

## Role of Endoscopy in Chronic Pancreatitis

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### INTRODUCTION

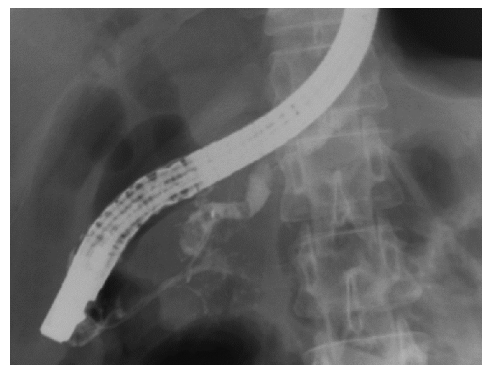
Patients with chronic pancreatitis can present with various clinical complex including steatorrhea, abdominal pain, pseudocyst and diabetes mellitus. The main concept of treating these patients is treating only symptomatic one. Currently it has been suggested to treat and investigate asymptomatic patient with chronic pancreatitis only when that strategy can prevent further attack of pancreatitis and excluding pancreatic cancer. There are three approaches for treating chronic pancreatitis; pharmacologic therapy, endoscopy with and without interventional radiology and surgery. In this review, information regarding the updated knowledge on endoscopic therapy for chronic pancreatitis will be provided. In addition, recent comparison with surgery will also be discussed.

### Treatment concept

Generally chronic pancreatitis patients with exocrine and/or endocrine insufficiency necessitate only pharmacologic therapy which mainly includes pancreatic enzyme supplement and insulin<sup>(1-3)</sup>. In contrast, patients who suffered from pancreatic type pain and duct leakage may require endoscopy and surgery as the sole therapy<sup>(4-6)</sup>. Since chronic pancreatitis is an irreversible damage of the pancreas and has no treatment that can completely restore the structure and function of the pancreas, then all therapies are aimed at improvement of patients' symptoms only. Quality of life improvement is the main concern for these patients<sup>(7)</sup>. Preferring one technique over the other is depended upon many factors including, efficacy, complication risks, long-term benefit and available expertise. Occasionally, prophylactic treatment is indicated for specific group with precancerous or suspicious for cancer<sup>(8)</sup>.

### Approach to pancreatic pain

Step up therapy from pharmacologic therapy to more invasive approaches such as endoscopy, percutaneous drainage and then surgery is highly recommended. Medical treatment consists of nothing peroral or if tolerable, low fat meal. To reduce pain by preventing biofeedback from secretin/CCK pathway, appropriate dose of non-enteric pancreatic enzyme was proposed<sup>(9)</sup>. However, a meta-analysis did not confirm the significance of this therapy<sup>(10)</sup>. Octreotide is considered to be beneficial for pain especially from pancreatic duct leakage. However, the real advantage of this agent is doubtful in patient with pain<sup>(11,12)</sup>. There are many pathways to explain the cause of pain in these patients. Visceral nerve entrapment and ischemia are among those hypotheses. In addition, luminal obstruction and inflammatory reaction in the pancreas and surrounding area have been proposed as the causes. Nevertheless, the main cause of pain is believed to be originated from pancreatic duct hypertension. Decompression of duct hypertension can be provided by either surgery or endoscopy.



**Figure 1** Demonstrating pancreatogram via minor papilla in patient with pancreatic stone

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Endoscopic technique includes stricture dilation, pancreatic stone removal with or without extracorporeal shock wave lithotripsy (ESWL) and stenting (Figure 1). The short term clinical response from endoscopic therapy appeared to be good and ranged from 74-100%<sup>(5,13-15)</sup>. However the long-term efficacy and pain relief from this technique are quite varies (47-94%) and depended up on the presence of stricture and stone

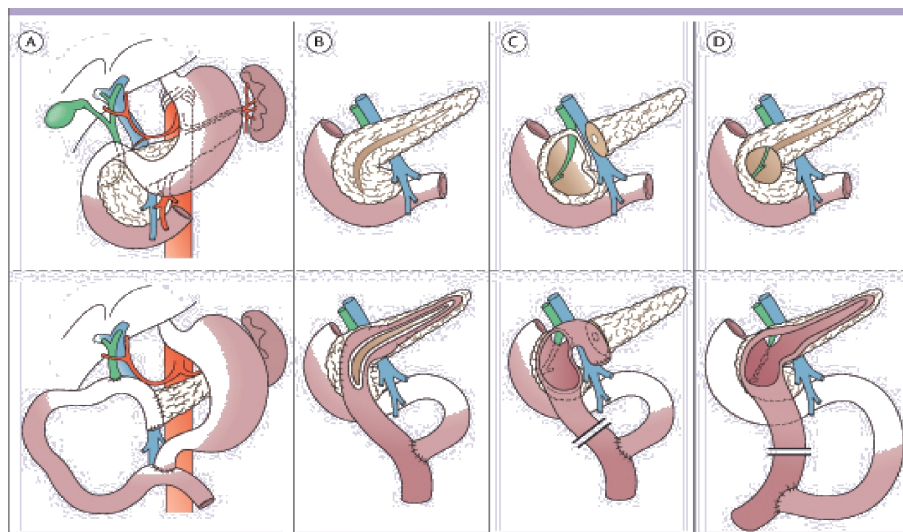
(Table 1, 2). Appropriate surgical decompression of the bile duct is usually the technique that can release the pressure from the main pancreatic duct (Puestow and Duval operations). Some special techniques may be better applied for patient with nerve entrapment, inflammation, and fibrosis at the pancreatic gland especially at the head of the pancreas (Beger and Frey operations). (Figure 2-5). A recent RCT comparing

**Table 1** Result of endoscopic pancreatic therapy with extracorporeal shock wave treatment on many series

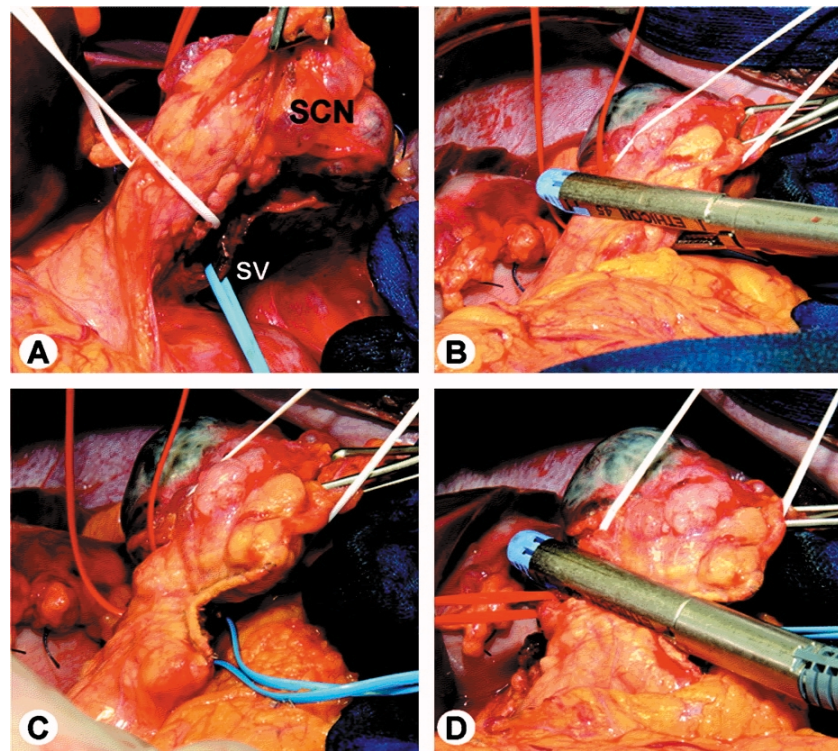
Author	N	Technique	Immedia pain relief (%)	Long-term pain relief (%)	F/U mo	Surgery (%)
Schneider 1994	50	ESWL + EPS	N/A	83	20	12
Dumoceau 1996	70	ESWL + EPS	95	54	60	5
Johanns 1996	35	ESWL + EPS	83	N/A	18	N/A
Ohara 1996	32	ESWL	N/A	79	44	N/A

**Table 2** The overall outcome from pancreatic endotherapy

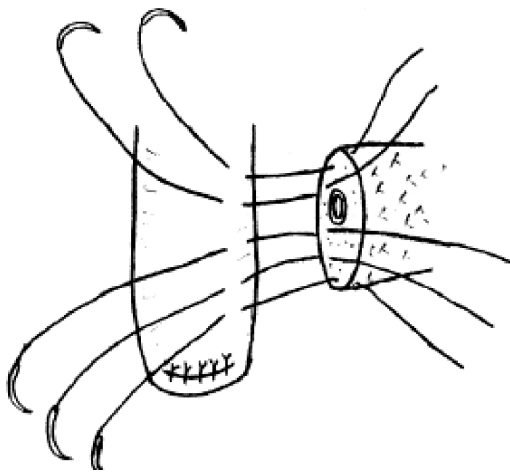
Author	N	Technique	Immedia pain relief (%)	Long-term pain relief (%)	F/U mo	Surgery (%)
1991-2002	1851	EPS ± stent ± SWL	74-100	47-94	8-59	8-26



**Figure 2** A Pyloric preserving Whipple operation  
 B Puestow operation (pancreatico-jejunostomy)  
 C Beger operation (duodenal preserving pancreatic head resection)  
 D Frey operation



**Figure 3** Distal pancreatectomy [Copied from: Kleeff J, *et al.* Ann Surg 2007; 245(4): 573-82.]



**Figure 4** Duval operation (end-to-side pancreatico-jejunostomy) [Modified from Imaizumi T, *et al.* J Hepatobiliary Pancreat Surg 2006; 13: 194-201.]



**Figure 5** From the operative field in Duval procedure [Modified from Imaizumi T, *et al.* J Hepatobiliary Pancreat Surg 2006; 13:194-201.]

the results from endoscopy with surgery for chronic pancreatitis pain has shown that the Izbicki pain score in the group who underwent surgery was lower than endoscopy group quite significantly (25% vs 51%,  $p < 0.001$ ) (16). In addition, the conversion rate to surgery in the endoscopy group was reported to be as high as 25%. However, this study does not imply that

there is no room for therapeutic endoscopy for chronic pancreatitis. There are many patients that endoscopy may be beneficial such as; distal duct stricture closed to the ampulla, pancreatic duct leakage, pancreas divisum, pancreatic sphincter of Oddi dysfunction and poor surgical candidate. Moreover, pain relief after pancreatic duct stenting is a good analogy to send



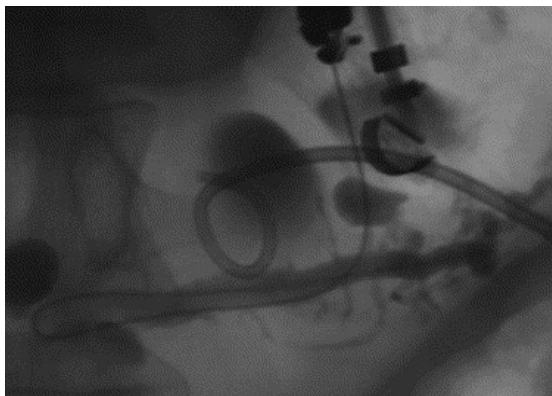
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patient for further surgical decompression of the pancreatic duct. Patient who does not respond to endoscopic decompression may require gland evacuation in addition to just duct decompression. Other use of endoscopic therapy that required more studies is transmural pancreatic duct drainage in patient with disconnected duct syndrome (Figure 6). Initial reports from advance endoscopic center showed the medium-term efficacy in term of pain relieving and decreasing pancreatic duct diameter after creation of transgastric fistula by endoscopic ultrasonoscope (EUS)<sup>(17,18)</sup>. It has to be noted that this is a technical demanding procedures which require special preprocedure evaluation and can be performed only in the special centers with availability of very high skill pancreatic endoscopists.

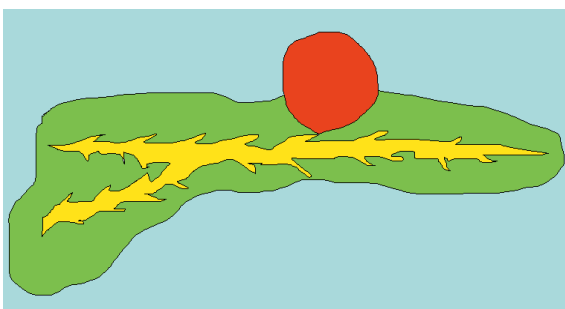
### Approach to pancreatic duct leakage

Pancreatic duct leakage can present in many ways including pseudocyst, pancreatic ascites, and pancreatic pleural effusion. The prognosis of fistula is depended up on the type of leakage that can be classified

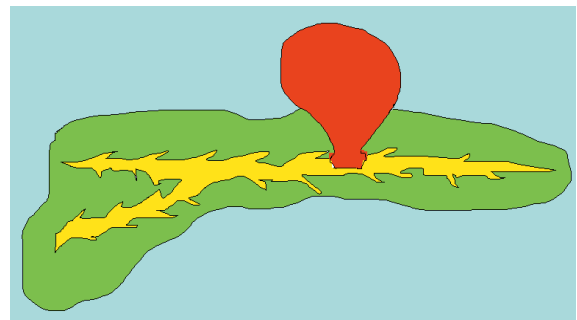
according to pancreatogram findings. Side branch or small duct leakage (Figure 7) can be conservatively sealed by pharmacological treatment. Partial main pancreatic duct disruption (Figure 8) typically requires endoscopic therapy to achieve rent closing<sup>(19,20)</sup>. Standard endoscopic therapy mainly involves pancreatic sphincterotomy and stenting (preferably across the leak site). Rarely patients who failed standard endotherapy would require special treatment such as injection of histoacryl (Figure 9-10) and coiling therapy (Figure 11). Patients with disconnected pancreatic duct (complete main pancreatic duct disruption) have the poorest prognosis (Figure 12). If the endoscopist is unable to bridge the ducts, the upstream segment will still producing pancreatic juice and then leakage will persist. Our data showed that more than 30% of this type of leakage had to undergo surgery after failed endotherapy<sup>(21)</sup> (Table 3).



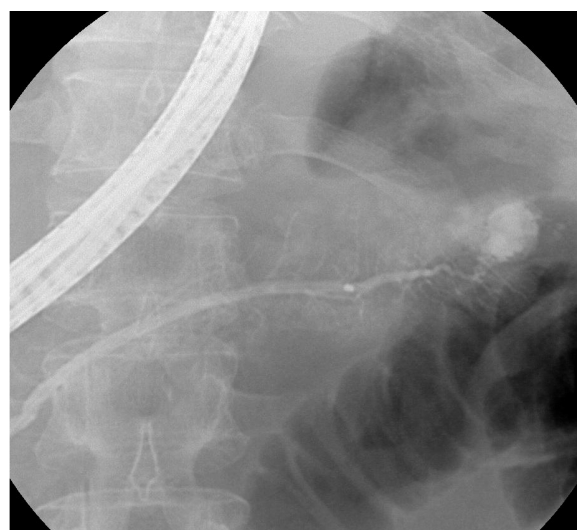
**Figure 6** Transgastric pancreatogram under EUS guided in patient with complete pancreatic duct obstruction [Modified from Kahaleh M, *et al.* Gastrointest Endosc. 2007; 65 (2): 224-30.]



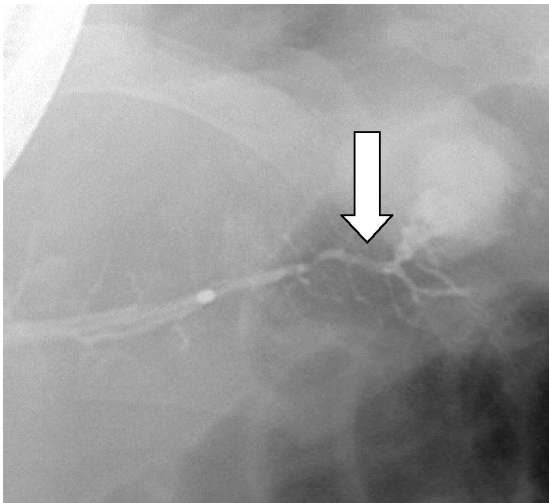
**Figure 7** Demonstrating side branch disruption



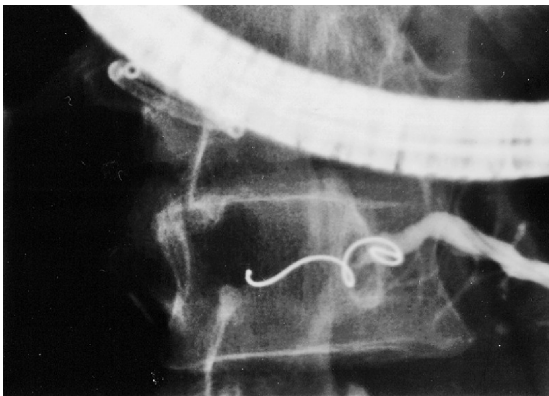
**Figure 8** Demonstrating partial duct disruption



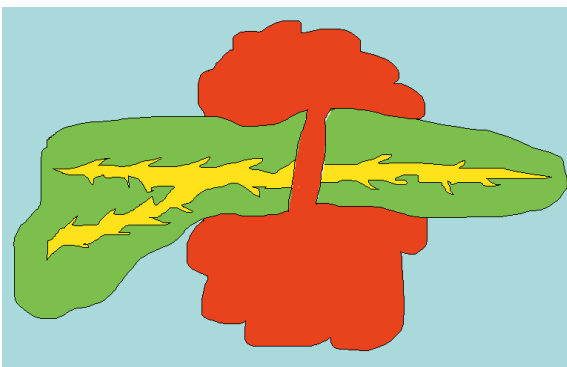
**Figure 9** Demonstrating catheter for histoacryl injection in patient with pseudocyst at the tail of pancreas [Copied from Lüthen R, *et al.* Permanent closure of a pancreatic duct leak by endoscopic coiling' Endoscopy 2007 (PMID:17285499)]



**Figure 10** After glue injection the leakage site was filled with mixture of histoacryl and lipiodol (white arrow) [Copied from Lüthen R, *et al.* Permanent closure of a pancreatic duct leak by endoscopic coiling' Endoscopy 2007 (PMID: 17285499)]



**Figure 11** Pancreatic duct after coil deployment in pancreatic leakage [Copied from Lüthen R, *et al.* Permanent closure of a pancreatic duct leak by endoscopic coiling' Endoscopy 2007 (PMID: 17285499)]



**Figure 12** Demonstrating complete main duct disruption or disconnected duct syndrome

**Table 3** Results of endotherapy in different types of pancreatic duct leakage

Leak type	CPPD	PPDD	SD	Total
Patient (n)	37	89	27	153
Direct to surgery	5	1	0	6
Endotherapy	20/32	79/81	8/8	102/121
Success/ attempt				
Mean procedure (n)	2.8	3.0	2.1	2.9
Surgery for failed endotherapy	12/32	2/81	0/8	19/121
Mean follow-up (month)	30	27	26	27

CPPD = Complete pancreatic duct disruption

PPDD = Partial pancreatic duct disruption

SD = Small duct leakage

Modified from Rerknimitr R, *et al.* Pancreatic duct leaks: results of endoscopic management. *Gastrointest Endosc* 2000; 51: AB 139.

### Future direction of therapy

As mentioned earlier, EUS has become an interesting tool for pancreatic endotherapy since it can convey the substance through the FNA channel. According to alcohol-induced pancreatitis theory, there is a necrosis-fibrosis sequence. Alpha-SMA (also known as ACTA2) can be the source of fibrogenesis in chronic pancreatitis and early adenocarcinoma of the pancreas<sup>(22)</sup>. Many studies reports data on fibrogenesis blocking agents<sup>(23-25)</sup>, Troglitazone, follistatin, CD 36, and peroxiome are found to inhibited filament protein production; hence fibrogenesis may decrease after direct injection of these agents to the pancreas. Nevertheless, over the next 5 years we probably will not see this progress in real practice yet but the research regarding this issue will definitely continue.

### CONCLUSION

The goal of pancreatic treatment is mainly for symptoms control and preemptive treatment is applied only for patient with risk for pancreatic cancer development. Medical treatment is always the first line therapy especially for exocrine and endocrine insufficiency. Endotherapy is usually indicated after failed pharmacologic therapy in patients with pain and duct leakage. Recently, excellent designed study reported a superior long-term outcome in selected patients who underwent surgery. However, endoscopic treatment still plays an important role as a preoperative thera-

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peutic duct decompression assessment and can be the best approach in some certain patients. EUS has become an interesting tool to negotiate in to the complete duct obstruction and duct disconnection patients. More data on this subject are awaited. Lastly, many research trials are working on agents that block fibrogenesis and EUS again may be the main equipment to deliver these agents.

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