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REVIEW

Management of delayed stenosis of pancreatico-enteric anastomosis following pancreatoduodenectomy



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KEYWORDS

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Pancreaticogastrostomy

Summary Stenosis of the pancreatico-enteric anastomosis following pancreatoduodenectomy (PD), a late post-operative complication that is seen mainly after PD for diseases with good prognosis, has been reported in less than 3% of cases in the literature. Most often asymptomatic, pancreatico-enteric anastomotic stenosis can lead to pancreatitis, pain or pancreatic insufficiency. Symptomatic stenosis is difficult to treat and its management is not standardized. Magnetic resonance cholangiopancreatography is the best investigation to confirm the diagnosis of stenosis. The Endoscopic UltraSonography (EUS) « rendezvous » technique, associating an endoscopic approach and EUS-guided puncture of the main pancreatic duct, has been available since 2010. Of note, however, the failure rate of the EUS series is as high as 25%, leading to repeat procedures. Surgical reconstruction of the anastomosis has been reported with good results in terms of morbidity. Surgical re-do of the pancreatico-enteric anastomosis for stenosis following PD carries a low risk of pancreatic fistula (around 5%) and an overall morbidity rate of around 20%.

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Introduction

Pancreatic fistula and bleeding are the main « early » complications observed after pancreatic surgery. Their prevalence in the literature ranges from 15–35% and 3–15%, respectively, according to the type of procedure [1–4]. “Late” complications are rarely observed, mainly because survival after pancreatoduodenectomy (PD) for malignant

disease is short and therefore these complications do not have the time to occur [5,6]. Notwithstanding, for patients who undergo pancreatic surgery for benign disease or for whom the prognosis is favorable, survival can be long enough for late complications to occur and one of the most frequent is pancreatico-enteric anastomotic stenosis. Effectively, pancreatico-enteric anastomotic stenosis is observed in 25–60% of radiological series that include magnetic resonance cholangiopancreatography (MRCP) [7–9]. Other late complications include stenosis of the bilio-enteric anastomotic, responsible for jaundice and/or cholangitis, and anastomotic ulceration with bleeding, in 2.5–8% [10,11] and 10–30% [12] of cases, respectively.

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Pancreatico-enteric anastomotic stenosis is most often asymptomatic [13]. However, in certain instances, stenosis leads to pancreatitis, pain or exocrine pancreatic insufficiency [14–16]. Therapeutic management of painful and symptomatic anastomotic stenosis is difficult because treatment is not standardized [17,18], unlike bilio-enteric anastomotic stenosis for which management is relatively well codified and has been widely published in the literature [19,20]. The goal of this study is to expose the different modalities to manage late pancreatico-enteric anastomotic complications, based on an analysis of the literature.

Methodology

The incidence of stenosis of the pancreatico-enteric anastomosis is an increasingly frequent problem because of both the progress made in survival for malignant disease [21] but also because of wider indications for PD, notably for less aggressive diseases associated with prolonged survival such as endocrine tumors, intraductal papillary mucinous neoplasms (IPMN), ampulloma, solid pseudo-papillary tumors (SPPT) or cystic tumors of the pancreas.

The key words used for our bibliographic search in Pubmed and Medline included “pancreaticodigestive, pancreaticojejunostomy, pancreaticogastrostomy, stenosis, stricture”. We selected 21 articles in the literature beginning in 2010 that appeared to be the most pertinent: 15 studies that analyzed the feasibility of endoscopic management (Table 1) and six studies that analyzed the feasibility, morbidity and mortality of re-do pancreatico-enteric anastomosis surgery (Table 2).

Occurrence of a pancreatico-enteric anastomotic stenosis has been reported in 1.5–11% of patients according to the studies, appearing after a median of 18 (8–120) months [11,17,22].

Diagnosis of the stenosis

The diagnosis of late anastomotic stenosis can arise under several different circumstances. While anastomotic stenosis can be perfectly asymptomatic [13] and discovered fortuitously, most often (77–100% of cases) [22–24], the patient complains of chronic pain due to pancreatitis [9,17]. Stenosis can also be responsible for exocrine pancreatic insufficiency [16] because of lack of pancreatic juice secretion into the gastro-intestinal tract. Kurosaki et al. [23] reported an anastomotic stenosis in 11 patients with normal diameter of the main pancreatic duct (MPD) after having undergone PD with pancreaticogastrostomy. The stenosis was asymptomatic in 45% of patients, associated with endocrine or exocrine pancreatic insufficiency in 36 and 27% of patients respectively and radiological signs of pancreatitis were present in 45% of patients.

The decision to treat the stenosis is based on the existence of symptoms (pain, pancreatitis).

Paraclinical investigations

MRCP is the investigation of reference for the diagnosis of stenosis, optionally coupled with secretin-enhancement [8,25,26]. Effectively, secretin stimulates the secretion of pancreatic juice and bicarbonates by the exocrine pancreas, resulting in increased intraductal pressure. It is

best to perform repeated, thick MR-CP slices before and then, every 15 to 30 seconds over 10–15 minutes after intravenous administration of one mL of secretin/10 kg of body weight [27] (Fig. 1).

Anastomotic stenosis is defined as a reduction in the diameter of the MPD at the level of the anastomosis associated with upstream dilatation. The median cut-off values of MPD diameter necessary for the diagnosis of anastomotic stenosis is 2.5 mm and 3.2 mm after injection of secretin [17,26]. This investigation confirms the exact site of the stricture and helps eliminate other diagnoses such as IPMN, intraductal carcinoma or pancreatitis.

Therapeutic management

Anastomotic stenosis leads to exocrine pancreatic insufficiency, occasionally acute but most commonly, chronic pancreatitis [23]. Management is based mainly on close surveillance in order to propose timely endoscopic or surgical intervention in case of symptoms. In the absence of symptoms, there is no evidence in the literature to show that preventive treatment is necessary, and in particular, to preserve pancreatic function.

Endoscopic approach

There are several possible endoscopic approaches:

- the “classical” endoscopic retrograde cholangiopancreatography (ERCP) approach;
- the EUS-guided « rendezvous » (approach);
- transgastric drainage of the main pancreatic duct;
- the pancreatic antegrade needle knife (PANK) technique;
- percutaneous approaches.

The “classical” ERCP approach consists of re-permeabilization of the anastomosis by a direct approach with a traditional endoscope. In the literature, the failure rate of this technique is about 80%. The three main reasons for failure include:

- difficulty in steering through the afferent limb of the anatomically modified Child assembly;
- the high risk of perforation with a traditional endoscope, especially when the operator is not experienced [28];
- inability to cannulate the MPD either because the stenosis is too tight or sometimes even total, or because the procedure is technically too difficult [22,29–34].

In patients with pancreaticogastrostomy, the anastomosis can be re-permeabilized in 57% of cases. It is generally easier to find the opening of the MPD with a side-viewing gastroscope, by dividing the gastric mucosa in the middle of the anastomotic area. Obviously, the risk of gastric perforation must not be underestimated [35]. The high failure rate observed with this “traditional” technique has led gastroenterologists to develop other therapeutic modalities.

Difficulty in identifying the opening of the MPD has driven endoscopists to the « rendezvous » technique, whose first step is EUS-guided transgastric puncture of the dilated MPD. After pancreatography to ensure that the placement is correct, a guide-wire is inserted in antegrade fashion into the MPD until it reaches the jejunum or stomach, according to the type of anastomosis (Fig. 2) [29,30]. The guide-wire is then grasped visualized endoscopically using a duodenoscope or colonoscope in the jejunum or stomach. Balloon dilatation (4mm) or insertion of a plastic stent

Table 1 Summary of the literature: endoscopic studies.

Author	Year	Indication	Number of cases anastomosis type	Technique	Reasons for failure	Complications
Ryou et al. [30]	2010	Pain	3 – PJ	ERCP EUS-RDV, then	3 – CPP not visible 3 – Anastomosis not passable Success	– – 1 pancreatitis
Ota et al. [31]	2010	Pain	1 – PJ	PANK ERCP, then EUS-RDV	CPP not visible Success	–
Kikuyama et al. [35]	2011	Pancreatitis	6 – PG/8 – PJ	ERCP, then EUS-RDV	ERCP: 8 MPD not accessible but all 8 anastomoses passable at EUS-RDV	–
Itoi et al. [29]	2011	Pancreatitis	2 – PJ	ERCP, then EUS-RDV	2 – CPP not visible Success	1 sepsis with retroperi- toneal collection
Mori et al. [36]	2012	Pancreatitis	1 – PJ	EUS-RDV	–	–
Takikawa et al. [33]	2013	Pain	1 – PJ	ERCP, Then EUS-RDV	Anastomosis not passable Success	–
Matsubayashi et al. [37]	2013	Pancreatitis	1 – PJ	EUS-RDV	Success	–
Hisa et al. [38]	2013	Pancreatitis	1 – PJ	EUS-RDV	Success	–
Kikuyama et al. [52]	2013	Pancreatitis	1 – PJ	ERCP via duodenoscope	Success	–
Kawakami et al. [34]	2014	Pancreatitis	1 – PG	ERCP, then EUS-RDV	Anastomosis not passable Success	–
Nakaji et al. [53]	2015	Pancreatitis	1 – PJ	ERCP, then ERCP anterior viewing endoscope	Anastomosis not passable Success	–
Kida et al. [54]	2016	Pancreatitis	3 – PJ	ERCP	3 – success	–
Chang et al. [39]	2016	Pain	1 – PG	ERCP EUS-RDV	Anastomosis not passable Success	Pancreatitis –
Yang and Yoon [44]	2016	Pancreatitis	1 – PJ	Percutaneous ERCP	Failure of progression through intestinal loop Success	– –
Kida et al. [55]	2017	Pancreatitis	1 – PJ	ERCP	Success	–

PJ: pancreaticojejunostomy; PG: pancreaticogastrostomy; ERCP: endoscopic retrograde cholangio pancreatography; EUS-RDV: Endoscopic UltraSound Guided–Rendezvous; PANK: pancreatic antegrade needle knife, MPD: main pancreatic duct.

(5–7 Fr) is then used to treat the stenosis. The success rate of this technique is higher (85%) with low morbidity [30,32–39]. However, the technique is complex requiring experienced operators as well as a well-adapted technical platform. Difficulty in snaking through a long and tortuous afferent loop, as sometimes occurs with the typical Child assembly, can be overcome by the use of a “single-balloon endoscope” that enhances the progression of the scope in the loop with a low risk of perforation [32,40]. In case of failure, the procedure must be repeated, leading to increased costs, morbidity and distress for the patients. In case of failure or when the anastomosis is not passable, an alternative is to perform a drainage between the MPD and the stomach or jejunum, as reported in several series

[41–43]. This technique consists of an echo-guided puncture of the MPD and fluoroscopic-guided insertion of a stent between the MPD and the stomach or jejunum.

Two other endoscopic techniques have been reported. One is the PANK technique wherein the stenosis is divided in an antegrade fashion from the MPD [30]. The patient is sedated and prophylactic antibiotic coverage is administered. A “needle-knife” is inserted and threaded under fluoroscopic guidance through the MPD up to the site of the anastomotic stenosis site. The stenosis is then balloon dilated and a stent is inserted. The stent will be replaced four to eight weeks later by a pancreaticojejunal or pancreaticogastric stent that will finally be removed another four to eight weeks later. This procedure is feasible particularly

Table 2 Summary of the literature: surgical studies.

Author	Year	Indication	Number of cases—Anastomosis	Pancreatic fistula	Overall morbidity	Mortality	Follow-up (months)	Long term success (%)
Sledzianowski et al. [9]	2004	Pancreatitis	1 – PJ	0	–	0	–	–
Kuroki et al. [47]	2008	Pancreatitis	1 – PJ	0	–	0	–	–
Morgan et al. [17]	2010	Pain and Pancreatitis	27 – PJ	2 (7.4%)	6 (22%)	0	56	26
Demirjian et al. [22]	2010	Pain and Pancreatitis	7 – PJ ^a	0	2 (28.6%)	0	18	57
Oida et al. [48]	2012	Pancreatitis	1 – PJ (hybrid technique)	0	–	0	–	–
Cioffi et al. [49]	2016	Pain and Pancreatitis	27 – PJ	1 (3.7%)	7 (26%)	0	30	60
Wagle et al. [18]	2017	Pain and Pancreatitis	5 – PJ 1 – PG	–	–	0	36	83

PJ: pancreaticojejunal; PG: pancreaticogastric.

^a 4 anastomotic reconstructions, 2 enlargements of the pancreaticojejunostomy and one failure due to adhesions preventing dissection.

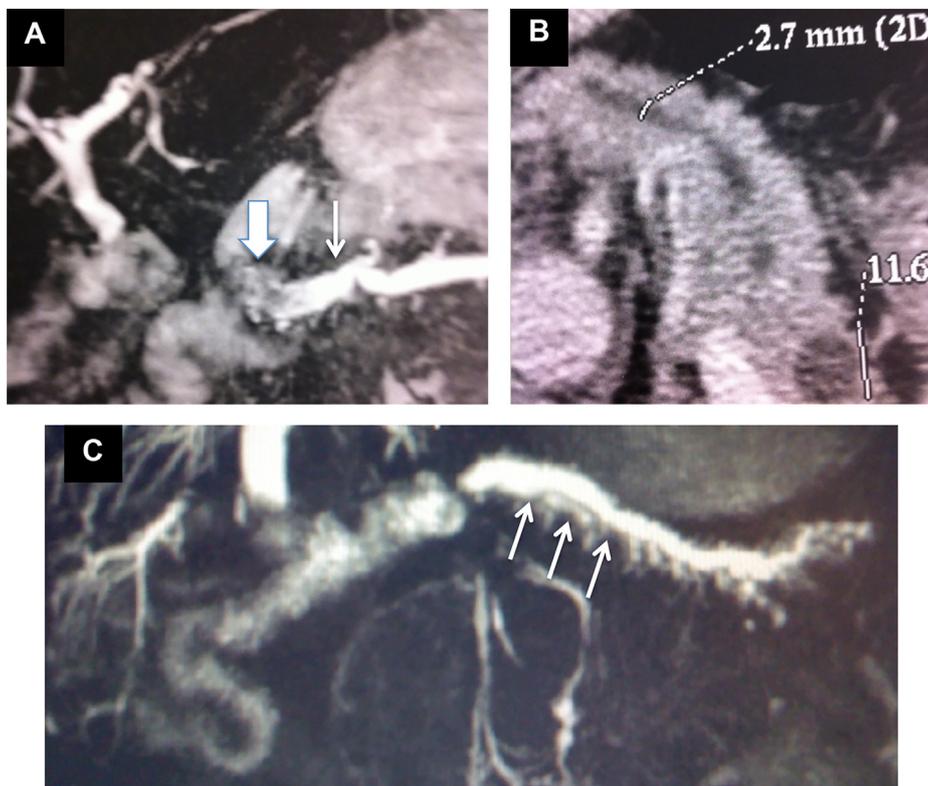


Figure 1. MRCP: pancreatico-enteric anastomotic stenosis with upstream dilatation of the MPD. A. Coronal slice; ductal obstruction originating from anastomotic stenosis (thick arrow); dilatation of the main pancreatic duct (thin arrow). B. Axial slice; dilatation of the MPD measuring 2.7 mm. C. Coronal slice: dilatation of MPD (thin arrows).

after failure of the “classical” ERCP or EUS-RDV approaches when the opening of the MPD cannot be visualized endolumenally.

Finally, the percutaneous approach, reported by Korean authors, consists of stenting the pancreatico-enteric anastomosis by percutaneous transhepatic passage through the bilio-enteric anastomosis [44]. The authors described a 21 G needle percutaneous transhepatic puncture of the intrahepatic bile duct of segment VI, identified under ultrasonographic guidance. After dilatation, an 8 Fr vascular

sheath was placed through the hepaticojejunostomy to facilitate the onward passage to the pancreaticojejunostomy. A 5 Fr catheter along with a guidewire was manipulated up to the pancreaticojejunostomy and used to opacify the anastomotic stenosis by retrograde filling. Next, the anastomosis was identified via a percutaneous transgastric puncture under fluoroscopic guidance. The previously described rendezvous technique allowed positioning a 7 Fr stent through the anastomosis. These two techniques are rarely reported in the literature, but lead to satisfactory

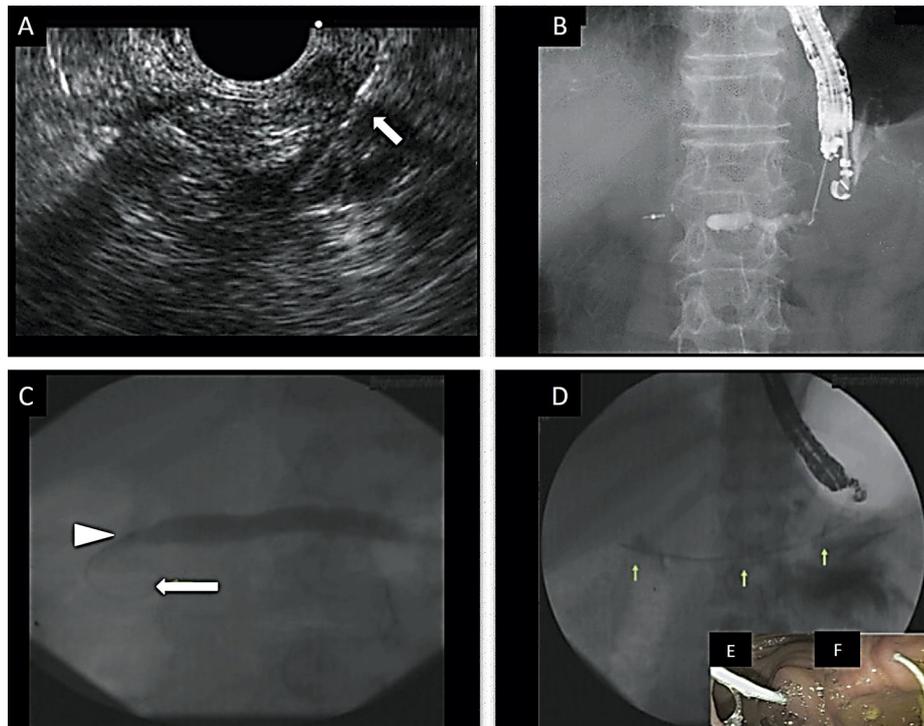


Figure 2. Endoscopic placement of a pancreatico-enteric stent. A. Puncture of the MPD with a 19 gauge needle (arrow). B. Radiography visualizing the pancreatic ducts by transgastric approach. C. Fluoroscopy – the full arrow shows the guide – the arrow head show the stenotic area. D. Placement of the gastro-pancreatico-jejunal stent – fluoroscopy – the arrows show the guide. E. Jejunal view of the stent. F. Gastric view of the stent. Source: Courtesy of Itoi et al. [29] and Ryou et al. [30].

results. One instance of pancreatitis was reported after the PANK procedure. All these endoscopic techniques must now be standardized and validated; they should be performed in centers specialized in interventional endoscopy.

Surgical approach

Seven studies have reported results of re-do surgical reconstruction of the anastomosis. In the majority of cases, a pancreaticojejunostomy stenosis had caused pancreatitis and pain. Surgery consisted of reconstruction of the pancreaticojejunostomy (or pancreaticogastrostomy in one case). It is well recognized that hard consistency of the pancreas and MPD dilatation are the best guarantees for a low-risk anastomosis [45,46]. When pancreatico-enteric stenosis leads to ductal obstruction, parenchymal fibrosis and ductal dilatation, the anastomosis is relatively easy to perform and associated with overall morbidity of 20% [9,17,18,47–49]. Oida et al. described an alternative hybrid technique consisting of a trans-anastomotic stent inserted after a surgical approach to the afferent limb [48]. Last, Demirjian et al. [22] published a series of seven patients, two of whom underwent a modified Puestow procedure consisting of a side-to-side pancreaticojejunostomy after making a 2 cm opening on the anterior aspect of the MPD. The advantage of this technique is that it does not require reconstruction of the Roux-en Y limb.

The choice between pancreaticojejunostomy or pancreatic-gastrostomy does not influence the fistula rate after PD [50]. It is therefore not possible to recommend one type of anastomosis over another during the re-do operation. The choice between the two techniques is therefore left to the discretion of the surgeon, according to experience and personal preferences as well as intra-operative findings.

Therapeutic sequence

Because of its mini-invasive character, improvements in the technique and the low rate of complications, the endoscopic approach should be privileged as the first-line management of these stenoses [22,35,51]. The traditional ERCP and rendezvous techniques are the most standardized today and are those most often performed by interventional gastroenterologists in many other settings [51,52]. Several tricks have been developed to cope with the main causes of failure of the traditional technique, essentially the impossibility to steer through the intestines in order to visualize the MPD opening, including the use of a balloon to facilitate the progression of the scope or use of a duodenoscope with anterior or lateral vision [29,52,53]. Faced with repeated failure of the endoscopic procedures, a pluridisciplinary discussion should be opened in order to treat the stenosis surgically in a timely and effective fashion [9,17].

Conclusion

Stenosis of the pancreatico-enteric anastomosis is a complication that occurs relatively late after surgery, but requires adapted and specific management, including eventually repeat surgical reconstruction. Initial interventional endoscopic management has made great strides and can be of help. As for many other affections of the pancreas, the final therapeutic decision should be taken by interventional radiologists, gastro-enterologists and surgeons. The available panel of therapeutic options and strategies is large and the best option is the least risky procedure, adapted to the patient. The endoscopic approach has the advantage of being mini-invasive. However, repetitive endoscopic

procedures should be avoided and it must always be kept in mind that surgical reconstruction of the anastomosis is technically possible and provides satisfactory results.

Disclosure of interest

The authors declare that they have no competing interest.

Key points

- Pancreatico-enteric stenosis, a late complication of pancreatoduodenectomy, is rarely symptomatic.
- Abdominal pain secondary to pancreatitis is the most frequent symptom.
- Exocrine pancreatic insufficiency is the ineluctable outcome.
- Progress in interventional endoscopy is an interesting therapeutic alternative but the procedure is complex.
- Echo-endoscopic guided “rendezvous” technique is the technique that provides the best results in terms of efficacy.
- If endoscopy is not possible, surgical reconstruction is an alternative with a low complication rate.

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