitagawa Y, Shimada M, Baba H, Tomita N, Nakagoe T, Sugihara K, Mori M. A pancreatoduodenectomy risk model developed from 8575 cases from a national single-race population (Japanese) using a web-based data entry system: the 30-day and in-hospital mortality rates for pancreatoduodenectomy. *Ann Surg* 2014; 259: 773-780 [PMID: 24253151 DOI: 10.1097/SLA.000000000000263]
3. Cameron JL. He J. Two thousand consecutive pancreaticoduodenectomies. *J Am Coll Surg* 2015; 220: 530-536 [PMID: 25724606 DOI: 10.1016/j.jacsurg.2014.12.031]
4. Bassi C, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M, Allen P, Andersson R, Asbnan HJ, Besselink MG, Conlon K, Del Chiaro M, Falconi M, Fernandez-Cruz L, Fernandez-Del Castillo C, Fingerhut A, Friess H, Gouna DJ, Hackert T, Izbski J, Lillemoe KD, Neoptolemos JP, Olah A, SCHulick R, Shrikhande SV, Takada T, Takaori K, Traverso W, Vollmer CR, Wolfgang CL, Yeo CJ, Salvia R, Buchler M. International Study Group on Pancreatic Surgery (ISGPS). The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. *Surgery* 2017; 161: 584-591 [PMID: 28040257 DOI: 10.1016/j.surg.2016.11.014]
5. Keck T, Wellner UF, Bahra M, Klein F, Sick O, Niedergethmann M, Wilhelm TJ, Farkas SA, Börner T, Bruns C, Kleespies A, Kleespies K, Mihaljevic AL, Uhl W, Chromik A, Fendrich V, Heeger K, Padberg W, Hecker A, Neumann UP, Junge K, Kaiff JC, Glöwka TR, Werner J, Knobel P, Piso P, Mayr M, Izbski J, Vashist Y, Bronsert P, Bruckner T, Limprecht R, Diener MK, Rossion I, Wegener I, Hopt UT. Pancreatogastrostomy Versus Pancreatocistojunostomy for REConstruction After PANCreastrod adenectomy (RECOPanC, DRKS 00000767)- Perioperative and Long-term Results of a Multicenter Randomized Controlled Trial. *Ann Surg* 2016; 263: 440-449 [PMID: 26135690 DOI: 10.1097/SLA.0000000000001288]
Su SJ, Shen SL, Li SQ, Hu WJ, Hua YP, Kuang M, Liang LJ, Peng BG. Risk factors and outcomes of postoperative pancreatic fistula after pancreatico-duodenumectomy: an audit of 532 consecutive cases. BMC Surg 2015; 15: 34 [PMID: 25588752 DOI: 10.1186/s12893-015-0011-2]

Chen BP, Bennett S, Hertens KA, Balaa FK, Martel G. Use and acceptance of the International Study Group for Pancreatic Fistula (ISGPF) definition and criteria in the surgical literature. HPB (Oxford) 2018; 20: 69-75 [PMID: 28927654 DOI: 10.1016/j.hpb.2017.08.022]

van der Gaag NA, Harmsen K, Eshuis WJ, Busch ORC, van Gulik TM, Gouma DJ. Pancreatoduodenectomy associated complications influence cancer recurrence and time interval to death. Eur J Surg Oncol 2014; 40: 551-558 [PMID: 24388408 DOI: 10.1016/j.ejso.2013.12.012]

Loos M, Strobel O, Legominski M, Dietrich M, Hinz U, Brenner T, Heininger A, Weigand MA, Bächler MW, Hackert T. Postoperative pancreatic fistula: Microbial growth determines outcome. Surgery 2018; 164: 1185-1190 [PMID: 30217397 DOI: 10.1016/j.surg.2018.07.007]

Hackert T, Hinz U, Pausch T, Fesenbeck I, Strobel O, Schneider L, Fritz S, Bächler MW. Postoperative pancreatic fistula: We need to redefine grades B and C. Surgery 2016; 159: 872-877 [PMID: 26603847 DOI: 10.1016/j.surg.2015.09.014]

Pedrazzoli S, Lissi G, Pasquall C, Ragazzi R, Berselli M, Spreti C. Postoperative pancreatic fistulas: preventing severe complications and reducing reoperation and mortality rate. Ann Surg 2009; 249: 97-104 [PMID: 19106683 DOI: 10.1097/SLA.0b013e318192746c]

Bassi C, Derenvis C, Butturini G, Fingerbut A, Yeo C, Izbicki J, Neoptolomos J, Sarr M, Traverso W, Buchler M; International Study Group on Pancreatic Fistula Definition. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery 2005; 138: 8-13 [PMID: 16003309]

Schäfer M, Möllhaupt B, Clavien PA. Evidence-based pancreatic head resection for pancreatic cancer and chronic pancreatitis. Ann Surg 2002; 236: 137-148 [PMID: 12170015]

Bassi C, Butturini G, Molinari E, Mascetta G, Salvia R, Falconi M, Gumbs A, Pederdzoli P. Pancreatic fistula rate after pancreatic resection. The importance of definitions. Dig Surg 2004; 21: 54-59 [PMID: 14707394]

Marchegiani G, Andranellio S, Salvia R, Bassi C. Current Definition of and Controversial Issues Regarding Postoperative Pancreatic Fistulas. Gut Liver 2019; 13: 149-153 [PMID: 30419630 DOI: 10.5009/gnl18229]

Kakita A, Takahashi T, Yoshida M, Furuta K. A simpler and more reliable technique of pancreatocjejunostomy anastomosis. Surg Today 1996; 26: 532-535 [PMID: 880437]

Furuta K, Yoshida M, Itohashi K, Katagiri H, Ishii K, Takahashi Y, Watanabe M. The advantage of Kakita’s method with pancreatocjejunostomy anastomosis for pancreatic resection. Surg Technol Int 2008; 17: 150-155 [PMID: 18802895]

Eshmuninov D, Schneider MA, Tschoor C, Raptis DA, Kambakamara P, Muller X, Lesert M, Clavien PA. Systematic review and meta-analysis of the postoperative pancreatic fistula rates after 462 distal pancreatectomies: staplers do not decrease fistula rates. J Gastrointest Surg 2008; 12: 1691-1697; discussion 1697-9 [PMID: 18704597 DOI: 10.1016/j.gastrsurg.2008.09.014]

Ferrone CR, Warshaw AL, Rattner DW, Berger D, Zheng H, Rawal B, Rodriguez R, Thayer SP, Ferrone CR. Pancreatic fistula rates after 462 distal pancreatectomies: staplers do not decrease fistula rates. J Gastrointest Surg 2008; 12: 1691-1697; discussion 1697-9 [PMID: 18704597 DOI: 10.1016/j.gastrsurg.2008.09.014]

Nakamura T, Kondo K, Iwasa H, Saito M, Fujita M, Morizane T. Risk factors for postoperative pancreatic fistula after distal pancreatectomy with pancreaticojejunostomy. J Gastrointest Surg 2007; 11: 311-317 [PMID: 17231785 DOI: 10.1007/s11608-009-1071-3]

Hu BY, Wan T, Zhang WZ, Dong JH. Risk factors for postoperative pancreatic fistula: Analysis of 539 successive cases of pancreaticoduodenectomy. World J Gastroenterol 2016; 22: 7797-7805 [PMID: 27678363 DOI: 10.3748/wjg.v22.i47.7797]

Pedrazzoli S. Pancreaticoduodenectomy (PD) and postoperative pancreatic fistula (POPF): a systematic review and analysis of the POPF-related mortality rate in 60,739 patients reported from the English literature published between 1990 and 2015. Medicine (Baltimore) 2017; 96: e6858 [PMID: 28489778 DOI: 10.1097/MD.0000000000006858]

Ke Z, Cui J, Hu N, Yang Z, Chen H, Hu J, Wang C, Wu H, Nie X, Xiong J. Risk factors for postoperative pancreatic fistula: Analysis of 170 consecutive cases of pancreaticoduodenectomy based on the updated 2016 ISGPS classification and grading system. Medicine (Baltimore) 2018; 97: e12151 [PMID: 30710457 DOI: 10.1097/MD.0000000000012157]

Yang YM, Tian XD, Zhang Y, Wang WM, Wan YL, Huang YT. Risk factors of pancreatic leakage after pancreaticoduodenectomy. World J Gastroenterol 2005; 11: 2456-2461 [PMID: 15832417]

Lin QY, Zhang WZ, Xia HT, Long JH, Wan T, Liang B, Yang T, Dong JH. Analysis of risk factors for postoperative pancreatic fistula following pancreaticoduodenectomy. World J Gastroenterol 2014; 20: 17491-17497 [PMID: 25516663 DOI: 10.3748/wjg.v20.i46.17491]

Anzorge C, Strömmen L, Andrén-Sandberg Å, Lundell L, Herrington MK, Segersvård R. Structured intraoperative assessment of pancreatic gland characteristics in predicting complications after pancreaticoduodenectomy. Br J Surg 2012; 99: 1676-1682 [PMID: 22016074 DOI: 10.1002/bjs.7874]

El Nakeeb A, Salah T, Sultan A, El Hemaly M, Askir W, Ezazti H, Handy E, Atef E, El Hanafy E, El-Geidie A, Abdel Wahab M, Abdallah T. Pancreatic anastomotic leakage after pancreaticoduodenectomy. Risk factors, clinical predictors, and management (single center experience). World Surg 2013; 37: 1405-1418 [PMID: 23944109 DOI: 10.1002/wsg.240-1632186746]

Fernández-Cruz L, Cosa R, Blanco L, López-Boado MA, Astudillo E. Pancreatogastrostomy with gastric partition after pylorus-preserving pancreaticoduodenectomy versus conventional pancreaticojunostomy: a prospective randomized study. Ann Surg 2008; 248: 930-938 [PMID: 19022337 DOI: 10.1097/SLA.0b013e3181767377]

Regarding Postoperative Pancreatic Fistulas. Gut Liver 2019; 13: 149-153 [PMID: 30419630 DOI: 10.5009/gnl18229]
Kawaida H et al. Surgical techniques and postoperative management to prevent POPF

10.1097/SLA.0b013e3181f6ef7

31 Wellner UF, Sick O, Oschewski M, Adam U, Hop UT, Keck T. Randomized controlled single-center trial comparing pancreatogastrostomy versus pancreaticojejunostomy after partial pancreaticoduodenectomy. J Gastrointest Surg 2012; 16: 1680-1695 [PMID: 22744638 DOI: 10.1007/s11605-012-1940-4]

32 Topal B, Fievous S, Aerts R, Weerts J, Feryn T, Roeyen G, Bertrand C, Hubert C, Janssens M, Closet J; Belgian Section of Hepatobiliary and Pancreatic Surgery. Pancreatieoujejunostomy versus pancreaticojejunostomy reconstruction after pancreaticoduodenectomy for pancreatic or periampullary tumours: a multicentre randomised trial. Lancet Oncol 2013; 14: 655-662 [PMID: 23643139 DOI: 10.1016/S1470-2045(13)70126-8]

33 Figueras J, Sabater L, Planellas P, Muñoz-Forner E, Lopez-Ben S, Falgueras L, Sala-Palau C, Albiol M, Ortega-Serrano J, Castro-Gutierrez E. Randomized clinical trial of pancreaticojejunostomy versus pancreaticojejunostomy on the rate and severity of pancreatic fistula after pancreaticoduodenectomy. Br J Surg 2013; 100: 1597-1605 [PMID: 24264781 DOI: 10.1002/bjs.8256]

34 El Nakeeb A, Hamdy E, Sultan AM, Salih T, Askrt W, Ezzat H, Said M, Zeied MA, Abdallah T. Isolated Roux loop pancreaticojejunostomy versus pancreaticogastrostomy after pancreaticoduodenectomy: a prospective randomized study. HPB (Oxford) 2014; 16: 713-722 [PMID: 24467711 DOI: 10.1111/hpb.12210]

35 Grendar J, Ouelle JF, Sutherland FR, Bathe OF, Ball CG, Dixon E. In search of the best reconstructive technique after pancreaticoduodenectomy: pancreaticojejunostomy versus pancreaticogastrostomy. Can J Surg 2015; 58: 154-159 [PMID: 25799130]

36 Zhou Y, Yu J, Wu L, Li B. Meta-analysis of pancreaticojejunostomy versus pancreaticojejunostomy on occurrences of postoperative pancreatic fistula after pancreaticoduodenectomy. Asian J Surg 2015; 38: 155-160 [PMID: 25913732 DOI: 10.1016/j.asjsur.2015.02.002]

37 Que W, Fang H, Yan B, Li J, Guo W, Zhai W, Zhang S. Pancreaticojejunostomy versus pancreaticojejunostomy after pancreaticoduodenectomy: a meta-analysis of randomized controlled trials. Am J Surg 2015; 209: 1074-1082 [PMID: 25743406 DOI: 10.1016/j.amjsurg.2014.07.019]

38 Menahem B, Guittet L, Mulliri A, Alves A, Labrado J. Pancreaticogastrostomy is superior to pancreaticojejunostomy for prevention of fistula after pancreaticoduodenectomy: an updated meta-analysis of randomized controlled trials. Ann Surg 2015; 261: 882-887 [PMID: 24979604 DOI: 10.1097/SLA.0000000000000806]

39 Liu FB, Chen JM, Geng W, Xie SX, Zhao YJ, Yu LQ, Geng XP. Pancreaticogastrostomy is associated with significantly less pancreatic fistula than pancreaticojejunostomy reconstruction after pancreaticoduodenectomy: a meta-analysis of seven randomized controlled trials. HPB (Oxford) 2015; 17: 123-130 [PMID: 24888576 DOI: 10.1111/hpb.12279]

40 Hallet J, Zih FS, Deobald RG, Scheer AS, Law CH, Coburn NG, Karanicolas PJ. The impact of pancreaticojejunostomy versus pancreaticogastrostomy reconstruction on pancreatic fistula after pancreaticoduodenectomy: meta-analysis of randomized controlled trials. HPB (Oxford) 2015; 17: 113-122 [PMID: 25040921 DOI: 10.1111/hpb.12229]

41 Xiong JJ, Tan CL, Szatmary P, Huang W, Ke NW, Hui WM, Nunes QM, Sutton R, Liu XB. Meta-analysis of pancreaticojejunostomy versus pancreaticogastrostomy after pancreaticoduodenectomy. Br J Surg 2014; 101: 1196-1208 [PMID: 25042859 DOI: 10.1002/bjs.9553]

42 Riceti 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: 805-813 [PMID: 28717243 DOI: 10.1016/j.pan.2017.07.003]

43 Crippa S, Cicorri C, Randolph J, Partelli S, Belfiori G, Piccioli A, Parisi A, Falconi M. Pancreaticogastrostomy is comparable to pancreaticojejunostomy after pancreaticoduodenectomy: an updated meta-analysis of randomized controlled trials. Langenbecks Arch Surg 2016; 401: 427-437 [PMID: 27102322 DOI: 10.1007/s00423-016-1418-z]

44 Lynn Y, Li T, Cheng Y, Wang B, Chen L, Zhao S. Pancreaticojejunostomy Versus Pancreaticogastrostomy After Pancreaticoduodenectomy: An Up-to-date Meta-analysis of RCTs Applying the ISGPS (2016) Criteria. Surg Laparosc Endosc Percutan Tech 2018; 28: 139-146 [PMID: 29683977 DOI: 10.1097/01.sle.0000000000000730]

45 Tomimaru Y, Takeda Y, Kobayashi S, Marubashi S, Lee CM, Tanemura M, Nagano H, Kitagawa T, Dono K, Umeshita K, Wakasa K, Monden M. Comparison of postoperative morphological changes in remnant pancreas between pancreaticogastrostomy and pancreaticojejunostomy after pancreaticoduodenectomy. Pancreas 2009; 38: 203-207 [PMID: 19304518 DOI: 10.1097/MPA.0b013e3181e7722]

46 Nakamura H, Murakami Y, Uemura K, Hayashidani Y, Sudo T, Ohge H, Sueda T. Predictive factors for exocrine pancreatic insufficiency after pancreaticoduodenectomy with pancreaticogastrostomy. J Gastrointest Surg 2009; 13: 1213-1227 [PMID: 19415402 DOI: 10.1007/s11605-009-0896-5]

47 Niedergelthmann M, Dusch N, Widyaniwong R, Weiss C, Kienle P, Post S. Risk-adapted anastomosis for partial pancreaticoduodenectomy reduces the risk of pancreatic fistula: a pilot study. World J Surg 2010; 34: 1579-1586 [PMID: 20333381 DOI: 10.1007/s00268-010-0521-5]

48 Tran TC, van H Hof G, Kazemier G, Hop WC, Peck C, van Toorenenbergen AW, van Dekken H, van Eijck CH. Pancreatic fistula correlates with exocrine pancreatic insufficiency after pancreaticoduodenectomy. Dig Surg 2008; 25: 313-318 [PMID: 18814895 DOI: 10.1159/000106625]

49 Perivolotis K, Sioka E, Tatsios A, Stefanidis I, Zintzaras E, Zachoroulis D. Pancreatogastrostomy versus Pancreaticojejunostomy: An Up-to-Date Meta-Analysis of RCTs. Int J Surg Oncol 2017; 2017: 7526494 [PMID: 28798875 DOI: 10.1155/2017/7526494]

50 Grobmyer SR, Kooby D, Blumgart LH, Hochwald SN. Novel pancreaticojejunostomy with a low rate of anastomotic failure-related complications. J Am Coll Surg 2010; 210: 54-59 [PMID: 20213322 DOI: 10.1016/j.jamcollsurg.2009.09.020]

51 Kleespies A, Rentsch M, Seeliger H, Albertsmeyer M, Jauch KW, Bruns CJ. Blumgart anastomosis for pancreaticojejunostomy minimizes severe complications after pancreatic head resection. Br J Surg 2009; 96: 741-750 [PMID: 19526614 DOI: 10.1002/bjs.6634]

52 Lee YN, Kim WY. Comparison of Blumgart versus conventional duct-to-mucosa anastomosis for pancreaticojejunostomy after pancreaticoduodenectomy. Ann Hepatobiliary Pancreat Surg 2018; 22: 253-260 [PMID: 30215047 DOI: 10.14701/ahbps.2018.22.3.253]

53 Fujii T, Sugimoto H, Yamada S, Kanda M, Suenga M, Takami H, Hattori M, Inokawa Y, Nomoto S, Fujiwara M, Kodera Y. Modified Blumgart anastomosis for pancreaticojejunostomy: technical improvement in matched historical control study. J Gastrointest Surg 2018; 18: 1108-1115 [PMID: 2932...
Hirono S, Kawai M, Okada KI, Miyazawa M, Kitahata Y, Hayami S, Ueno M, Yamaue H. Modified Blumgart Mattress Suture Versus Conventional Interrupted Suture in Pancreaticojejunostomy During Pancreatectoduodenectomy: Randomized Controlled Trial. *Ann Surg* 2019; 209: 243-251 [PMID: 29697455 DOI: 10.1097/SLA.0000000000002322]

Kawakatsu S, Inoue Y, Mise Y, Ishizawa T, Ito H, Takahashi Y, Sairua A. Comparison of pancreaticojejunostomy techniques in patients with a soft pancreas: Kakita anastomosis and Blumgart anastomosis. *BMC Surg* 2018; 18: 88 [PMID: 30235532 DOI: 10.1186/s12893-018-0420-5]

Peng SY, Wang JW, Lau WY, Cai XJ, Mou YP, Liu YR, Li JT. Conventional versus binding pancreaticojejunostomy after pancreatoduodenectomy: a prospective randomized trial. *Ann Surg* 2007; 245: 692-698 [PMID: 17457161]

Berger AC, Howard TJ, Kennedy EP, Sauter PK, Bower-Cherry M, Dutkevitch S, Hyslop T, Schmidt CM, Rosato EL, Laru H, Nakeeb A, Pitt HA, Lillemoe KD, Yeo CJ. Does type of pancreaticojejunostomy after pancreaticoduodenectomy affect postoperative pancreatic fistula rate? A randomized, prospective, dual-institution trial. *J Am Coll Surg* 2009; 208: 738-747; discussion 747-749 [PMID: 19476827 DOI: 10.1016/j.jamcollsurg.2008.12.031]

Senda Y, Shimizu Y, Natsuume S, Ito S, Komori K, Abe T, Matsuo K, Sano T. Randomized clinical trial of duct-to-mucosa versus invagination pancreaticojejunostomy after pancreatoduodenectomy. *Br J Surg* 2018; 105: 48-57 [PMID: 29265404 DOI: 10.1002/bjs.10727]

Bai X, Zhang Q, Gao S, Lou J, Li G, Zhang Y, Ma T, Zhang Y, Xu Y, Liang T. Duct-to-Mucosa vs Invagination for Pancreaticojejunostomy after Pancreatoduodenectomy: A Prospective, Randomized Controlled Trial from a Single Surgeon. *J Am Coll Surg* 2016; 222: 10-18 [PMID: 25677499 DOI: 10.1016/j.jamcollsurg.2015.10.003]

El Nakeeb A, El Henawy M, Ashk W, Abd Ellatif M, Hamed H, Elghawalaby A, Attia M, Abdallah T, Abd EIWahab M. Comparative study between duct to mucosa and invagination pancreaticojejunostomy after pancreatoduodenectomy: a prospective randomized study. *Int J Surg* 2015; 16: 1-6 [PMID: 25682724 DOI: 10.1016/j.ijsu.2015.02.002]

Singh AN, Pal S, Mangla V, Kilambi R, George J, Dash NR, Chattopadhyay TK, Sahni P. Pancreaticojejunostomy: Does the technique matter? A randomized trial. *J Surg Oncol* 2018; 117: 389-396 [PMID: 29044532 DOI: 10.1002/jso.24873]

Maggioli L, Sauvanet A, Nagarajan G, Dokmak S, Aussilhou B, Belghiti J. Binding versus conventional pancreaticojejunostomy after pancreatoduodenectomy: a case-matched study. *J Gastrointest Surg* 2010; 14: 1385-1400 [PMID: 20777228 DOI: 10.1007/s11605-010-1222-0]

Sun X, Zhang Q, Zhang J, Lou Y, Fu Q, Zhang X, Liang T, Bai X. Meta-analysis of invagination and duct-to-mucosa pancreaticojejunostomy after pancreatoduodenectomy: An update. *Int J Surg* 2016; 36: 240-247 [PMID: 27820480 DOI: 10.1016/j.ijsu.2016.11.008]

Lyu Y, Li T, Wang B, Cheng Y, Zhao S. Selection of pancreaticojejunostomy technique after pancreaticoduodenectomy: duct-to-mucosa anastomosis is not better than invagination anastomosis: A meta-analysis. *Medicine (Baltimore)* 2018; 97: e12621 [PMID: 30290634 DOI: 10.1097/MD.0000000000012621]

Motoi F, Egawa S, Rikiyama T, Katayose Y, Umino M. Randomized clinical trial of external stent drainage of the pancreatic duct to reduce postoperative pancreatic fistula after pancreaticojejunostomy. *Br J Surg* 2012; 99: 524-531 [PMID: 22497024]

Poon RT, Fan ST, Lo CM, Ng KK, Yuen WK, Yeung C, Wong J. External drainage of pancreatic duct with a stent to reduce leakage rate of pancreaticojejunostomy after pancreatoduodenectomy: a prospective randomized trial. *Ann Surg* 2007; 246: 425-433; discussion 433-435 [PMID: 17717446]

Kuroki T, Tajima Y, Kitanou A, Adachi T, Kanematsu T. Stenting versus non-stenting in pancreaticojejunostomy: a prospective study limited to a normal pancreas without fibrosis sorted by usingdynamic MRI. *Pancreas* 2011; 40: 25-29 [PMID: 20717066 DOI: 10.1097/MPA.0b013e3181e8616a]

Pessaux P, Sauvanet A, Mariette C, Paye F, Muscari F, Cunha AS, Sastre B, Arnaud JP; Fédération de Recherche en Chirurgie (French). External pancreatic duct stent decreases pancreatic fistula rate after pancreaticoduodenectomy: prospective multicenter randomized trial. *Ann Surg* 2011; 253: 879-885 [PMID: 21366858 DOI: 10.1097/SLA.0b013e31821219a7]

Bin X, Lian B, Jianping G, Bin T. Comparison of patient outcomes with and without stenting tube in pancreaticojejunostomy. *J Int Med Res* 2018; 46: 403-410 [PMID: 28718685 DOI: 10.1177/0306041817717400]

Patel K, Teta A, Sukharamwala P, Thoons J, Szaczmacher M, DeVito P. External pancreatic duct stent reduces pancreatic fistula: a meta-analysis and systematic review. *Int J Surg* 2014; 12: 827-832 [PMID: 25003575 DOI: 10.1016/j.ijsu.2014.06.008]

Hong S, Wang H, Yang S, Yang K. External stent versus no stent for pancreaticojejunostomy: a meta-analysis of randomized controlled trials. *J Gastrointest Surg* 2013; 17: 1516-1525 [PMID: 23568149 DOI: 10.1007/s11605-013-2187-4]

Ohwada S, Tanahashi Y, Ogawa T, Kawate S, Hamada K, Tago KI, Yamada T, Morishita Y. In situ vs ex situ pancreatic duct stents of duct-to-mucosa pancreaticojejunostomy after pancreatoduodenectomy with bilroth i-type reconstruction. *Arch Surg* 2002; 137: 1289-1293 [PMID: 12413321]

Suzuki S, Kaji S, Koike N, Harada N, Tanaka S, Hayashi T, Suzuki S, Hamay F. Pancreaticojejunostomy: Does the technique matter? A randomized, prospective, dual-institution trial. *Ann Surg* 2009; 198: 51-54 [PMID: 19217599 DOI: 10.1097/SLA.0b013e3182c12204]

Wang H, Xiu D, Tao M. The pancreatic juice length in the stent tube as the predicting factor of clinical relevant postoperative pancreatic fistula after pancreatoduodenectomy. *Medicine (Baltimore)* 2017; 96: e8481 [PMID: 29092590 DOI: 10.1097/MD.0000000000001845]

Zhang GQ, Li XH, Ye XJ, Chen HB, Fu NT, Wu AT, Li Y. Internal Versus External Drainage With A Pancreatic Duct Stent For Pancreaticojejunostomy During Pancreatoduodenectomy For Patients at High Risk for Pancreatic Fistula: A Comparative Study. *J Surg Res* 2018; 232: 247-256 [PMID: 30463725 DOI: 10.1016/j.jss.2018.06.033]

Jang JY, Chang YR, Kim SW, Choi SH, Park SJ, Lee SE, Lim CS, Kang MJ, Lee H, Heo JS. Randomized multicentre trial comparing external and internal pancreatic stenting during pancreatoduodenectomy. *Br J Surg* 2016; 103: 668-675 [PMID: 27040594 DOI: 10.1002/bjs.10160]

Tani M, Kawai M, Hirono S, Ina S, Miyazawa M, Shimizu A, Yamaue H. A prospective randomized controlled trial of internal versus external drainage with pancreaticojejunostomy for pancreatoduodenectomy. *Am J Surg* 2010; 199: 759-764 [PMID: 20074691 DOI: 10.1016/j.amjsurg.2009.06.023]
Surgical techniques and postoperative management to prevent POPF

Kawaida H et al.

WJG 2019; 25(28): 17295-17303

DOI: 10.1016/j.amjsurg.2019.06.017

Kamoda Y, Fujino Y, Matsumoto I, Shinzeki M, Sakai T, Kuroda Y. Usefulness of performing a pancreaticojjunostomy with an internal stent after a pancreateoduodenectomy. Surg Today 2008; 38: 524-528 [PMID: 18516532 DOI: 10.1007/s00595-007-3662-x]

Smyrniosit V, Arkadopoulos N, Kyriazi MA, Derpapas M, Theodosopoulos T, Gennatas C, Kondi-Paphiti A, Vassiliou I. Does internal stenting of the pancreaticojjunostomy improve outcomes after pancreateoduodenectomy? A prospective study. Langenbecks Arch Surg 2010; 395: 195-200 [PMID: 20802994 DOI: 10.1007/s00423-009-0585-6]

Imazumi T, Hatori T, Tobita K, Fukuda A, Takasaki K, Makucchi H. Pancreaticojjunostomy using duct-to-mucosa anastomosis without a stenting tube. J Hepatobiliary Pancreat Surg 2006; 13: 194-201 [PMID: 16708294]

Ochiai T, Sonoyama T, Soga K, Inoue K, Ikoma H, Shiozaki A, Kuriru Y, Kubota T, Nakanishi M, Kikuchi S, Ichikawa D, Fujiwara H, Sakakura C, Okamoto K, Kubo Y, Onui E. Application of polyethylene glycolic acid felt with fibrin seal in pancreateoduodenectomy. J Gastrointest Surg 2010; 14: 884-890 [PMID: 20177808 DOI: 10.1007/s11605-009-1149-3]

Gong J, He S, Cheng Y, Cheng N, Gong J, Zeng Z. Fibrin sealants for the prevention of postoperative pancreatic fistula following pancreatic surgery. Cochrane Database Syst Rev 2018; 6: CD009962 [PMID: 29234987 DOI: 10.1002/14651858.CD009962.pub3]

Martin I, Ar K. Does fibrin glue sealant decrease the rate of anastomotic leak after a pancreateoduodenectomy? Results of a prospective randomized trial. HPB (Oxford) 2013; 15: 561-566 [PMID: 23484477 DOI: 10.1111/hpb.2013.15.00421]

Lillehoo KD, Cameron JL, Kim MP, Campbell KA, Sauter PK, Coleman JA, Yeo CJ. Does fibrin glue sealant decrease the rate of pancreatic fistula after pancreateoduodenectomy? Results of a prospective randomized trial. J Gastrointest Surg 2004; 8: 766-772; discussion 772-774 [PMID: 15531229]

Schindl M, Függer R, Götzinger P, Lingle F, Zitt M, Stătăñer S, Kornprat P, Saharaki H, Hlauschek D, Gnant M; Austrian Breast and Colorectal Cancer Study Group. Randomized clinical trial of the effect of a fibrin sealant patch on pancreatic fistula formation after pancreateoduodenectomy. Br J Surg 2018; 105: 811-819 [PMID: 29664999 DOI: 10.1002/bjs.10840]

Tian Y, Ma H, Peng Y, Li G, Yang H. Preventive effect of omental flap in pancreaticoduodenectomy against postoperative complications: a meta-analysis. Hepatogastroenterology 2015; 62: 187-189 [PMID: 25911894]

Shah OM, Bangri SA, Singh M, Lattoo RA, Bhat MY. Omental flaps reduces complications after pancreateoduodenectomy. Hepatobiliary Pancreat Dis Int 2015; 14: 313-319 [PMID: 26063034]

Tani M, Kawai M, Hirono S, Hatori T, Imazumi T, Nakao A, Egawa S, Asano T, Nagakawa T, Yamaze H. Use of omentum or falciform ligament does not decrease complications after pancreateoduodenectomy: nationwide survey of the Japanese Society of Pancreatic Surgery. Surgery 2012; 151: 183-191 [PMID: 21982073 DOI: 10.1016/j.surng.2011.07.023]

Ramia JM, de la Plaza R, Adel F, Ramiro C, Arteaga V, Garcia-Parreño J. Wrapping in pancreatic surgery: a systematic review. ANZ J Surg 2014; 84: 921-924 [PMID: 25720806 DOI: 10.1111/ans.12491]

Eguchi H, Nagano H, Tanemura M, Takeda Y, Murashishi S, Kobayashi S, Wada H, Umeshita K, Mori M, Doki Y. A thick pancreas is a risk factor for pancreatic fistula after a distal pancreatectomy: selection of the closure technique according to the thickness. Dig Surg 2011; 28: 50-56 [PMID: 21293132 DOI: 10.1159/000322406]

Yoshikoa R, Sairau A, Koga R, Seki M, Kishi Y, Morimura R, Yamamoto J, Yamaguchi T. Risk factors for clinical pancreatic fistula after distal pancreatectomy: analysis of consecutive 100 patients. World J Surg 2010; 34: 121-125 [PMID: 20020297 DOI: 10.1007/s00268-009-0300-3]

Kawaida H, Komi H, Watanabe M, Hosomura N, Amemiya H, Fujii H. Risk factors of postoperative pancreatic fistula after distal pancreatectomy using a triple-row stapler. Surg Today 2018; 48: 95-100 [PMID: 28600634 DOI: 10.1007/s00595-017-1554-2]

Ban D, Shimada K, Konishi M, Sairau A, Hashimoto M, Uesaka K. Stapler and nonstapler closure of the pancreatic remnant after distal pancreatectomy: multicenter retrospective analysis of 388 patients. World J Surg 2012; 36: 1866-1873 [PMID: 22326040 DOI: 10.1007/s00268-012-1505-2]

Subhedar PD, Patel SH, Kneuertz PJ, Maithel SK, Staley CA, Sarmiento JM, Galloway JR, Kooby DA. Risk factors for pancreatic fistula after stapled gland transaction. Am Surg 2011; 77: 965-970 [PMID: 21944507]

Sugimoto M, Gotobda N, Kato Y, Takahashi S, Kinoshita T, Shibashaki H, Nomura S, Konishi M, Kaneko H. Risk factor analysis and prevention of postoperative pancreatic fistula after distal pancreatectomy with stapler use. J Hepatobiliary Pancreat Sci 2013; 20: 538-544 [PMID: 23430851 DOI: 10.1007/s11605-013-0596-0]

Kawai M, Tani M, Okada K, Hirono S, Miyazawa M, Shimizu A, Kitahata Y, Yamaue H. Use of a thick pancreas using stapler closure increases pancreatic fistula after distal pancreatectomy. J Gastrointest Surg 2013; 16: 352-359 [PMID: 23806829 DOI: 10.1007/jamssurg.2012.11.023]

Pratt W, Mathiel SK, Vanounou T, Callery MP, Vollmer CM. Postoperative pancreatic fistulas are not equivalent at proximal, distal, and central pancreatectomy. J Gastrointest Surg 2006; 10: 1264-1278; discussion 1278-1279 [PMID: 1714013]

PrattBalcom JH 4th, Rattner DW, Warshaw AL, Chang Y, Fernandez-del Castillo C. Ten-year experience with 733 pancreatic resections: changing indications, older patients, and decreasing length of hospitalization. Arch Surg 2001; 136: 391-398 [PMID: 11296108]

Kleeff J, Dierker MK, Zgraggen K, Hinz U, Wagner M, Bachmann J, Zehetner J, Müller MW, Fries H, Bächler MW. Distal pancreatectomy: risk factors for surgical failure in 302 consecutive cases. Ann Surg 2007; 245: 573-582 [PMID: 17414066]

Zhou W, Lv R, Wang X, Mou Y, Cai X, Herr I. Stapler vs suture closure of pancreatic remnant after distal pancreatectomy: a meta-analysis. Am J Surg 2010; 200: 529-536 [PMID: 20538249 DOI: 10.1016/j.amjsurg.2009.12.022]

Diener MK, Seiler CM, Rossion I, Kleeff J, Glänenmann M, Butttermann G, Tornazic A, Brunns CJ, Bosch OR, Farkas S, Belenav O, Neoptolomos JP, Halloran C, Keck T, Niedergethmann G, Gellert K, Witzgall M, Kollmar O, Langer P, Steger U, Neudecker J, Berrevoet F, Gänzner S, Heiss MM, Luntz SP, Bruckner T, Kieser M, Bächler MW. Efficacy of staple versus hand-sewn closure after distal pancreatectomy (DISPACT): a randomised, controlled multicentre trial. Lanceet 2011; 377: 1514-1522 [PMID: 21529927 DOI: 10.1016/s0140-6736(11)60237-7]

Park JS, Lee DH, Jang JY, Han Y, Yoon DS, Kim JK, Han HS, Yoon Y, Hwang D, Kang CM, Hwang
Wang S, Shi N, You L, Dai M, Zhao Y. Minimally invasive surgical approach versus open procedure for pancreaticoduodenectomy: systematic review and meta-analysis. Langenbecks Arch Surg 2016; 401: 151-159 [PMID: 26897031 DOI: 10.1007/s00423-016-1382-7]

Hassenplug M, Hinz U, Strobel O, Volpert J, knebel P, Diener MK, werner J, Hackert T, Bächler MW. Teres ligament Patch reduces Relevant morbidity after Distal pancreatectomy (the DISCOVER Randomized Controlled Trial). Ann Surg 2016; 264: 723-730 [PMID: 27455155 DOI: 10.1097/SLA.0000000000001364]

Kawai M, Hiroto S, okada K, Satoi S, yanagimoto H, Kon M, murakami Y, Kondo N, Sho M, akahori T, Toyama H, fukumoto T, Fuji T, matsutomato I, eguchi H, Ikoma H, Takeda Y, fujimoto J, yamaue H. Reinforced staplers for distal pancreatectomy. Langenbecks Arch Surg 2017; 402: 1197-1204 [PMID: 28112814 DOI: 10.1007/s00423-016-1382-7]

Jensen EH, Porschtsy PR, Chownieck J, Teng M. Meta-analysis of bioabsorbable staple line reinforcement and risk of fistula following pancreatic resection. J Gastrointest Surg 2013; 17: 267-272 [PMID: 22948840 DOI: 10.1007/s11605-012-2031-5]

Jang JY, shin YC, Han Y, Park JS, Han HS, Hwang HK, Yoon DS, Kim JK, Yoon YS, Hwang DW, Kang CM, Lee WJ, Heo JS, Kang MJ, Chang YR, Chang J, Jung W, Kim SW. Effect of Polyglycolic Acid Mesh for prevention of Pancreatic Fistula Following Distal Pancreatectomy: A Randomized Clinical Trial. JAMA Surg 2017; 152: 150-155 [PMID: 27784046 DOI: 10.1001/jamasurg.2016.3644]

Kondo N, Uemura K, Nakagawa N, Okada K, Kuroda S, Suo T, Hadano N, matsutomo H, Sato D, Sasaki M, Ate T, Fukushima O, okuda A, nakanishi A, Hashimoto Y, oehl M, Murakami Y, Hiroshina Surgical Study Group of Clinical Oncology: A Multicenter, Randomized, Controlled Trial Comparing Reinforced Staplers with Bare staplers During Distal Pancreatectomy (HISCO-07 Trial). Ann Surg Oncol 2019; 26: 1519-1527 [PMID: 30783854 DOI: 10.1245/s10434-019-07222-0]

Wagner M, Gloor B, Ambühl M, Worni M, Lutz JA, Angus E, Candinas D. Roux-en-Y drainage of the pancreatic stump decreases pancreatic fistula after distal pancreatic resection. J Gastrointest Surg 2007; 11: 303-308 [PMID: 17458602]

Klein F, Glanemann M, Faber W, Gill S, Neuhau P, Acceptance an anastomosis or direct closure of the pancreatic remnant after a distal pancreatectomy: a single-centre experience. HPB (Oxford) 2012; 14: 799-804 [PMID: 22534380 DOI: 10.1111/j.1440-1807.2012.05535.x]

Meniconi RL, Caronna R, Borreca D, Schiratti M, Chirletti P. Pancreato-jejunostomy versus hand-sewn closure of the pancreatic stump to prevent pancreatic fistula after distal pancreatic resection: a retrospective analysis. BMC Surg 2013; 13: 23 [PMID: 23819892 DOI: 10.1186/1471-2482-13-23]

Kawai M, Hiroto S, Okada K, Sho M, Nakajima Y, Eguchi H, nagano H, Ikoma H, morimura R, Takeda Y, Nakahara S, Suzumura K, fujimoto J, yamaue H. Randomized Controlled Trial of Pancreatointejunostomy versus Stapler closure of the pancreatic stump during distal pancreatectomy to reduce pancreatic fistula. Ann Surg 2016; 264: 180-187 [PMID: 26473652 DOI: 10.1097/SLA.0000000000001395]

Uemura K, Satoi S, Motori F, Kwon M, Unno M, murakami Y. Randomized clinical trial of duct-to-mucosa pancreaticojejunostomy versus handsown closure after distal pancreatectomy. Br J Surg 2017; 104: 536-543 [PMID: 28112814 DOI: 10.1002/bjs.10458]

Nakamura M, Wakabayashi G, Miyazaka Y, Tanaka M, Morikawa T, Unno M, Tajima H, Kumamoto Y, Satoi S, Kwon M, Toyama H, Ku Y, Yoshihori H, Nara S, Shimada K, Yokoyama T, Miyagawa S, Toyama Y, Yanaga K, Fuji T, Koderaw Y, Study group of JHBPS, Kondoh M, Takahara T, Beppeu T, Yamaue H, Miyazaki M, Takeda T. Multicenter comparative study of laparoscopic and open distal pancreatectomy using propensity score-matching. J Hepatobiliary Pancreat Sci 2015; 22: 731-736 [PMID: 26087943 DOI: 10.1002/hebp.268]

Senthilnathan P, Chinnusamy P, Ramakrishnan P, Athavale PR, Ramakrishnan P, Subbiah R, Comparison of Pathological Radicality between open and Laparoscopic Pancreaticoduodenectomy in a Tertiary Centre. Indian J Surg Oncol 2015; 6: 20-25 [PMID: 25937759 DOI: 10.1007/s11605-014-0372-x]

Mehrabi A, hafezi M, Arvin J, Esmailizadeh G, Maroussi C, Emami G, Müller-Stich BP, Bächler MW, Hackert T, Diener MK. A systematic review and meta-analysis of laparoscopic versus open distal pancreatectomy for benign and malignant lesions of the pancreas. Surgery 2015; 157: 45-55 [PMID: 25482464 DOI: 10.1016/j.surg.2014.06.081]

Gavrilidis P, Lim C, Menahem L, Lahat E, Salloum C, Azoulay D. Robotic versus laparoscopic distal pancreatectomy - The first meta-analysis. HPB (Oxford) 2016; 18: 567-574 [PMID: 27346136 DOI: 10.1111/hpb.13080]

Huang B, Feng L, zhao J. Systematic review and meta-analysis of robotic versus laparoscopic distal pancreatectomy for benign and malignant lesions. Surg Endosc 2016; 30: 4078-4085 [PMID: 26743110 DOI: 10.1007/s00464-015-4723-7]

Guerrini GP, lauretta A, Bellufo C, Oliveri M, forlin M, Bassio S, Breda B, Bertoli G, Di Benedetto F. Robotic versus laparoscopic distal pancreatectomy: an up-to-date meta-analysis. BMC Surg 2017; 17: 105 [PMID: 29121885 DOI: 10.1186/s12993-017-0301-3]

Correa-Gallego C, Dinkelspiel HE, Sulimanoff I, Fischer S, Vinuela EF, Kingdom TP, Fong Y, DeMatteo RP, D’Angelica MI, Jarnagin WR, Allen PJ. Minimally-invasive vs open pancreaticoduodenectomy: systematic review and meta-analysis. J Am Coll Surg 2014; 218: 129-139 [PMID: 24276074 DOI: 10.1016/j.jamcollsurg.2013.09.005]

Wang S, Shi N, You L, Dui M, Zhao Y. Minimally invasive surgical approach versus open procedure for pancreatic resection. J Hepatobiliary Pancreat Sci 2016; 23: 110-117 [PMID: 26681272 DOI: 10.1002/jhbp.310]

Sa Cunha A, Carrere N, Meunier B, Fabre JM, Saussant A, Pessaux P, Ortega-Deballon P, Fingerhut A, Lacaine F. French Fédération de Recherche en Chirurgie (FRENCH). Staple closure reinforcement with absorbable fibrin collagen sealant sponge (TachoSil) does not prevent pancreatic fistula after distal pancreatectomy: the FIABLE multicenter randomized study. Am J Surg 2015; 210: 739-748 [PMID: 26160763 DOI: 10.1016/j.amjsurg.2015.04.015]

Montorsi M, Zerbi A, Bassi C, Capussotti L, Coppola R, Sacchi M; Italian Tachosil Study Group. Efficacy of an absorbable fibrin sealant patch (TachoSil) after distal pancreatectomy: a multicenter, randomized, controlled trial. Ann Surg 2012; 256: 853-9; discussion 859-60 [PMID: 23095631 DOI: 10.1097/SLA.0b013e3182272dec]

Hüttner FJ, Mihalicek AL, Hackert T, Ulrich A, Bächler MW, Diener MK. Effectiveness of TachoSil® in the prevention of postoperative pancreatic fistula after distal pancreatectomy: a systematic review and meta-analysis. Langenbecks Arch Surg 2016; 401: 151-159 [PMID: 26897031 DOI: 10.1007/s00423-016-1382-7]
pancreatocoduodenectomy: A systematic review and meta-analysis. Medicine (Baltimore) 2017; 96: e6619

124 Kantor O, Pitt HA, Talanmonti MS, Roggin KK, Bentrem DJ, Prinz RA, Baker MS. Minimally invasive pancreatocoduodenectomy: is the incidence of clinically relevant postoperative fistula comparable to that after open pancreatectomy? Surgery 2018; 163: 587-593 [PMID: 29454444 DOI: 10.1016/j.surg.2017.12.001]

125 Nassour I, Wang SC, Porembka MR, Yopp AC, Choti MA, Augustine MM, Polanco PM, Mansour JC, Minter RM. Robotic Versus Laparoscopic Pancreatocoduodenectomy: a nOSIPQ Analysis. J Gastrointest Surg 2017; 21: 1784-1792 [PMID: 28918866 DOI: 10.1007/s11605-017-3543-6]

126 Zimmerman AM, Roye DG, Charpentier KP. A comparison of outcomes between open, laparoscopic and robotic pancreatectomy. HPB (Oxford) 2018; 20: 364-369 [PMID: 29183703 DOI: 10.1002/hpb.21008]

127 Poves I, Morató O, Buello F, Grande L. Laparoscopic-adapted Blumgart pancreatojejunostomy in laparoscopic pancreatectomy. Surg Endosc 2017; 31: 2837-2845 [PMID: 27904043 DOI: 10.1007/s00464-016-5294-y]

128 Cai Y, Luo H, Li Y, Gao P, Peng B. A novel technique of pancreatojejunostomy for laparoscopic pancreatectomy. Surg Endosc 2019; 33: 1572-1577 [PMID: 30203206 DOI: 10.1007/s00464-018-6446-z]

129 Behrmann SW, Zarraur BL, Parram A, Riall TS, Hall BL, Pitt HA. Routine drainage of the operative bed following elective distal pancreatectomy does not reduce the occurrence of complications. J Gastrointest Surg 2015; 19: 72-9; discussion 79 [PMID: 25115324 DOI: 10.1007/s11605-014-2608-z]

130 BehrmanVan Buren G 2nd, Bloomston M, Schmidt CR, Behrman SW, Zyromski NJ, Ball CG, Morgan KA, Hughes SJ, Karanicolas PJ, Allendorf JD, Vollmer CM Jr, Ly Q, Brown KM, Velanovich V, Winter JM, McElhaney AL, Muscarella P 2nd, Schmidt CM, House MG, Dixon E, Dillhoff ME, Trevino JG, Hallett J, Coburn NSG, Nakeeb A, Behrns KE, Sasson AR, Ceppa EP, Abdel-Misih SRZ, Riall TS, Silberfein EJ, Ellison EC, Adams DB, Hsu C, Tran Cao HS, Mohammed S, Villafañe-Ferriol N, Barakat O, Massareh NN, Chang C, Mendez-Reyes JE, Fang A, Jo E, Mo Q, Fisher WE. A Prospective Randomized Multicenter Trial of Distal Pancreatectomy With and Without Routine Intrapерitoneal Drainage. Ann Surg 2017; 266: 421-431 [PMID: 28692468 DOI: 10.1097/SLA.0000000000002375]

131 Fisher WE, Hodges SE, Silberfein EJ, Artinyan A, Ahern CH, Jo E, Bruniciardi FC. Pancreatic resection without routine intraperitoneal drainage. HPB (Oxford) 2011; 13: 503-510 [PMID: 21692324 DOI: 10.1111/j.1477-2578.2011.00331.x]

132 Čečka F, Loveček M, Jon B, Skálikč P, Šubr Z, Neoral Č, Ferko A. Intra-abdominal drainage following pancreatectomy: A systematic review. World J Gastroenterol 2015; 21: 11458-11468 [PMID: 26523110 DOI: 10.3748/wjg.v21.i40.11485]

133 Witzigmann H, Diener MK, Kienkötter S, Rossion J, Bruckner T, Bärbel Werner, Pridddli O, Radulova-Maasrberger O, Lauer H, Knebel P, Ulrich A, Strobel O, Hacker T, Büchler MW. No Need for Routine Drainage After Pancreatic Head Resection: The Dual-Center, Randomized, Controlled PANDRA Trial (ISRCTN04937707). Ann Surg 2016; 264: 528-537 [PMID: 27531357 DOI: 10.1097/SLA.0000000000001859]

134 FisherVan Buren G 2nd, Bloomston M, Hughes SJ, Winter J, Behrman SW, Zyromski NJ, Vollmer C, Velanovich V, Riall T, Muscarella P, Trevino J, Nakeeb A, Schmidt CM, Behrns K, Ellison EC, Barakat O, Perry KA, Driscoll LJ, Silberfein EJ, Goldsin B, Brown K, Mohammed S, Hodges SE, McElhaney A, Issazadeh M, Jo E, Mo Q, Fisher WE. A randomized prospective multicenter trial of pancreatectomy with or without routine intraperitoneal drainage. Ann Surg 2014; 259: 605-612 [PMID: 24374131 DOI: 10.1097/SLA.0000000000004460]

135 Wang YC, Szathmáry F, Zhu JQ, Xiong JJ, Huang W, Gomatos J, Nines QM, Sutton R, Liu XB. Prophylactic intra-peritoneal drain placement following pancreatectomy: a systematic review and meta-analysis. World J Gastroenterol 2015; 21: 2510-2521 [PMID: 25741162 DOI: 10.3748/wjg.v21.i18.2510]

136 Kawai M, Tani M, Terasawa H, Ina S, Hiroso S, Nishikawa R, Miyaizawa M, Uchiyama K, Yamane H. Early removal of prophylactic drains reduces the risk of intra-abdominal infections in patients with pancreatic head resection: prospective study for 104 consecutive patients. Ann Surg 2006; 244: 1-7 [PMID: 16794381]

137 Adachi T, Kuroki T, Kitasato A, Hirabaru M, Matsushima H, Soayama A, Hidaka M, Takatsuki M, Eguchi S. Safety and efficacy of early drain removal and triple-dug therapy to prevent pancreatic fistula after distal pancreatectomy. Pancreatology 2015; 15: 411-416 [PMID: 26073457 DOI: 10.1016/j.pan.2015.05.468]

138 Bassi C, Molinari E, Mallo G, Crippa S, Butturini G, Salvia R, Talamini G, Pederzoli P. Early versus late drain removal after standard pancreatic resections: results of a prospective randomized trial. Ann Surg 2010; 252: 207-214 [PMID: 20622661 DOI: 10.1097/SLA.0b013e3181e16489]

139 Nagakawa Y, Matsudo T, Hijioka Y, Kikuchi S, Bunso K, Suzuki Y, Kasuya K, Tsuchida A. Bacterial contamination in ascitic fluid is associated with the development of clinically relevant pancreatic fistula after pancreatectomy. AM J Gastroenterol 2013; 108: 701-706 [PMID: 23429407 DOI: 10.1038/ajg.2012.541 PMID: 21576985]

140 Harris AG. Somatostatin and somatostatin analogues: pharmacokinetics and pharmacodynamic effects. Gut 1994; 35: S1-S4 [PMID: 7914414]

141 Shan YS, Sy ED, Lin PW. Role of somatostatin in the prevention of pancreatic stump-related morbidity following elective pancreatectomy in high-risk patients and elimination of surgeon-related factors: prospective, randomized, controlled trial. World J Surg 2003; 27: 709-714 [PMID: 12732998]

142 Gossillar C, Chipponi J, Baulieux J, Partensky C, Schan R, Gayet P, Barbe P, Chastagner P. Randomized multicentre trial of somatostatin infusion after pancreatectomy. Br J Surg 2001; 88: 1456-1462 [PMID: 11683740]

143 Suc B, Miska S, Piccinini M, Fourtieran G, Hay JM, Flament Y, Fingerhat A, Fagniez PL, Chipponi J, French Associations for Surgical Research. Octreotide in the prevention of intra-abdominal complications following elective pancreatic resection: a prospective, multicenter randomized controlled trial. Arch Surg 2004; 139: 288-94; discussion 295 [PMID: 15066886]

144 Sarr MG. Pancreatic Surgery Group. The potent somatostatin analogue vaptrode does not decrease pancreas-specific complications after elective pancreatectomy: a prospective, multicenter, double-blinded, randomized, placebo-controlled trial. J Am Coll Surg 2003; 196: 556-64; discussion 564-5; author reply 565 [PMID: 12691930]
145 Yeo CJ, Cameron JL, Lillemoe KD, Sauter PK, Coleman J, Sohn TA, Campbell KA, Choti MA. Does prophylactic octreotide decrease the rates of pancreatic fistula and other complications after pancreaticoduodenectomy? Results of a prospective randomized placebo-controlled trial. Ann Surg 2000; 232: 419-429 [PMID: 10977392]

146 Kurumboor P, Palaniswami KN, Pramil K, George D, Aikot S. Does Not Prevent Pancreatic Fistula Following Pancreateoduodenectomy in Patients with Soft Pancreas and Non-dilated Duct: A Prospective Randomised Controlled Trial. J Gastrointest Surg 2015; 19: 2038-2044 [PMID: 26302879 DOI: 10.1007/s11605-015-2925-x]

147 Fernández-Cruz I, Jiménez Chavarría E, Taurá P, Closa D, Bondo MA, Fjørtoft T. Prospective randomized trial of the effect of octreotide on pancreatic juice output after pancreaticoduodenectomy in relation to histological diagnosis, duct size and leakage. HPB (Oxford) 2013; 15: 392-399 [PMID: 23557411 DOI: 10.1111/j.1477-2574.2012.00608.x]

148 Droessler RA, Coleman J, Moussavian MR, Schilling MK, Kollmar O. Octreotide prophylaxis is not beneficial for biochemical activity and clinical severity of postoperative pancreatic fistula after pancreatic surgery. Dig Surg 2012; 29: 484-491 [PMID: 23392293 DOI: 10.1159/000345874]

149 Graham JA, Johnson LB, Haddad N, Al-Kawas F, Carroll J, Jha R, Maglalis D, Mertens S, Fishbein T. A prospective study of prophylactic long-acting octreotide in high-risk patients undergoing pancreaticoduodenectomy. Am J Surg 2011; 201: 481-485 [PMID: 21421102 DOI: 10.1016/j.amjsurg.2010.06.038]

150 Koti RS, Gurusamy KS, Davidson BR. Meta-analysis of randomized controlled trials on the effectiveness of somatostatin analogues for pancreatic surgery: a Cochrane review. HPB (Oxford) 2010; 12: 155-165 [PMID: 20590882 DOI: 10.1111/j.1477-2574.2010.00157.x]

151 Jin K, Zhou H, Zhang J, Wang W, Sun Y, Ruan C, Hu Z, Wang Y. Systematic review and meta-analysis of somatostatin analogues in the prevention of postoperative complications after pancreaticoduodenectomy. Langenbecks Arch Surg 2015; 32: 196-207 [PMID: 25872003]

152 El Nakeeb A, ElGawalby A, A Ali M, Shehta A, Hamed H, El Raefee A, Abd El Raefee A. Efficacy of octreotide in the prevention of complications after pancreaticoduodenectomy in patients with soft pancreas and non-dilated duct: A prospective randomized trial. Hepatobiliary Pancreat Dis Int 2018; 17: 59-63 [PMID: 29428106 DOI: 10.1016/j.hjpdi.2018.01.015]

153 Allen PJ, Brennan MF, Bucknor AA, Robinson LM, Pappas MM, Carlucci KE, D’Angelica MI, DeMatteo RP, Jarnagin WR. Pasireotide for postoperative pancreatic fistula. N Engl J Med 2014; 370: 2014-2022 [PMID: 24849084 DOI: 10.1056/NEJMoa1311688]

154 Youn S, Sung ML, Jutila J, DiFronzo LA, O’Connor VV. Pasireotide is not effective in reducing the development of postoperative pancreatic fistula. HPB (Oxford) 2018; 20: 834-840 [PMID: 30069144 DOI: 10.1016/j.hpb.2018.03.007]

155 Elliott IA, Dann AM, Ghukasyan R, Damato L, Girgis MD, King JC, Hines OJ, Reber HA, Donahue TR. Pasireotide does not prevent postoperative pancreatic fistula: a prospective study. HPB 2018; 20: 418-422 [PMID: 29398479 DOI: 10.1111/hpb.2017.10.018]

156 Goyert N, Eeson G, Kagedan DJ, Behman R, Lemke M, Halter J, Mittmann N, Law C, Karanicolas PJ, Coburn NG. Pasireotide for the Prevention of Pancreatic Fistula Following Pancreaticoduodenectomy: A Cost-effectiveness Analysis. Ann Surg 2017; 265: 2-10 [PMID: 27573539 DOI: 10.1097/SLA.0000000000001899]

157 Ma LW, Dominguez-Rosado J, Gennarelli RL, Bach PB, Gonen M, D’Angelica MI, DeMatteo RP, Jarnagin WR. The Cost of Pasireotide: Results from a Prospective Randomized Trial. Ann Surg 2017; 265: 11-16 [PMID: 27428029 DOI: 10.1097/SLA.0000000000001892]

158 Welsch T, Musile J, Distler M, Knobl H, Weitz J, Höckel D. Cost-effectiveness comparison of prophylactic octreotide and pasireotide for prevention of fistula after pancreatic surgery. Langenbecks Arch Surg 2016; 401: 1027-1035 [PMID: 27233242 DOI: 10.1007/s00423-016-1456-6]
