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CLINICAL REVIEW

Approach to management of pancreatic strictures: the gastroenterologist's perspective

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Abstract
Pancreatic strictures represent a complex clinical problem which often requires multidisciplinary management with a team of gastroenterologists, surgeons and radiologists. Dominant strictures are largely due to inflammatory processes of the pancreas like chronic pancreatitis. However, differentiating benign from malignant processes of the pancreas, leading to strictures is imperative and remains a challenge. With advances in endoscopic management, options for therapy include endoscopic retrograde cholangiopancreatography (ERCP), and endoscopic ultrasound-guided pancreatic drainage (EUS-PD) in situations where ERCP is not feasible or fails. However, endoscopic therapy is suited for a select group of patients and surgery remains key to management in many patients. In this narrative review, we look at the gastroenterologist's perspective and approach to pancreatic ductal strictures, including endoscopic and surgical management.

Keywords Chronic pancreatitis · Stricture · ERCP · EUS

Introduction

Pancreatic duct (PD) strictures are one of the most challenging diagnostic and therapeutic conditions for treating gastroenterologists. The principal diagnostic consideration is to rule out underlying malignancy. Management of these strictures can be challenging for endoscopists due to the complexity of the underlying disease leading to the stricture or associated PD stones in benign disease like chronic pancreatitis (CP) and leaks leading to recurrent collections related to post-traumatic strictures. PD strictures can be arbitrarily classified as benign or malignant, single or multiple and dominant or non-dominant [1]. Dominant stricture has been defined by upstream dilatation of the main pancreatic duct to 6 mm or more in diameter, occlusion of contrast outflow alongside a 6-Fr size catheter placed upstream from the stricture or provocation of symptoms, mainly abdominal pain during continuous infusion of 1 l saline at the upstream area using a nasopancreatic catheter for 12–24 h [2]. Knowledge of each of these categories in addition to location of stricture in the main pancreatic duct (head, genu, body and tail) and anatomical ductal variations (pancreatic divisum or ansa) is critical for formulating effective management strategy.

Endoscopic management is a first-line therapy in symptomatic single-dominant pancreatic strictures in view of its feasibility and lower rates of morbidity and mortality as compared to surgery [3]. Emerging diagnostic and therapeutic tools are now available to manage PD strictures and associated conditions. This review will focus on clinical presentation and concise differential diagnosis of the etiologies of PD stricture along with emerging diagnostic modalities and rapidly advancing endoscopic management options and role of surgery.

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Clinical presentation

Patients with symptomatic PD strictures usually present with persistent or recurrent abdominal pain, particularly in the setting of CP. Ductal hypertension due to obstruction caused by dominant strictures with or without associated stones is one of pathophysiologic mechanism of pain in these patients [4]. Weight loss and steatorrhea secondary to exocrine pancreatic insufficiency (EPI) and pancreatic outflow obstruction can be other presenting complaints in these patients. Coexisting pseudocysts can cause gastric or duodenal compression resulting in nausea and vomiting in some patients. Jaundice and cholangitis may be initial presentations in patients with associated biliary strictures, in autoimmune pancreatitis (AIP) and immunoglobulin G4-related sclerosing cholangitis (IgG4-SC). Primary pancreatic ductal adenocarcinoma can obstruct the main PD and cause symptoms of acute pancreatitis or EPI.

Etiology of PD strictures

Depending upon etiology, PD strictures can be classified into two categories: benign and malignant. Table 1 depicts the etiologies of benign PD strictures. PD strictures secondary to malignancy can either directly involve the duct or cause extrinsic compression on duct due to mass effect. Meticulous history with documentation of alcohol abuse and previous episodes of pancreatitis along with physical examination could be a guide to the etiology, followed by cross-sectional imaging or endoscopic ultrasound (EUS), or any combination of these modalities, to accurately evaluate the pancreatic parenchymal and ductal abnormalities [5].

Ruling out the underlying malignancy is the first step in the evaluation of PD stricture [6]. Younger age, history of pancreatitis, absence of jaundice, normal bile duct, strictures in the body or tail of the pancreas, diffuse ductal irregularity and multiple strictures, pancreatic divisum anatomy, irregular side branches and presence of associated main pancreatic duct stones may point toward benign nature of stricture [7, 8], whereas isolated PD stricture with upstream dilatation, associated mass, stricture in head and neck of pancreas and simultaneous PD and common bile duct stricture (double duct sign) favor malignancy [4, 7, 8]. However, it is noteworthy to mention that none of these features are absolute for ruling out a particular etiology, as AIP can present with obstructive jaundice and a diffusely enlarged pancreas and/or low-attenuation mass in the head of the pancreas. Also, approximately 2% of patients with "newly diagnosed" CP may have underlying pancreatic malignancy [9] and patients with a history of quiescent CP who present with new-onset alarm symptoms should be approached with suspicion to rule out a malignancy [8].

CP is the most common cause of pancreatic stricture, and the presence of dominant PD stricture leads to ductal obstruction resulting in pain or superimposed episodes of acute on chronic pancreatitis [10]. Associated stone in the PD will lead to additional injury causing inflammatory cascade activation resulting in further fibrosis and progression of stricture [11]. In a large study of patients with CP undergoing pancreatic endotherapy for MPD obstruction, PD stricture was the most common etiology of obstruction (47%), while isolated PD stone was present in 18% and a combination of stricture and stone was seen in 32% cases [12].

Autoimmune pancreatitis (AIP) is another less common, but medically treatable cause of PD strictures and can also be associated with biliary stricture in the setting of immunoglobulin G4 (IgG4)-related sclerosing cholangitis (IgG4-SC). Apart from the typical imaging features of AIP which include diffuse enlargement of pancreas or a discrete mass, PD strictures can result from AIP. Features suggestive of AIP-associated PD stricture are: (i) long stricture involving more than one-third of length of PD, (ii) lack of upstream dilatation (PD diameter < 5 mm), (iii) multiple strictures, and (iv) side branches arising from strictured segment [13–18]. EUS-guided pancreatic parenchymal biopsy may be performed to confirm AIP on histology and to exclude malignancy [19]. Other less common causes of PD stricture include trauma, iatrogenic triggers from placement of a PD stent, or post-pancreatic surgery.

Table 1 Etiology of benign pancreatic strictures

Causes of benign pancreatic duct strictures [6, 10]
Chronic pancreatitis
Recurrent acute pancreatitis
Trauma
Pancreatic pseudocyst
IgG4 related disease (Autoimmune pancreatitis and IgG4 related sclerosing cholangitis)
Previous pancreatic surgery
Benign pancreatic neoplasm
Iatrogenic (Placement of PD stent, previous ERCP instrumentation)

Role of cross-sectional imaging in evaluation of PD strictures

The possibility of underlying malignancy necessitates investigation with high-quality cross-sectional imaging. European guidelines recommend performing a high-quality pancreatic computed tomography (CT) scan and/or magnetic resonance imaging (MRI) with cholangiopancreatography (MRCP) to

rule out pancreatic cancer in patients of CP [2], which is a most common cause for PD strictures. A meta-analysis of 52 studies found that CT scan and MRI present similar diagnostic accuracies for the diagnosis of pancreatic cancer [20]. Additionally, MRCP has excellent accuracy for delineation of ductal abnormalities including strictures, dilation, and intra-ductal stones; in two retrospective studies, its diagnostic accuracy for ductal abnormalities was 73.2% (41 children with CP) and 92.2% (30 adults with CP) [21, 22].

Role of endoscopy in evaluation of PD strictures

EUS can be utilized for evaluation of both parenchymal and ductal changes. The role of EUS for diagnosis of CP comes only if CT and MRI are normal and the suspicion for CP is still high, especially in patients with recurrent acute pancreatitis due to low specificity and high inter-observer variability [23]. Major benefit of EUS as diagnostic tool in patients of PD stricture is that it allows tissue sampling where malignancy or AIP is suspected due to higher success rate and fewer post-procedural complications as compared to ERCP [24]. EUS-guided parenchymal biopsy has a sensitivity of approximately 80% for diagnosis of AIP via histology alone with minimal resultant risk of acute pancreatitis [19]. It should be noted that EUS-FNA (fine needle aspiration) of lesions in the setting of CP is less sensitive according to a retrospective and a prospective study (54% and 74% vs. 89% and 91% in the presence vs. the absence of CP, respectively) [2]. In a recent prospective and multicenter analysis in China, EUS-guided FNB (fine needle biopsy) samples produced more accurate diagnoses than samples collected by EUS-guided FNA in pancreatic masses [25].

Given the non-invasive nature of MRCP and highly reliable ductal findings, ERCP has shifted to primarily a therapeutic procedure in management of PD strictures. However, it offers the endoscopist the modality to take brushings for cytology for ruling out occult malignancy at the time of intervention, particularly in the absence of mass on cross-sectional imaging and chance to use emerging diagnostic tools as discussed below in evaluation of PD strictures [3, 10]. The tissue yield of brush cytology of pancreatic duct can be improved by stricture dilation [26].

Peroral pancreatoscopy with the newest platform SpyGlass DS™, single-operator, single-use cholangiopancreatoscopy system (Boston Scientific, Natick, Massachusetts, USA), provides high-quality images for determining the etiology of indeterminate PD strictures and pathology, including main duct intraductal papillary mucinous neoplasms and malignancy both by endoscopic appearance and improved sampling via biopsy instead of brushings with sensitivities of up to 91% [6, 27–29]. Post-ERCP pancreatitis (PEP) prophylaxis should be utilized after pancreatoscopy in view of increased risk of this complication [29].

Serial pancreatic juice aspiration cytologic examination (SPACE) is a diagnostic method which involves collection of pancreatic juice by a nasopancreatic tube placed via the major papilla, followed by cytological analysis. In the first study of 20 patients, diagnosis of pancreatic cancer was made with a sensitivity of 100%, specificity of 83.3%, and accuracy of 95%. None of the patients had acute pancreatitis after drainage tube placement [30]. Subsequently, another study reported 92% sensitivity of SPACE for diagnosis of pancreatic cancer and concluded that SPACE can be useful for the diagnosis of small pancreatic cancers which could not be recognized by EUS [31].

Emerging endoscopic tools for evaluation of indeterminate PD strictures include confocal laser endomicroscopy (CLE) and optical coherence tomography (OCT). CLE is a novel endoscopic imaging technique that can provide real-time optical biopsies from PD strictures [32]. During this procedure, currently available CholangioFlex miniprobe (Cellvizio; Mauna Kea Technologies, Paris, France) is passed through the ERCP catheter and fluorescein dye is administered to produce high-resolution images of the PD stricture at a microscopic level. CLE probes visualize biliary epithelium by transmitting low-power laser and detecting light reflected back from the tissue [32, 33]. Its role in evaluation of PD strictures is supported by only small case series and studies [33, 34]; therefore, large-scale data and standardized classification systems as developed for biliary strictures are needed before its widespread use. OCT is a technology that uses infrared light to obtain high-resolution, cross-sectional tomographic imaging of the tissue microstructure below the surface that can be interpreted in vivo. The latest version of this technology, NVision Volumetric Laser Endomicroscopy (VLE) (Ninepoint; Bedford, MA), allows for a wider and deeper field of vision and higher-quality images unlike earlier versions [35]. This technique requires advancing the catheter with probe through the working channel of the duodenoscope into the PD adjacent to the wire to the area of interest and then performing 90-s scan for capturing and interpreting images in vivo [6, 35]. The addition of performing OCT during ERCP does not seem to add risk to the procedure as evidenced by the low rate of adverse events [36]. Despite having several advantages over current diagnostic modalities for indeterminate PD strictures like allowing under-the-surface evaluation unlike cholangioscopy, which allows examination of only surface mucosa, allowing circumferential evaluation across 6 cm of tissue in 90 s unlike CLE, which evaluates only small focal areas at one time, and having smaller diameter probe than cholangioscope, which can be easily advanced in narrow strictures, its optimal utility is recommended in combination with other diagnostic modalities [35].

Role of serum markers in evaluation of PD strictures

Serum markers such as IgG4 in AIP or CA 19–9 in pancreatic cancer can also be useful in determining the etiology of the stricture [24]. A combination of IgG4 levels and CA19-9 has been shown to be effective in differentiating between AIP and pancreatic cancer. CA19-9 levels less than 74 IU/ml with IgG4 levels > 1.0 g/L helped identify patients with AIP with 94% sensitivity and 100% specificity [37]. In another study from Taiwan, CA19-9 levels < 85 IU/ml with IgG4 levels > 2.8 g/l had the best diagnostic accuracy of 85% for AIP, as compared to pancreatic cancer [38].

Management of pancreatic duct strictures

Management of pancreatic stricture depends upon the etiology, presence of symptoms, age, comorbidities, anatomy of the stricture (number and location), and availability of expertise (endoscopic vs. surgical). Asymptomatic strictures do not require any intervention if malignancy has been excluded by cross-sectional imaging and brush cytology. The primary aim of management is relief of pain and strategies include medical, endoscopic and surgical techniques. Among all the above-mentioned etiologies of pancreatic stricture, autoimmune pancreatitis is the only condition which can be managed by medical therapy. Induction of remission is usually achieved with glucocorticoids, while there is a difference of opinion regarding maintenance therapy in these patients. Other medical management common to all etiologies include removal of the causative agent like alcohol and smoking, and management of exocrine insufficiency through pancreatic enzyme replacement therapy.

Endoscopic management

Endoscopic therapy is usually the first line of management for pancreatic strictures in the majority of centers. Endoscopic management includes pancreatic sphincterotomy, followed by dilatation of stricture and PD stent placement (Figs. 1 and 2). Multiple options are available for dilatation of stricture which include balloon or Bougie dilators and Soehendra stent retriever if the dilator cannot traverse the stricture [5, 39]. A recent study evaluated the use of 6-Fr cystotome (diathermy catheter) as an alternative method for dilation of recalcitrant pancreatic strictures after the failure of conventional modalities [40]. PD strictures being tight and resilient are not effectively decompressed by dilatation alone and hence should be followed by stenting [41].

Preference of stent

Plastic stent placement has been recommended by both ASGE and ESGE guidelines, which can be placed for a prolonged period or exchanged on a scheduled basis or upon recurrence of symptoms. Both guidelines recommend placement of a single 10-Fr plastic stent across the dominant stricture as smaller stents are prone to occlusion, thus, increasing the number of hospital admissions for pain [2, 41]. ESGE defines refractory MPD strictures as persistent or recurrent symptomatic dominant strictures even after 1 year of single pancreatic stent placement [2]. Although ESGE suggests consideration of multiple side-by-side plastic stents for refractory strictures, some experts prefer multiple stent placement at the initial session only to avoid blockage of side branches. In a multicentric study on long-term outcome after multiple plastic stenting for refractory pancreatic stricture in CP, 74.4% (32/43) of the patients were asymptomatic during a mean follow-up of 9.5 years (0.3–15.5 years) after

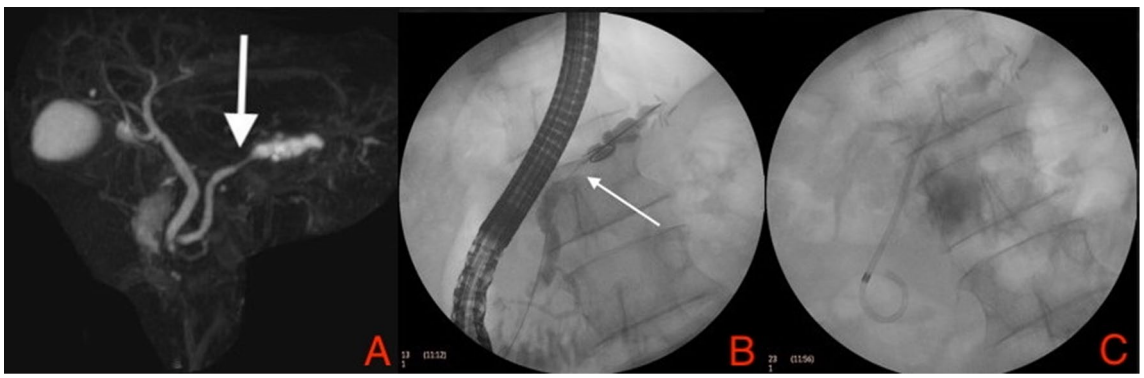

Fig. 1 **A** Patient with adenocarcinoma of the tail of the pancreas post-distal pancreatectomy with dominant stricture (arrow) in the pancreatic body. **B** Pancreatogram showing a dominant stricture (arrow). Brush cytology revealed adenocarcinoma. **C** Pancreatic stent was placed to achieve complete drainage

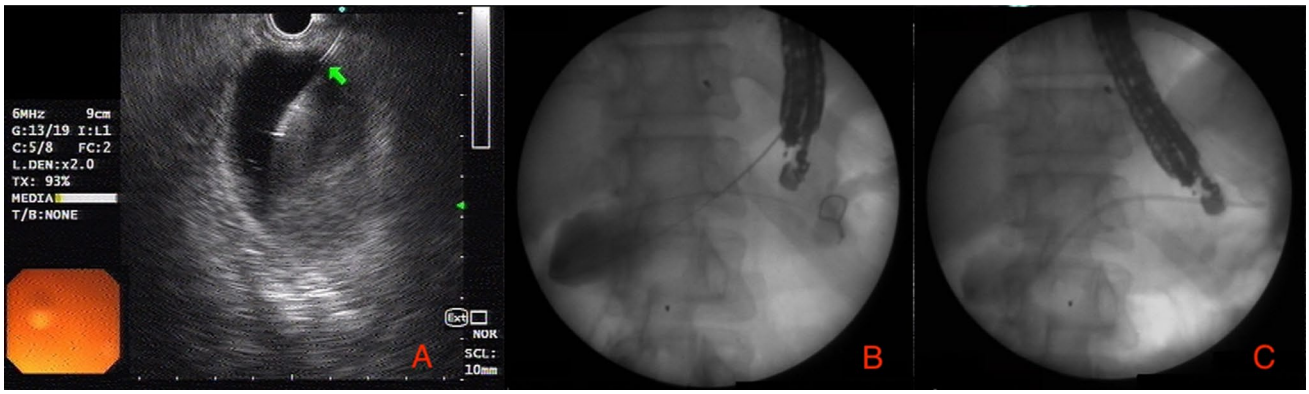

Fig. 2 Dominant stricture in the neck of the pancreas in an 11-year-old boy presenting with abdominal pain (big arrow) with long common channel (double-headed arrow) with bile duct also opacified on injection in the MPD (small arrow). This is representative of a pancreaticobiliary malunion

stent removal [42]. However, there are neither any trials comparing single large diameter vs. multiple side-by-side smaller diameter plastic stents for PD stricture therapy nor comparing scheduled vs. on demand stent exchange. There are no recommendations regarding the length of the stent, and the length of the stent used depends on the location and length of the stenosis.

Technical success is defined as placement of stent across the dominant MPD stricture or the most proximal stricture in case of multiple strictures which is aimed at decompression of the MPD to reduce pain and persistently dilate the stricture(s). The number of strictures and location of stricture are the major factors determining the success of endotherapy. So, a single stricture in the head of the pancreas is an ideal candidate for ERCP with stenting compared to stricture in tail or multiple strictures. ERCP has a technical failure rate of 3–10% and the common reasons include failure of cannulation of the main pancreatic duct, severe strictures, pancreatic stones, or altered anatomy. In such patients, EUS-guided PD drainage has evolved as a minimally invasive alternative to surgery. Clinical success has not been defined for these patients, but absence of pain on follow-up is an acceptable definition. Multiple studies have shown an immediate clinical success rate of 83–100% with long-term clinical success rate of 52–84% with use of plastic stents [43–49]. A meta-analysis of 16 studies reported an immediate pain relief in 88% and long-term pain relief in 67% of patients with CP undergoing endotherapy [50]. Long-term stricture resolution rate after removal of plastic stent varies from 58 to 74.4% [42, 45].

Fully covered self-expandable metal stents (FCSEMS) have been evaluated for treatment of pancreatic stricture in multiple small studies. A recent meta-analysis of ten studies with 163 patients showed a stricture resolution rate of 93% (95%CI 84–99%) with overall rate of adverse events being 34.9% compared to complication rate of 7.85% with plastic stents [50, 51]. Another meta-analysis comparing FCSEMS and multiple plastic stent in refractory PD stricture reported similar improvement in pain after stenting, risk of recurrence of pain after stent removal and stricture resolution with significantly higher risk of adverse events with FCSEMS [52]. Lack of long-term data and clinical experience with high complication rate warrants further evaluation before FCSEMS can be recommended for pancreatic strictures.

EUS-guided pancreatic duct drainage (EUS-PD)

Failure of transpapillary drainage of PD by conventional ERCP or inaccessible papilla due to surgically altered anatomy (Whipple's procedure, Billroth II, Roux-en-Y gastric bypass) are the two main indications of EUS-guided pancreatic duct drainage. Other indications and contraindications to EUS-guided pancreatic drainage are summarized in Table 2.

Technique of EUS-PD

There are two distinct techniques for EUS-PD: (i) EUS-guided rendezvous (EUS-RV), and (ii) EUS-guided pancreatic transmural stenting (EUS-PTS).

There are two access routes to PD: transgastric and transduodenal. After visualization of PD by EUS, puncture is usually made with a 22-gauze needle with a 0.018-inch hydrophilic guidewire or a 19- gauze needle with a 0.025-inch or 0.035-inch wire. A 19-G needle is the preferred size, while a 22-G needle is used when the pancreas is fibrotic or MPD is < 5 mm. Apart from needle size, sharpness of the needle is also an important factor, as stiff parenchyma in a case of chronic pancreatitis will prevent smooth puncture in the absence of a sharp tip. In EUS-RV, after transmural puncture, the wire is guided across the stenosis to

Table 2 EUS guided Pancreatic Drainage- Indications and Contraindications (Adapted from Reference number 53)

Indications for EUS-PD	Contraindications for EUS-PD
MPD dilation caused by strictures or stones	Unable to visualize MPD on EUS
Inaccessible to pancreaticojejunal anastomosis	Multifocal MPD strictures
Difficulty in accessing MPD by ERCP	Presence of blood vessels interning in the puncture route
MPD disruption	Long distance from puncture site to MPD
	Coagulopathy, bleeding tendency

ERCP endoscopic retrograde cholangiopancreatography, *EUS* endoscopic ultrasound, *MPD* main pancreatic duct

pass through papilla into the duodenum. Then EUS scope is exchanged for a duodenoscope, followed by grasping the wire and performing endotherapy over the guidewire.

EUS-PTS is done when the guidewire cannot pass across the stenosis or there is a previous surgery precluding access to papilla. After passage of guidewire into the PD, the next step involves dilatation of tract which can be achieved with electrocautery or non-electrocautery devices. Electrocautery includes diathermic sheath (prototype Cysto-Gastro set, EndoFlex, Voerde, Germany) or cystotome (Cook Medical) while non-electrocautery includes mechanical dilators and balloon dilators. There is no clear consensus on which device to be preferred, but data from small studies on EUS-PD and extrapolated data from EUS-guided biliary drainage show that non-electrocautery devices have lower rate of adverse events and, hence, should be used as the primary dilation device. Although cautery-assisted devices may prove to be more efficacious for tract dilatation in fibrotic parenchyma, they should be used only as a rescue technique when other approaches fail [54–59]. Post-dilatation of tract stent placement is done over the guidewire with preferential placement of plastic stents (Fig. 3), although FCSEMS have also been used.

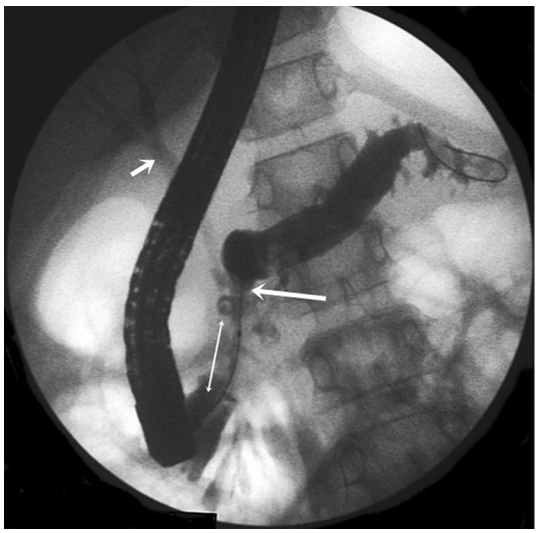

Fig. 3 Dominant stricture in the neck of the pancreas leading to grossly dilated main pancreatic duct with pain and failed ERCP planned for EUS-guided pancreaticogastrostomy. **A** EUS showing dilated duct with puncture taken with 19-G EUS FNA needle. **B** Pancreatogram showing grossly dilated main pancreatic duct with coiled guidewire. **C** Plastic stent placed in the MPD through the pancreaticogastrostomy access

Outcomes of EUS-PD

The first large series on EUS-PD published by Tessier et al. reported a technical success rate of 92% and clinical success rate of 76%. Indications were CP with complete obstruction, inaccessible papilla, anastomotic stenosis after Whipple procedure, and complete MPD rupture after acute pancreatitis or trauma. Adverse events were observed in 14% cases [60]. In the largest study of 94 patients, the technical success rate was 100%, while clinical success, as indicated by reduced or absence of further pain after the EUS-guided intervention was achieved in 81.9% cases over a median follow-up period of 28 months. The complication rate was only 8% [61]. In a systemic review of nine studies, the overall technical and clinical success rates were 85% (range 63–100%) and 88% (range 76–100%), respectively. Short-term adverse events were observed in overall 25% of the cases, while 5% of the patients had severe adverse events which included acute pancreatitis, pancreatic fluid collections, perforation, abscess and bleeding [53].

In a small study comparing the outcome of EUS-PD in patients with benign and malignant PD strictures, the technical success rates for benign and malignant strictures were 75% vs. 100%, respectively, with lower rate of adverse event in malignant cases. The authors stated that failed ERCP in a case of obstructive pancreatitis associated with a pancreatic tumor is an indication for EUS-PD [62].

While ERCP is the first-line treatment in patients with normal anatomy, there is controversy regarding ERCP vs. EUS-PD in patients with surgically altered anatomy. In a multicentric retrospective study comparing EUS-PD with enteroscopy-assisted endoscopic retrograde pancreatography (e-ERP) in patients with post-Whipple anatomy, EUS-PD was associated with a higher technical success rate (92.5%

vs. 20%) and higher clinical success rate (87.5% vs. 23.1%), but also had a higher rate of adverse events (35% vs. 2.9%) [63]. A recent systematic review also reported a similar finding with EUS-guided approach being superior to an ERP-guided approach with regard to pancreatic duct opacification (87% vs. 30%), cannulation success (79% vs. 26%), and stent placement (72% vs. 20%). However, adverse event rate between the two modalities could not be compared due to insufficient data [64].

Data regarding long-term clinical outcome of EUS-PD is scarce, with reported clinical success rate of 92% and development of delayed adverse events such as stent migration and stent blockage in 25–44% cases [65, 66]. A study on long-term outcome of EUS-PD with FCSEMS showed a late adverse event rate of 25% when followed up for a median period of 27.2 months [67]. EUS-RV should be the first choice when patient has an intact anatomy as the complication rate is lower. EUS-guided pancreaticoduodenostomy is recommended for stenosis of MPD in the head of the pancreas, while EUS-guided pancreaticogastrostomy is largely reserved for surgically altered anatomy.

Surgical management

Technical or clinical failure of endoscopic therapy warrants surgical therapy for management of pancreatic strictures. Surgeries for PD strictures can be classified into resection procedures, drainage procedures or a combination of both, and the decision regarding type of surgery depends on etiology of stricture, size of the PD, location of the stricture, and presence of pancreatic head mass [68]. Resection procedures like Whipple procedure are done for patients with disease confined to the pancreatic head, while a distal pancreatectomy is preferred for disease limited to the tail of the pancreas [69–71]. Duodenum-preserving pancreatic head resection surgeries such as Beger procedure and Berne procedure are done for patients with inflammatory head mass with bile duct obstruction [69–72]. Total pancreatectomy with islet cell auto-transplantation is reserved for patients with small duct disease or hereditary forms of chronic pancreatitis (high risk of malignancy) [69–71]. Pure drainage procedures such as lateral pancreatojejunostomy are preferred when MPD is dilated significantly without an associated inflammatory head mass. On the other hand, dilated MPD with inflammatory head mass is best treated by Frey's procedure, which is a combined resection and drainage procedure involving pancreatic head coring with lateral

Table 3 Different surgical techniques for treatment of pancreatic stricture (Data from studies in patients with chronic pancreatitis) [69–72]

Procedure	Technique	Comments
Lateral pancreaticojejunostomy	Longitudinal opening of pancreatic duct with Rouxen-Y pancreaticojejunostomy	Postoperative mortality rate up to 4% Initial pain control in > 90% but long-term pain relief only in 33–53% 25% become insulin dependent within 5 years
Pancreaticoduodenectomy	Resection of pancreatic head and duodenum with pancreaticojejunal, hepaticojejunal, and gastrojejunal anastomosis	Postoperative mortality rate < 3%, morbidity in 16–53% High rate of long-term endocrine insufficiency (up to 48%)
Duodenum preserving pancreatic head resections		
Beger procedure	Transection of pancreas at the level of portal vein, subtotal resection of the pancreatic head, and two pancreaticojejunal anastomoses	Compared to resection procedures Slightly lower rate of long-term pain relief Lower rate of morbidity and mortality
Berne procedure	Coring out pancreatic head with one pancreaticojejunal anastomosis	Lower risk of endocrine insufficiency
Frey procedure	Coring out pancreatic head, longitudinal opening of the pancreatic duct, and pancreaticojejunal anastomosis	
V-shaped excision	Removal of pancreatic tissue from the anterior surface of pancreas and pancreaticojejunal anastomosis	Useful for patients with small duct CP with lower morbidity and comparable pain relief
Distal pancreatectomy	Resection of the distal part of pancreas and closing pancreatic resection line	Highest rate of endocrine insufficiency Lower rates of diabetes with spleen-sparing procedures
Total pancreatectomy (with islet cell autotransplantation)	Removal of the whole pancreas and duodenum	Minimize developing diabetes by preserving glycemic control

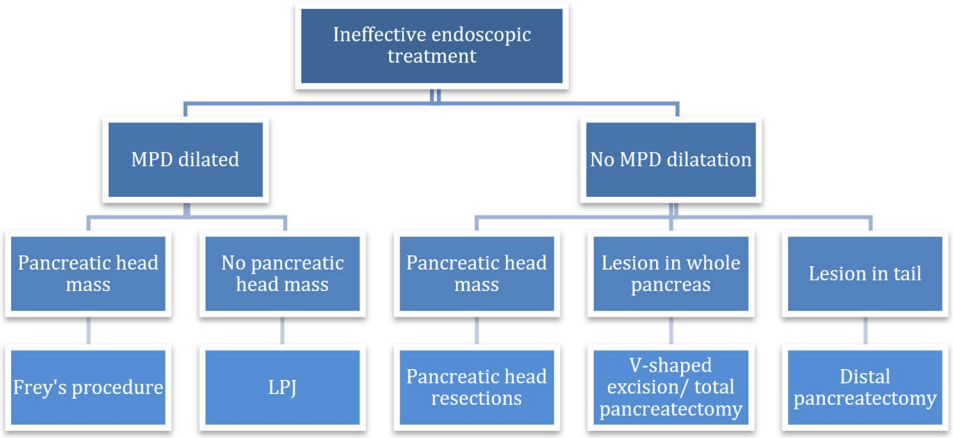

Fig. 4 Algorithm for surgical management of pancreatic strictures (*LPJ* lateral pancreaticojejunostomy)

pancreaticojejunal anastomosis [73]. Table 3 summarizes the surgical therapies for management of pancreatic stricture, mostly in cases with chronic pancreatitis. Figure 4 shows the algorithm for surgical management of pancreatic stricture.

A Cochrane Database systemic review and meta-analysis of two RCTS comparing endoscopic (excluding any trials with ESWL) and surgical interventions for painful CP showed that the surgical group had significantly higher proportion of pain relief at both medium (2–5 years; relative risk 1.62; 95% CI 1.22–2.15) and long-term (≥ 5 years; relative risk 1.56; 95% CI 1.18–2.05) follow-up [68]. A recent ESCAPE trial reported that patients who underwent early surgery for pain in CP had lower Izbicki pain score compared to endotherapy, during the 18 months follow-up period. However, complete or partial pain relief at the end of the follow-up period was not significantly different [74]. Although surgical management has been shown to have better long-term outcome, they are associated with higher morbidity and, hence, studies with larger sample size are required before recommending early surgery in patients with pancreatic strictures. Figure 5 summarizes the algorithm for management of pancreatic strictures.

Conclusion

Strictures in the pancreas are sequelae to inflammatory or malignant processes of the pancreas. Imaging modalities, especially MRCP and tumor markers (CA-19.9) can help differentiate benign from malignant etiologies. Management is endoscopic in patients with single dominant strictures of the pancreas, with need for surgical intervention in patients with multiple strictures or multiple calculi with strictures. Further large prospective studies on the management of pancreatic strictures are needed.

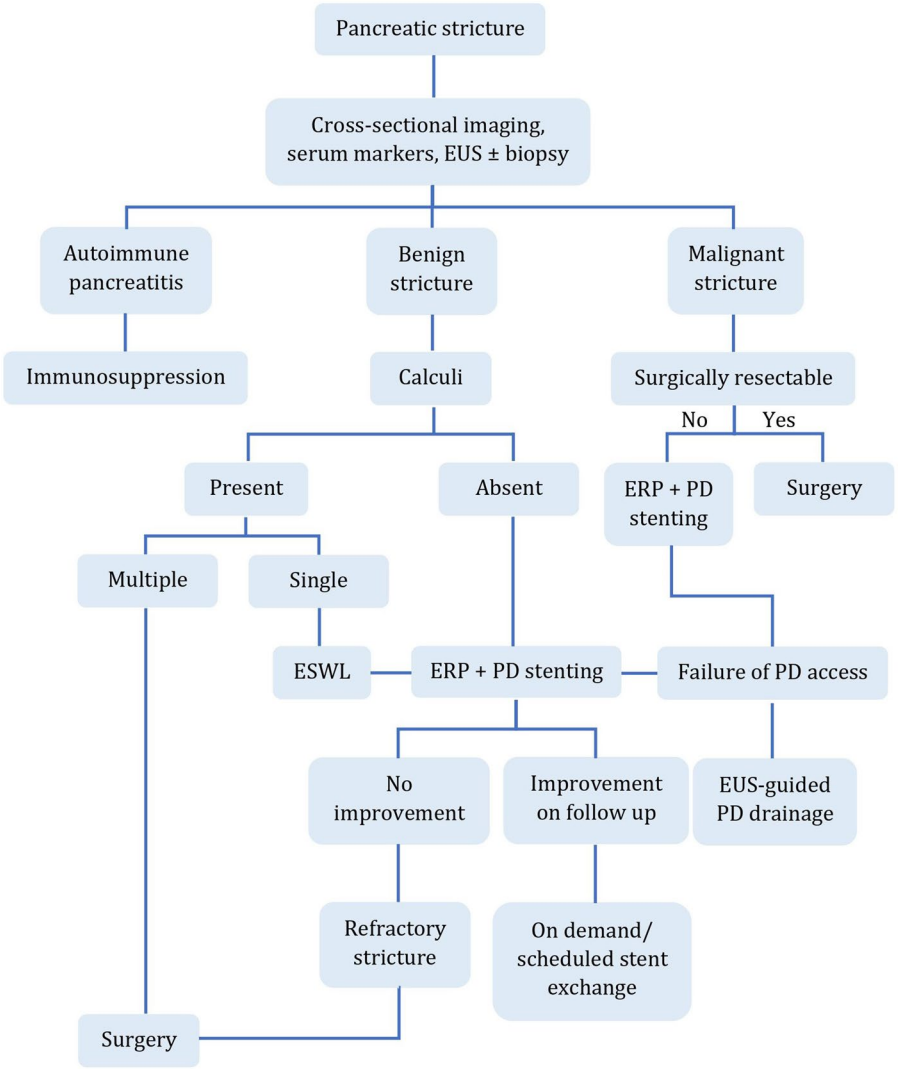

Fig. 5 Algorithm for management of dominant pancreatic strictures

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Declarations

Conflict of interest Vaneet Jearth, Suprabhat Giri and Sridhar Sundaram have no conflicts ofinterest to declare.

Human Rights All procedures followed have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed Consent nformed consent was obtained from all patients for being included in the study.

References

1. Delhaye M, Matos C, Devière J. Endoscopic management of chronic pancreatitis. Gastrointest Endosc Clin N Am. 2003;13:717–42.
2. Dumonceau J, Delhaye M, Tringali A, Arvanitakis M, Sanchez-Yague A, Vaysse T, et al. Endoscopic treatment of chronic pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) Guideline – Updated August 2018. Endoscopy. 2019;51(02):179–93.
3. Alkhiari R, Kahaleh M. Management of Benign Pancreatic Strictures. Adv ERCP Complic Refract Biliary Pancreat Dis 2019;147–152.
4. Catalano M. Endoscopic treatment of pancreatic duct strictures. Tech Gastrointest Endosc. 1999;1(4):168–74.
5. Dumonceau JM. Endoscopic therapy for chronic pancreatitis. Gastrointest Endosc Clin N Am. 2013;23(4):821–32.
6. Alkhiari R, Kahaleh M. Characteristics of Benign Pancreatic Duct Stricture. Adv ERCP Complic Refract Biliary Pancreat Dis 2019;143–146.
7. Kalady M, Peterson B, Baillie J. Pancreatic duct strictures: identifying risk of malignancy. Ann Surg Oncol. 2004;11(6):581–8.
8. Cohen S, Siegel J, Kasmin F. Treatment of pancreatic strictures. Curr Treat Options Gastroenterol. 2007;10(5):347–54.
9. Munigala S, Kanwal F, Xian H, et al. New diagnosis of chronic pancreatitis: risk of missing an underlying pancreatic cancer. Am J Gastroenterol. 2014;109:1824–30.

10. Chandrasekhara V, Chathadi K, Acosta R, Decker G, Early D, Eloubeidi M, et al. The role of endoscopy in benign pancreatic disease. Gastrointest Endosc. 2015;82(2):203–14.
11. Adler JM, Gardner TB. Endoscopic therapies for chronic pancreatitis. Dig Dis Sci. 2017;62(7):1729–37.
12. Rösch T, Daniel S, Scholz M, et al. Endoscopic treatment of chronic pancreatitis: a multicenter study of 1000 patients with long-term follow up. Endoscopy. 2002;34:765–71.
13. Kanno A, Masamune A, Shimosegawa T. Endoscopic approaches for the diagnosis of autoimmune pancreatitis. Dig Endosc. 2015;27(2):250–8.
14. Shimosegawa T, Chari ST, Frulloni L, et al. International consensus diagnostic criteria for autoimmune pancreatitis: Guidelines of the International Association of Pancreatology. Pancreas. 2011;40:352–8.
15. Farrell JJ, Garber J, Sahani D, Brugge WR. EUS findings in patients with autoimmune pancreatitis. Gastrointest Endosc. 2004;60:927–36.
16. Moon SH, Kim MH. The role of endoscopy in the diagnosis of autoimmune pancreatitis. Gastrointest Endosc. 2012;76:645–56.
17. Hoki N, Mizuno N, Sawaki A, et al. Diagnosis of autoimmune pancreatitis using endoscopic ultrasonography. J Gastroenterol. 2009;44:154–9.
18. Sugumar A, Levy MJ, Kamisawa T, et al. Endoscopic retrograde pancreatography criteria to diagnose autoimmune pancreatitis: an international multicentre study. Gut. 2011;60:666–70.
19. Jung JG, Lee JK, Lee KH, Lee KT, Woo YS, Paik WH, et al. Comparison of endoscopic retrograde cholangiopancreatography with papillary biopsy and endoscopic ultrasound-guided pancreatic biopsy in the diagnosis of autoimmune pancreatitis. Pancreatology. 2015;15(3):259–64.
20. Toft J, Hadden WJ, Laurence JM, et al. Imaging modalities in the diagnosis of pancreatic adenocarcinoma: A systematic review and metaanalysis of sensitivity, specificity and diagnostic accuracy. Eur J Radiol. 2017;92:17–23.
21. Kolodziejczyk E, Jurkiewicz E, Pertkiewicz J, et al. MRCP versus ERCP in the evaluation of chronic pancreatitis in children: which is the better choice? Pancreas. 2016;45:1115–9.
22. Sica GT, Braver J, Cooney MJ, et al. Comparison of endoscopic retrograde cholangiopancreatography with MR cholangiopancreatography in patients with pancreatitis. Radiology. 1999;210:605–10.
23. Singh VK, Yadav D, Garg PK. Diagnosis and management of chronic pancreatitis: a review. JAMA. 2019;322(24):2422–34.
24. Dawod E, Kahaleh M. Management of benign and malignant pancreatic duct strictures. Clin Endosc. 2018;51(2):156–60.
25. Cheng B, Zhang Y, Chen Q, et al. Analysis of fine-needle biopsy vs fine-needle aspiration in diagnosis of pancreatic and abdominal masses: a prospective, multicenter. Randomized Controlled Trial Clin Gastroenterol Hepatol. 2018;16(8):1314–21.
26. Brugge WR, De Witt J, Klapman JB, Ashfaq R, Shidham V, Chhieng D, Kwon R, Baloch Z, Zarka M, Staerkel G. Techniques for cytologic sampling of pancreatic and bile duct lesions: The Papanicolaou Society of Cytopathology Guidelines. Cytojournal. 2014;11(Suppl 1):2. https://doi.org/10.4103/1742-6413.133311.
27. Arnelo U, Siiki A, Swahn F, et al. Single-operator pancreatoscopy is helpful in the evaluation of suspected intraductal papillary mucinous neoplasms (IPMN). Pancreatology. 2014;14(6):510–4.
28. El_Hajj II, Brauer BC, Wani S, Fukami N, Attwell AR, Shah RJ. Role of per-oral pancreatoscopy in the evaluation of suspected pancreatic duct neoplasia: a 13-year US single-center experience. Gastrointest Endosc. 2017;85(4):737–45.
29. De Luca L, Repici A, Koçollari A, Auriemma F, Bianchetti M, Mangiavillano B. Pancreatoscopy: An update. World J Gastrointest Endosc. 2019;11(1):22–30. https://doi.org/10.4253/wjge.v11.i1.22.PMID:30705729;PMCID:PMC6354109.
30. Iiboshi T, Hanada K, Fukuda T, Yonehara S, Sasaki T, Chayama K. Value of cytodiagnosis using endoscopic nasopancreatic drainage for early diagnosis of pancreatic cancer: establishing a new method for the early detection of pancreatic carcinoma in situ. Pancreas. 2012;41(4):523–9.
31. Terada S, Kikuyama M, Kawaguchi S, Kanemoto H, Yokoi Y, Kamisawa T, et al. Proposal for endoscopic ultrasonography classification for small pancreatic cancer. Diagnostics (Basel). 2019;9(1):15.
32. Dorrell R, Pawa S, Zhou Y, Lalwani N, Pawa R. The Diagnostic dilemma of malignant biliary strictures. Diagnostics. 2020;10(5):337.
33. Karia K, Kahaleh M. A review of probe-based confocal laser endomicroscopy for pancreaticobiliary disease. Clin Endosc. 2016;49(5):462–6. https://doi.org/10.5946/ce.2016.086.
34. Kahaleh M, Turner BG, Bezak K, Sharaiha RZ, Sarkaria S, Lieberman M, et al. Probe-based confocal laser endomicroscopy in the pancreatic duct provides direct visualization of ductal structures and aids in clinical management. Dig Liver Dis. 2015;47:202–4.
35. Tyberg A, Raijman I, Novikov A, Sejpal D, Benias P, Trindade A, et al. Optical coherence tomography of the pancreatic and bile ducts: are we ready for prime time? Endosc Int Open. 2020;08(05):E644–9.
36. Tyberg A, Xu M, Gaidhane M, Kahaleh M. Second generation optical coherence tomography: Preliminary experience in pancreatic and biliary strictures. Dig Liver Dis. 2018;50(11):1214–7.
37. Chang MC, Liang PC, Jan S, et al. Increase diagnostic accuracy in differentiating focal type autoimmune pancreatitis from pancreatic cancer with combined serum IgG4 and CA19-9 levels. Pancreatology. 2014;14(5):366–72.
38. van Heerde MJ, Buijs J, Hansen BE, et al. Serum level of Ca 19–9 increases ability of IgG4 test to distinguish patients with autoimmune pancreatitis from those with pancreatic carcinoma. Dig Dis Sci. 2014;59(6):1322–9.
39. Ziebert JJ, DiSario JA. Dilation of refractory pancreatic duct strictures: the turn of the screw. Gastrointest Endosc. 1999;49:632–5.
40. Sundaram S, Choksi D, Kale A, Giri S, Patra B, Bhatia S, et al. Outcomes of dilation of recalcitrant pancreatic strictures using a wire-guided cystotome. Clin Endosc. 2021.
41. Chathadi KV, et al. The role of ERCP in benign diseases of the biliary tract. Gastrointest Endosc. 2015;81:795–803.
42. Tringali A, Bove V, di Prampero SFV, Boškoski I, Familiari P, Perri V, Costamagna G. Long-term follow-up after multiple plastic stenting for refractory pancreatic duct strictures in chronic pancreatitis. Endoscopy. 2019;51(10):930–5.
43. Costamagna G, Bulajic M, Tringali A, et al. Multiple stenting of refractory pancreatic duct strictures in severe chronic pancreatitis: long-term results. Endoscopy. 2006;38:254–9.
44. Sauer BG, Gurka MJ, Ellen K, Shami VM, Kahaleh M. Effect of pancreatic duct stent diameter on hospitalization in chronic pancreatitis: does size matter? Pancreas. 2009;38:728–31.
45. Eleftherladis N, Dinu F, Delhaye M, et al. Long-term outcome after pancreatic stenting in severe chronic pancreatitis. Endoscopy. 2005;37:223–30.
46. Cremer M, Devière J, Delhaye M, Baize M, Vandermeeren A. Stenting in severe chronic pancreatitis: results of medium-term follow-up in seventy-six patients. Endoscopy. 1991;23:171–6.
47. Rösch T, Daniel S, Scholz M, et al. Endoscopic treatment of chronic pancreatitis: a multicenter study of 1000 patients with long-term follow-up. Endoscopy. 2002;34:765–71.
48. Vitale GC, Cothron K, Vitale EA, et al. Role of pancreatic duct stenting in the treatment of chronic pancreatitis. Surg Endosc. 2004;18:1431–4.

49. Weber A, Schneider J, Neu B, et al. Endoscopic stent therapy for patients with chronic pancreatitis: results from a prospective follow-up study. Pancreas. 2007;34:287–94.
50. Jafri M, Sachdev A, Sadiq J, Lee D, Taur T, Goodman A, Gress F. Efficacy of endotherapy in the treatment of pain associated with chronic pancreatitis: a systematic review and meta-analysis. JOP. 2017;18(2):125–32.
51. Li TT, Song SL, Xiao LN, Wang CH. Efficacy of fully covered self-expandable metal stents for the management of pancreatic duct strictures in chronic pancreatitis: A systematic review and meta-analysis. J Gastroenterol Hepatol. 2020;35(7):1099–106.
52. Sofi AA, Khan MA, Ahmad S, Khan Z, Peerzada MM, Sunguk J, Vargo J. Comparison of clinical outcomes of multiple plastic stents and covered metal stent in refractory pancreatic ductal strictures in chronic pancreatitis- a systematic review and meta-analysis. Pancreatology. 2021;S1424–3903(21):00132.
53. Imoto A, Ogura T, Higuchi K. Endoscopic ultrasound-guided pancreatic duct drainage: techniques and literature review of transmural stenting. Clin Endosc. 2020;53(5):525–34.
54. Honjo M, Itoi T, Tsuchiya T, et al. Safety and efficacy of ultra-tapered mechanical dilator for EUS-guided hepaticogastrostomy and pancreatic duct drainage compared with electrocautery dilator (with video). Endosc Ultrasound. 2018;7:376–82.
55. Kitamura K, Yamamiya A, Ishii Y, Nomoto T, Honma T, Yoshida H. Electrocautery vs non-electrocautery dilation catheters in endoscopic ultrasonography-guided pancreatic fluid collection drainage. World J Gastrointest Endosc. 2016;8:458–65.
56. Kahaleh M, Artifon EL, Perez-Miranda M, et al. Endoscopic ultrasonography guided biliary drainage: summary of consortium meeting, May 7th, 2011, Chicago. World J Gastroenterol. 2013;19:1372–9.
57. Fujii-Lau LL, Levy MJ. Endoscopic ultrasound-guided pancreatic duct drainage. J Hepatobiliary Pancreat Sci. 2015;22:51–7.
58. Chapman CG, Waxman I, Siddiqui UD. Endoscopic ultrasound (EUS)-guided pancreatic duct drainage: the basics of when and how to perform EUS-guided pancreatic duct interventions. Clin Endosc. 2016;49:161–7.
59. Park DH, Jang JW, Lee SS, Seo DW, Lee SK, Kim MH. EUS-guided biliary drainage with transluminal stenting after failed ERCP: predictors of adverse events and long-term results. Gastrointest Endosc. 2011;74:1276–84.
60. Tessier G, Bories E, Arvanitakis M, Hittelet A, Pesenti C, Le Moine O, et al. EUS-guided pancreatogastrostomy and pancreatobulbostomy for the treatment of pain in patients with pancreatic ductal dilatation inaccessible for transpapillary endoscopic therapy. Gastrointest Endosc. 2007;65(2):233–41.
61. Will U, Reichel A, Fueldner F, Meyer F. Endoscopic ultrasonography-guided drainage for patients with symptomatic obstruction and enlargement of the pancreatic duct. World J Gastroenterol. 2015;21(46):13140–51.
62. Uchida D, Kato H, Saragai Y, Takada S, Mizukawa S, Muro S, et al. Indications for endoscopic ultrasound-guided pancreatic drainage: for benign or malignant cases? Can J Gastroenterol Hepatol. 2018;2018:8216109.
63. Chen YI, Levy MJ, Moreels TG, Hajijeva G, Will U, Artifon EL, et al. An international multicenter study comparing EUS-guided pancreatic duct drainage with enteroscopy-assisted endoscopic retrograde pancreatography after Whipple surgery. Gastrointest Endosc. 2017;85(1):170–7.
64. Basiliya K, Veldhuijzen G, Gerges C, Maubach J, Will U, Elmunzer BJ, et al. Endoscopic retrograde pancreatography-guided versus endoscopic ultrasound-guided technique for pancreatic duct cannulation in patients with pancreaticojejunostomy stenosis: a systematic literature review. Endoscopy. 2021;53(3):266–76.
65. Matsunami Y, Itoi T, Sofuni A, et al. Evaluation of a new stent for EUS-guided pancreatic duct drainage: long-term follow-up outcome. Endosc Int Open. 2018;6:E505–12.
66. Dalal A, Patil G, Maydeo A. Six-year retrospective analysis of endoscopic ultrasonography-guided pancreatic ductal interventions at a tertiary referral center. Dig Endosc. 2020;32:409–16.
67. Oh D, Park DH, Song TJ, et al. Long-term outcome of endoscopic ultrasound- guided pancreatic duct drainage using a fully covered self-expandable metal stent for pancreaticojejunal anastomosis stricture. J Gastroenterol Hepatol. 2020;35:994–1001.
68. Ahmed_Ali U, Pahlplatz JM, Nealon WH, van Goor H, Gooszen HG, Boermeester MA. Endoscopic or surgical intervention for painful obstructive chronic pancreatitis. Cochrane Database Syst Rev. 2015;3:CD007884.
69. Tillou JD, Tatum JA, Jolissaint JS, et al. Operative management of chronic pancreatitis: a review. Am J Surg. 2017;214:347–57.
70. Dominguez-Munoz JE, Drewes AM, Lindkvist B, et al. Recommendations from the United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis. Pancreatology. 2018;18:847–54.
71. Udd M, Kylänpää L, Kokkola A. The role of endoscopic and surgical treatment in chronic pancreatitis. Scand J Surg. 2020;109(1):69–78.
72. Jawad ZAR, Tsim N, Pai M, et al. Short and long-term post-operative outcomes of duodenum preserving pancreatic head resection for chronic pancreatitis affecting the head of pancreas: A systematic review and meta-analysis. HPB. 2016;18(2):121–8.
73. The pancreas: an integrated textbook of basic science, medicine, and surgery / edited by Hans G. Beger, Andrew L. Warshaw, Ralph H. Hruban, Markus W. Büchler, Markus M. Lerch, John P. Neoptolemos, Tooru Shimosegawa, David C. Whitcomb. Third edition. Hoboken, NJ: John Wiley & Sons, Inc., 2018.
74. Issa Y, Kempeneers MA, Bruno MJ, Fockens P, Poley JW, Ahmed Ali U, et al. Effect of early surgery vs endoscopy-first approach on pain in patients with chronic pancreatitis: The ESCAPE randomized clinical trial. JAMA. 2020;323(3):237–47.