Erciyes Med J 2022; 44(2): 123–8 • DOI: 10.14744/etd.2021.26628
INVITED REVIEW – OPEN ACCESS

Pancreaticojejunostomy Anastomosis Techniques After Pancreaticoduodenectomy: A Critical Review

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ABSTRACT

Despite advanced new anastomosis techniques and auxiliary anastomosis materials, unfortunately, the rate of pancreaticojejunostomy (PJ) anastomotic fistula developing after pancreatoduodenectomy (PD) has not fallen to the anticipated level. The aim of this review was to evaluate different PJ techniques in the context of the current literature. The method used for PJ anastomosis is one of the most critical risk factors. Also, the rate of pancreatic fistula after the operation (PFAO) is exceptionally high in patients with a soft pancreas, narrow pancreatic duct diameter, or a posteriorly located pancreatic duct. Meta-analyses comparing duct-mucosa-PJ (dm-PJ) and invagination-PJ (i-PJ) have demonstrated similar rates of PFAO, morbidity, and mortality. Although a lower rate of PFAO was originally reported when using the binding-PJ approach, recent studies have contradicted this, showing similar rates of PFAO, morbidity, and mortality. A recent meta-analysis comparing Blumgart anastomosis (BA) and conventional pancreaticojejunostomy (c-PJ) reported that BA was significantly associated with a lower grade B/C PFAO ratio. However, in a subgroup analysis, there was no significant impact on grade B/C PFAO in patients with soft pancreatic stumps. The literature also includes reports of internal or external stents and prophylactic octreotide being used to reduce the rate of PFAO. In conclusion, pancreatic fistula development after PD is multifactorial. The surgeon can reduce bleeding and avoid sepsis with meticulous dissection and taking extra care throughout the entire operation. Based on the results of meta-analyses, standard dm-PJ anastomosis and BA techniques performed carefully can be recommended as a standard, leading to a more controlled PFAO rate.

Keywords: Pancreatic fistula, pancreaticoduodenectomy, pancreaticojejunostomy, risk factor

Cite this article as:
Aziret M. Pancreaticojejunostomy Anastomosis Techniques After Pancreaticoduodenectomy: A Critical Review. Erciyes Med J 2022; 44(2): 123-8.

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Submitted
27.07.2021

Accepted
20.09.2021

Available Online
21.01.2022

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INTRODUCTION

Pancreatic head carcinoma is associated with a poor prognosis, with a 5-year relative survival rate of only 9%, and most patients (75–80%) are diagnosed as metastatic at initial presentation (1). Pancreaticoduodenectomy (PD) or the Whipple procedure is a potentially curative treatment for carcinomas in the periampullary area, head, or processus uncinatus of the pancreas (2). However, the Whipple procedure is challenging for both the surgeon and the patient, as resection of the organ and tissue, combined with the essential reconstruction involved, can lead to significant complications and death (3).

Pancreatic fistula is one of the most important complications that can develop following PD. Various studies in the literature report a wide range of pancreatic fistula after operation (PFAO) rates, ranging from 13% to 45% (3–6), and many authors have studied this wide distribution over the past 50 years. PFAO is associated with life-threatening complications, such as intra-abdominal hemorrhage and sepsis (3, 4). The overall mortality rate for all PFAO cases has been reported to be 1%, while the rate for grade C cases has been as high as 25% (5). Although new techniques and studies have been developed over the last 30 years to reduce PFAO formation, a satisfactory improvement in fistula rates has not yet been achieved (6).

Additional risk factors for POPF after PD include factors directly related to the pancreas itself (soft pancreas, decreased blood flow, posterior location of the pancreatic duct, and narrow diameter of the pancreatic duct), and a high body mass index (BMI), preoperative malnutrition, massive intraoperative bleeding, the volume of the pancreatic remnant, surgeon and center experience, and the anastomosis technique (7–12). The pancreatojejunostomy (PJ) technique is one of the more critical risk factors associated with high morbidity and mortality. The present review is an evaluation of various pancreaticojejunostomy techniques that may lead to the development of pancreatic fistula after a Whipple procedure.

Pancreaticojejunostomy Anastomosis Techniques

PD is a critical, technically demanding pancreatic resection that involves the retroperitoneal lymph nodes, gallbladder, common bile duct, antrectomy (sparing the pylorus in some cases), duodenum, and 10 to 15 cm of the

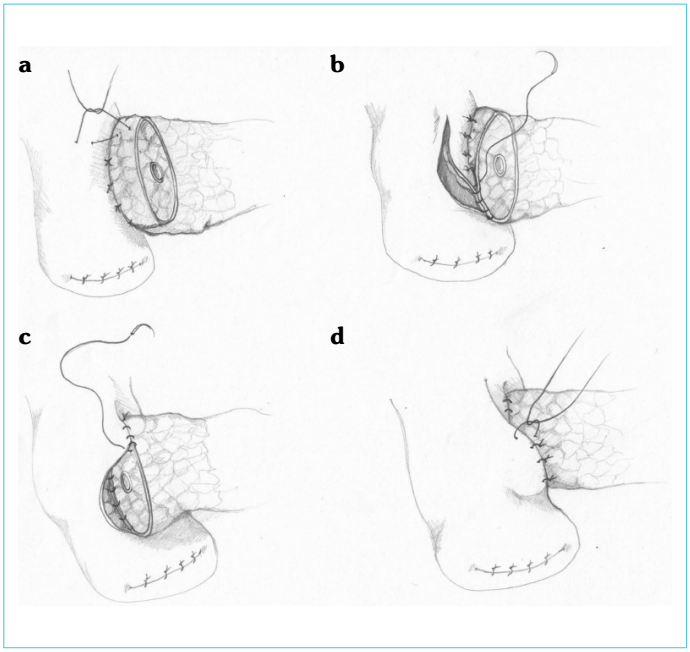

Figure 1. Conventional invagination technique (14)

proximal jejunum. Surgical reconstruction options include Child's surgery, known as PJ, hepaticojejunostomy (HJ), and the standard S-Child gastrojejunostomy (GJ) (12). The best surgical management of pancreatic remnants is still debated, and no optimal PJ surgical technique to reduce PFAO rates has been demonstrated. As a result, there is wide variation in the choice of surgical technique by pancreatic surgeons.

End-to-end or End-to-side Invagination Pancreaticojejunostomy

Many recently developed PJ techniques have been described in the literature. The main goal of these techniques is to prevent or reduce the anastomotic leak rate. End-to-end or end-to-side intussusception is a PJ anastomosis technique used occasionally at some tertiary centers in patients with a soft pancreas and a narrow pancreatic duct diameter (3 mm). The fistula rate recorded in the literature for this method ranges from 1% to 15%. End-to-end invagination involves transferring the pancreatic remnant to the jejunal lumen. Then, a 2-row anastomosis with nonabsorbable and absorbable sutures is performed. This invagination technique has a critical disadvantage: If PJ anastomosis leakage occurs, the entire jejunal lumen may open, leading to uncontrolled PFAO outflow, resulting in sepsis, massive bleeding, and multiorgan failure (13) (Fig. 1).

Standard Duct-to-mucosa Pancreaticojejunostomy

Duct-to-mucosa PJ (dm-PJ) is one of the most commonly cited techniques in the literature. The dm-PJ is a safe and effective approach to intussusception that involves an anastomosis performed between the pancreatic duct and the jejunal wall. First, the pancreatic duct is prepared for the anastomosis with a gastric tube internal stent. The internal stent is mostly used in cases with a soft pancreas and a pancreatic duct diameter of <3 mm (Fig. 2a). Next, a double-needle absorbable suture, polydioxanone (4/0-6/0), is usually used at 10-12-14 with corner sutures on the anterior pancreatic duct (Fig. 2b).

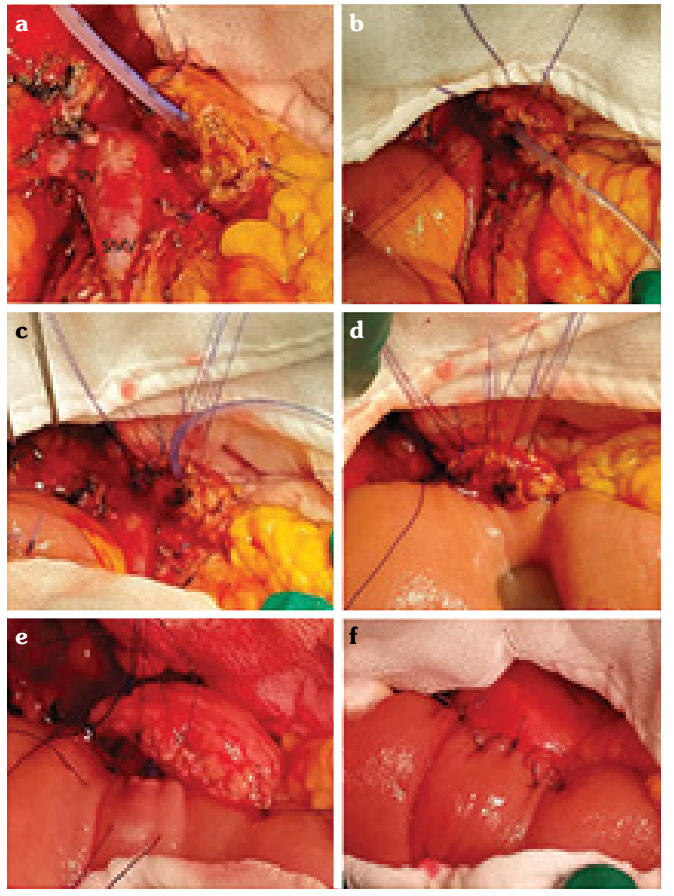

Figure 2. (a) Preparing the pancreatic duct with internal stent; (b, c), separately suturing the anterior and posterior pancreatic duct; (d) suturing and tying between posterior outer wall and jejunum; (e, f) fixation of the internal stent, suturing, and tying the stitch in rear pancreatic duct with jejunum, anterior pancreatic duct with jejunum, and anterior pancreatic wall with jejunum

PV: Portal vein; SMV: Superior mesenteric vein

Similarly, a suture passed through a catheter inserted into the pancreatic duct is passed at 4-6-8 at the posterior pancreatic duct (Fig. 2c). Next, a nonabsorbable suture or an absorbable suture is usually used continuously or singly on the posterior outer wall, and the suture is passed through the pancreatic capsule to the seromuscular layer of the jejunum. The sutures passed through the pancreas and jejunum are tied off (Fig. 2d). A tiny hole of about 3 to 4 mm is opened in the jejunum, and another tip of the double needle that has passed through the posterior pancreatic duct is passed from the outer to the inner jejunum in a clockwise direction following the sutures passing through the jejunum, and the sutures are tied. At this point, an internal catheter can be fixed in the jejunum (Fig. 2e). Following the same procedure connecting the anterior pancreatic duct to the jejunum, the sutures passing through the anterior pancreatic wall and the seromuscular layer of the jejunum are tied (14) (Fig. 2 e, f).

Blumgart Anastomosis

Blumgart anastomosis (BA) is a combination of the techniques of intussusception and duct-to-mucosa anastomosis (Fig. 3). Four

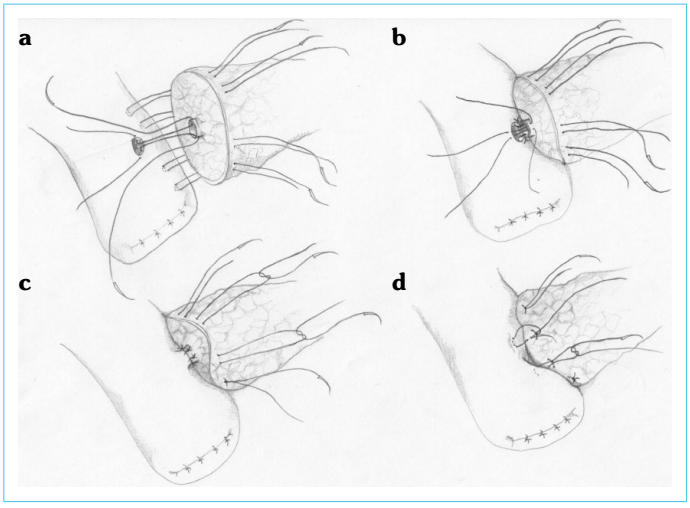

Figure 3. Blumgart anastomosis technique (14). Suturing through the entire thickness of the anterior to the posterior wall of the pancreas and threaded through the seromuscular layer of the jejunal segments. (a) The rear and anterior walls of the pancreas are joined with full-thickness sutures, and (b, c) a duct-to-mucosa anastomosis is performed. (d) Next, the sutures are passed from the front of the jejunum seromuscularly and tied

to 8 polyglactin (Vicryl; Ethicon, Inc., Somerville, NJ, USA) sutures are passed through the entire thickness of the anterior to the posterior wall of the pancreas at 0.75 cm intervals. These sutures are then threaded through the seromuscular layer of the jejunal segments. Finally, the posterior and anterior walls of the pancreas are joined with full-thickness sutures. Once the transpancreatic sutures are placed, they are left open to form the jejunal sutures. After a mini-incision of the jejunal segment, a duct-to-mucosa anastomosis is performed with monofilament sutures (4/0-6/0 polydioxanone). The dm-PJ anastomosis is often performed as an end-to-side anastomosis. The hanging sutures are seromuscular, passed from the front of the jejunum, and then tied. The jejunal serosa is wrapped to cover the remaining pancreatic tissue completely (13, 15, 16).

Peng's Binding Approach Pancreaticojejunostomy

The binding approach or pancreaticojejunostomy was introduced by Peng et al. in 2003 (17). First, approximately 3 cm of the pancreatic stump is isolated (1), then a corresponding 3 cm jejunal segment is inverted, followed by cauterization of the mucosa with electrocautery or eradication with 10% carbolic acid. A pancreatic anastomosis is created between the pancreatic stump and the outward-facing mucosa with absorbable sutures. After invagination, the jejunum is gradually narrowed with an absorbable surgical material, such as polyglactin, at a distance of 1.5 to 2 cm from the proximal end of the invaginated pancreatic tissue (17) (Fig. 4).

Other Techniques

Modified PJ techniques, such as the Pair-Watch, Heidelberg, and Cattell-Warren techniques, may also be used in specific referral centers after PD. These methods include different combinations of canal-to-mucosa anastomosis and intussusception techniques.

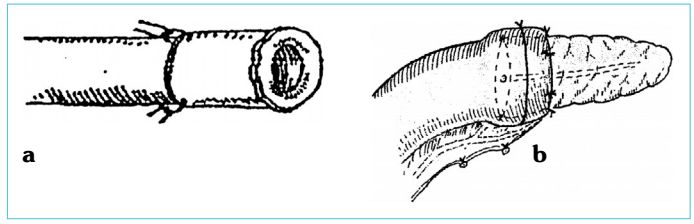

Figure 4. Peng's binding technique (17). (a) Preparing the isolated pancreatic stump (≈3 cm), the corresponding jejunal segment is inverted, followed by cauterization of the mucosa. (b) A pancreatic anastomosis is then created, and after invagination, the jejunum is gradually narrowed at a distance of 1.5–2 cm from the proximal end of the invaginated pancreatic tissue

Risk Factors, Description, and Classification

Risk Factors

While management of the pancreatic stump is one of the most critical causes of PFAO, there are other important risk factors, such as those related to the pancreas (soft pancreas, reduced blood supply, posterior location of the pancreatic duct, and narrow duct diameter [3 mm]), a greater BMI, massive intra-abdominal hemorrhage, the volume of residual pancreatic tissue, poor preoperative nutrition, and surgeon and center experience. Therefore, a combination of risk factors must often be considered in the management of PFAO (7–11).

Description and Classification

Before the turn of the millennium, there were various definitions of pancreatic fistula depending on the surgeon, hospital, and country. The International Study Group of Pancreatic Fistula (ISGPF) first offered a standard definition of pancreatic fistula in 2005. The International Study Group of Pancreatic Surgery (ISGPS) updated the classification in 2016 to limit it to cases in which the drainage fluid measured more than 3 times the upper limit for amylase on postoperative day 3 (7, 8). The definition was amended to include only clinically significant conditions directly related to PFAO (8). The ISGPS also classified pancreatic fistulas as grade A, B, and C, according to clinical severity.

Biochemical fistula (grade A fistula): The ISGPS redefined a grade A fistula and adopted the term biochemical fistula (BF), as it does not cause any change in the clinical course. In this case, the fistula or complication is not of long duration or demonstrates no abnormal clinical entity.

Grade B fistula: A grade B fistula is of clinical significance with the likelihood of abdominal pain, fever, and an elevated leukocyte count. When parenteral or enteral nutrition is initiated, the length of hospital stay and hospital costs increase. PFAO persists for >3 weeks.

Grade C fistula: This is a life-threatening condition and requires significant changes in postoperative follow-up. A grade B fistula is redefined as grade C if it causes clinical instability leading to organ failure or requires repeat laparotomy.

RESULTS

Duct-to-Mucosa Versus Invagination Pancreaticojejunostomy Anastomosis

The duct-to-mucosa pancreaticojejunostomy (dm-PJ) and the invagination pancreaticojejunostomy (i-PJ) are the most common methods

of managing the pancreatic stump (18, 19). The i-PJ is the more commonly used technique because it is straightforward and requires less time than the dm-PJ technique. The dm-PJ is more complex; the difficulty of exposing the pancreatic duct requires more attention and time. A meta-analysis of the 2 techniques performed by Poon et al. (20), concluded that although many techniques have been described to reduce PFAO, further randomized-controlled trials are needed to establish the most suitable method of PJ anastomosis after PD (20). Lai et al. (21) also suggested that high-volume randomized-controlled studies are needed to determine optimal anastomotic techniques and the most useful pharmacological interventions. In a systematic review and meta-analysis conducted by Yang et al. (22), it was reported that no single pancreatic reconstruction technique is appropriate for every type of pancreatic remnant after PD. Some newer techniques, such as binding-PJ and modified pancreaticogastrostomy, should be evaluated further in the future. Bai et al. (23) also noted similar rates of PFAO in a comparison of dm-PJ and i-PJ.

Hashimoto et al. (24) noted that successful management of pancreatic anastomosis is more dependent on meticulous surgical technique, the experience of the surgical center, and other treatment parameters, than the type of anastomotic technique employed. They also stated that binding-PJ and the use of external stents should be investigated with further randomized-controlled studies. A metanalysis of dm-PJ versus i-PJ anastomosis by Li et al. (25) found no significant difference in PFAO, reoperation, or mortality. They also found no significant difference between binding-PJ and standard PJ (including dm-PJ and i-PJ). In 2015, while comparing i-PJ and dm-PJ metanalyses, Hua et al. (26) reported less clinically significant PFAO with i-PJ. On the other hand, another meta-analysis comparing these 2 anastomotic techniques that included 7 randomized controlled trials (RCTs), conducted by Sun et al. (27), presented similar PFAO, morbidity, mortality, and reoperation rates. They also note a shorter hospital stay when the dmPJ technique was used. Kilambi et al. (28) found similar overall and clinically relevant PFAO rates. In 2018, Lyu et al. (29) found no significant difference between dmPJ and i-PJ in terms of PFAO, clinically relevant PFAO, or other complications.

Binding Pancreaticojejunostomy versus Other PJ Anastomosis

Peng et al. (17) detected a lower PFAO rate in their series of 150 consecutive patients. The meta-analysis by Li et al. (25) found no significant difference between binding-PG and conventional PJ (including both dmPJ and i-PJ). A meta-analysis that included RCTs performed by Yang et al. (22) reported that no single pancreas reconstruction method would be suitable for all forms of remnant pancreas tissue but recommended that binding-PJ be considered for further studies. In 2017, a meta-analysis on binding-PJ versus conventional PJ by Zhang et al. (10) found similar PFAO, morbidity, and mortality rates; however, they pointed out that the binding-PJ approach resulted in higher total hospital costs. The authors concluded that surgeons should perform the reconstruction method of their choice.

Blumgart versus Standard Pancreaticojejunostomy or Interrupted Transpancreatic Suture

Some advantage has been attributed to BA in the literature (30, 31). A meta-analysis comparing BA and dm-PJ or i-PJ performed by Li et al. (30) found that BA decreased the rate of grade B/C PFAO. However, there was no significant difference between the BA group and the groups without BA in terms of grade B/C PFAO in the subgroup analysis. Another meta-analysis comparing modified Blumgart anastomosis (m-BA) and interrupted transpancreatic suture (ITS) found that m-BA was superior in terms of grade B/C PFAO and intra-abdominal abscess (31).

Conventional Reconstruction versus Isolated-Pancreaticojejunostomy Anastomosis

In the literature, it has been reported in some important studies that isolated pancreatic anastomosis can reduce the rate of PFAO (32, 33). However, Li et al. (25) found in their meta-analysis focusing on a comparison of isolated-PJ anastomosis versus conventional reconstruction that isolated-PJ (Roux-en-Y reconstruction) did not appear to reduce the incidence of PFAO. Furthermore, in 2020, Lyu et al. (34) observed no significant difference in the rate of PFAO, clinically relevant PFAO, morbidity, or mortality in their meta-analysis comparing i-PJ, isolated-PJ, and conventional PJ.

Standard Pancreaticojejunostomy versus Braun Enteroenterostomy or Isolated Pancreaticojejunostomy Anastomosis

Several anastomosis techniques have been developed with the goal of reducing morbidity and mortality after PD. The Child reconstruction technique is one example. It is defined primarily as a pancreaticojejunostomy/PJ followed by a hepaticojejunostomy/HJ and a gastrojejunostomy/GJ (s-Child). Recently, a meta-analysis showed that s-Child reconstruction with an additional Braun enteroenterostomy was superior to a standard/s-Child or isolated-Roux-en-Y-pancreaticojejunostomy in terms of postoperative complications, such as clinically relevant PFAO and bile leaks (35).

DISCUSSION

Pancreatic cancer is the second most common digestive system tumor, with a high annual incidence and death rate in both sexes in the United States (1). The diagnosis of periampullary region and pancreatic head cancers is usually delayed because these tumors are located deep in the retroperitoneal region. In particular, a pancreatic head tumor is often diagnosed at the terminal stage, and only 20% to 25% of all patients can be resected curatively (2). The carcinogenesis of pancreatic cancer generally follows a heterogeneous pattern (2, 3).

PD is performed in patients with carcinomas of the pancreatic head and uncinates, duodenum, distal common bile duct, or the ampulla (4, 5). PD can be a curative treatment approach in the periampullary area; however, it is complex and carries a high risk for patients due to worrisome levels of morbidity and mortality (6–8). The mortality rate has decreased significantly in the last 2 decades as PD has become a routinely used surgical approach in experienced centers. Nonetheless, successful management depends on proper patient selection, a high level of experience, advanced perioperative care, and a multidisciplinary approach. Even in experienced centers, the morbidity and mortality rates are still 30% to 50% and 3% to 5%, respectively (7–8). PFAO is one of the most important complications that may develop after PD. It is believed that PFAO can cause other serious complications, and an incidence of PFAO of 5% to 45% has been reported (8–10).

Risk factors for PFAO include gender, BMI, malnutrition, periampullary disease pathology, pancreatic resection material, soft pancreatic stump, pancreatic duct diameter, operative time, type of resection, pancreatic anastomosis technique, and intraoperative bleeding (2, 7, 8, 10–17). Recent studies have noted that surgeon experience and surgical centers are also risk factors (8, 18, 19). Despite the importance of associated risk factors, PJ is still a popular method for pancreatic stump management. Different anastomotic techniques are used by different centers and countries around the world. Since invagination PJ (i-PJ) is uncomplicated and dm-PJ offers a safe and effective option, they are often the methods of choice in cases of PFAO and are routinely used worldwide. In a literature review comparing dmPJ and i-PJ, the rates of PFAO, morbidity, and mortality were similar (20–25). However, in 2015, a new finding was reported in the literature; Hua et al. (26) found that i-PJ had a significantly lower clinically relevant PFAO ratio. However, the study emphasized the need for well-designed RCTs. Later meta-analyses (27–29) found that dm-PJ and i-PJ had similar rates of PFAO, morbidity, and mortality.

New techniques are continually being explored in the hope of reducing the rate of PFAO, as the incidence of PFAO in conventional PJ (c-PJ) anastomoses ranges from 3% to 45%. Yang et al. (22), in their meta-analysis, and Hashimoto et al (24), reported that the bandage PJ technique should be considered for future clinical trials and that new RCT studies are needed. However, Li et al. (25) and Zhang et al. (10) claimed that the bandage PJ and c-PJ techniques have similar PFAO, morbidity, and mortality rates, and noted that the total hospital costs for bandage PJ are higher than those of c-PJ. They suggested that surgeons should decide which reconstruction method they prefer (10).

BA is a critical anastomotic technique in some tertiary centers. The distinctive feature of this technique is the emphasis on reinforcement of the anterior and posterior pancreas with full-thickness sutures passing through the pancreatic remnant, in addition to the duct-mucosa anastomosis (30, 31). A recent meta-analysis conducted by Li et al. (30) comparing BA and c-PJ reported that BA was significantly associated with a lower grade B/C PFAO ratio. However, no significant difference was found in a subgroup analysis in patients with a soft pancreatic stump for grade B/C PFAO (3).

Pancreaticojejunostomy, hepaticojejunostomy, and gastrojejunostomy are commonly performed to reconstruct the pancreatic stump after PD. It has been suggested that the rate of PFAO could be reduced if pancreatic secretions are sent through an alternative jejunal loop. However, the superiority of an isolated PJ anastomosis has not demonstrated a statistically significant improvement in the rate of PFAO and other complications (32–35).

The addition of Braun's enteroenterostomy to a standard reconstruction after PD is a method widely used in many clinics to reduce morbidity. Braun enteroenterostomy is performed approximately 40 cm distal to the hepaticojejunostomy anastomosis and 20 to 30 cm distal to the pancreaticogastrostomy anastomosis. In a meta-analysis, Schorn et al. (35) reported that adding a Braun enterostomy to the standard reconstruction resulted in significantly better clinically relevant PFAO.

This review article has some limitations. Firstly, the inclusion of retrospective studies may have led to bias and anomalous results. Secondly, there is no clear information about the characteristics, numbers, and removal times of drains used in the studies. Thirdly, a meta-analysis involving only soft pancreatic anastomosis included studies with small sample sizes or was inconclusive. Therefore, optimal results could not be achieved for the leading group expected to have anastomotic leaks. In addition to these points, pancreaticogastrostomy was not evaluated in this review.

CONCLUSION

The development of a pancreatic fistula after PD is multifactorial. Therefore, the surgeon must perform the entire surgery from dissection to anastomosis meticulously. The results of dm-PJ-based anastomoses are similar in patients with non-soft pancreatic tissue and a wide diameter of the pancreatic duct. Therefore, the main risk factors for morbidity and mortality seem to be the soft tissue of the pancreatic remnant, a narrow duct, and a posterior-located duct. Recently, the BA technique has helped to significantly lower the PFAO rate in grade B/C patients, although no significant difference has been detected in cases with a soft pancreatic stump. In patients with a soft pancreas or a narrow pancreatic duct, an external stent can be added to the standard duct-to-mucosa anastomosis. Furthermore, the addition of Braun enteroenterostomy to the standard reconstruction can reduce the clinically relevant PFAO rate. It is to be hoped that future developments may add to the surgeon's toolbox in treating these patients.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The author have no conflict of interest to declare.

Financial Disclosure: The author declared that this study has received no financial support.

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