Management of Pancreatic Fistulae

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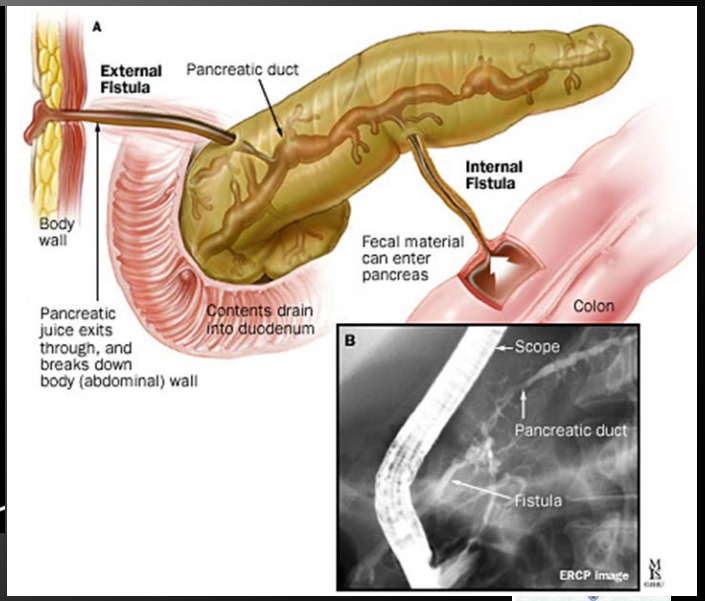
Fistula definition

- A Fistula is a permanent abnormal passageway between two organs (epithelial lined structures) in the body or between an organ and the exterior of the body.
- What is a pancreatic fistula?



Definition of PF

- Leakage of pancreatic ductal fluid
  - Ductal injury
  - Amylase content high
- May be contained by surrounding structures (pseudocyst)
- May communicate with other structures (fistula)

Post-operative fistula

Postoperative pancreatic fistula: An international study group (ISGPF) definition *Bassi et al Surgery 2005;138:8-13*

"drain output of any volume on or after postoperative day 3 with an amylase greater than 3 times the serum level"

Previous definitions

1. Output > 10 mL/d of amylase-rich fluid postoperative (postop) day 5 or for > 5 days.
2. Output > 10 mL/d of amylase-rich fluid after postop day 8 or for > 8 days.
3. Output between 25 mL/d and 100 mL/d of amylase-rich fluid after postop day 8 or for > 8 days.
4. Output > than 50 mL/d of amylase-rich fluid after postop day 11 or for > 11 days.

Bassi et al Dig Surg 2004;21:54-9.

Consequences of duct disruption

- Enclosed collection
  - Pseudocyst
- Communication with peritoneal cavity
  - Pancreatic ascites
- Communication with pleura
  - Pleural effusion
- Communication with skin
  - External fistula
- Communication with bowel
  - Pancreatico-enteric or -colic fistula

Grading of PF

Table II. Main parameters for POPF grading

Grade	*A*	*B*	*C*
Clinical conditions	Well	Often well	Ill appearing/ bad
Specific teatment*	No	Yes/no	Yes
US/CT (if obtained)	Negative	Negative/ positive	Positive
Persistent drainage (after 3 weeks)†	No	Usually yes	Yes
Reoperation	No	No	Yes
Death related to POPF	No	No	Possibly yes
Signs of infections	No	Yes	Yes
Sepsis	No	No	Yes
Readmission	No	Yes/no	Yes/no

US, Ultrasonography; *CT*, computed tomographic scan; *POPF*, postoperative pancreatic fistula.

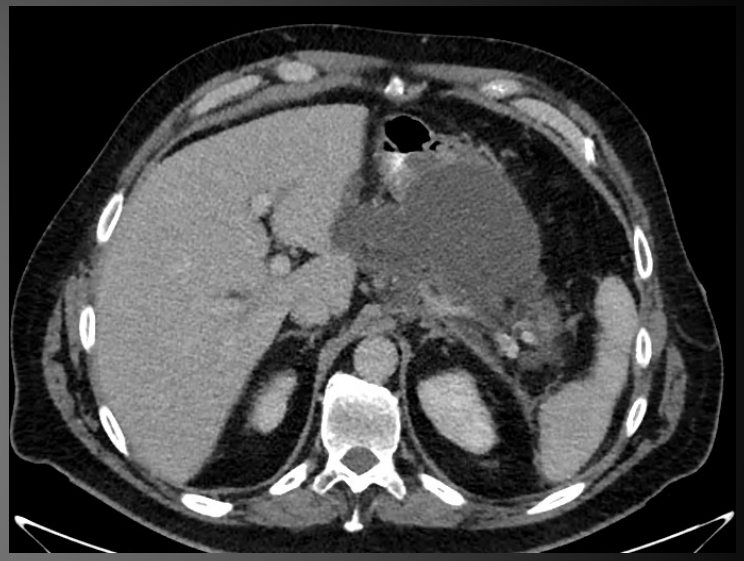
*Partial (peripheral) or total parenteral nutrition, antibiotics, enteral nutrition, somatostatin analogue and/or minimal invasive drainage.

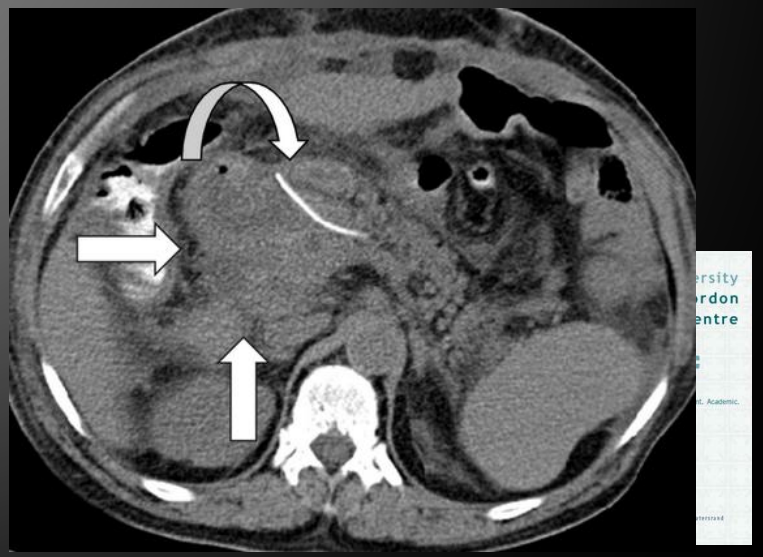
†With or without a drain in situ.

Bassi et al Surgery 2005;138:8-13

Aetiology of PF

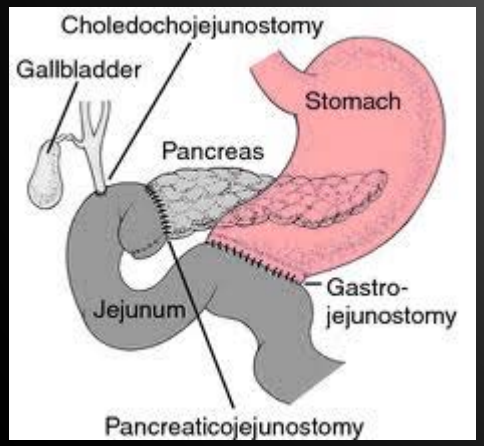
- Post-inflammatory (55%)
  - Acute pancreatitis
  - Chronic pancreatitis
- Iatrogenic (35%)
  - Surgery
  - Biopsy
  - Percutaneous drainage of pseudocysts
- Trauma (10%)

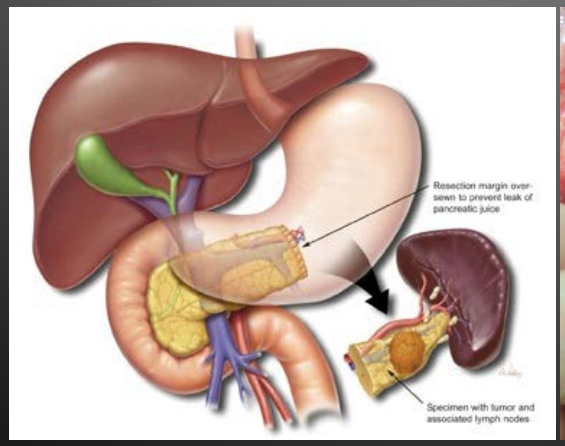


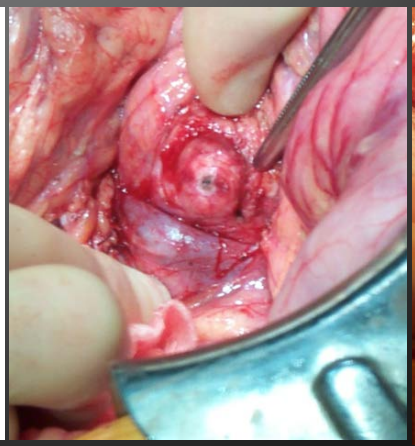


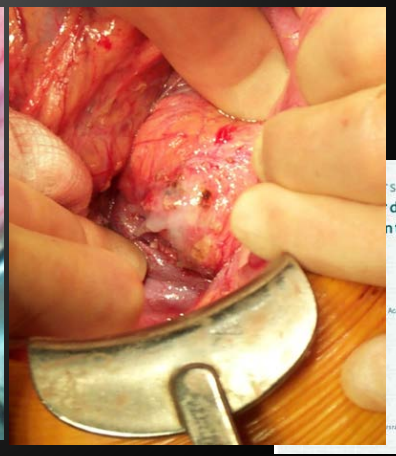
Surgical causes of PF

- Whipple – 5-30% (13%)
- Distal pancreatectomy – 13-31% (20%)
- Central pancreatectomy
- Enucleation / partial resection
- Pancreatico-enteric or -gastric anastomosis









Risk factors for PF after PD

Table 1 Fistula Risk Score for the prediction of clinically relevant fistula (CR-POPF) after pancreatoduodenectomy

Risk factor	Parameter	Points
Gland texture	*Firm*	0
	Soft	2
Pathology	*Pancreatic adenocarcinoma or pancreatitis*	0
	Ampullary, duodenal, cystic, islet cell, etc...	1
Pancreatic duct diameter	*≥5 mm*	0
	4 mm	1
	3 mm	2
	2 mm	3
	≤1 mm	4
Intraoperative blood loss	*≤400 ml*	0
	401–700 ml	1
	701–1,000 ml	2
	>1,000 ml	3
		Total 0 to 10 points

From Callery et al., *JACS*, 2013

Table 1 Selected trials performed to evaluate rates of POPF

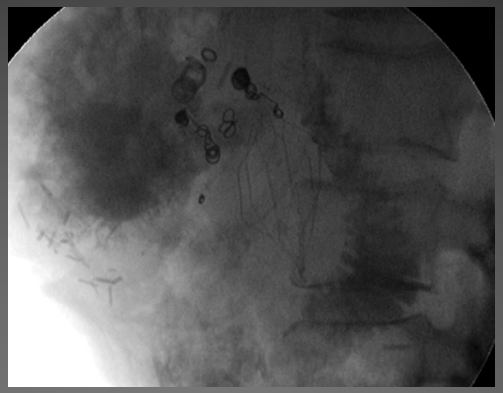
Study	Trial arm(s)	N	Fistula (%)	Conclusion
Berger, 2009	Duct-to-mucosa Pancreaticojejunostomy (PJ)	100	12 (12%)	Fewer POPF in invagination group
	Invagination PJ	97	23 (24%)	
Grobmyer, 2010	Modified duct-to-mucosa PJ (Blumgart anastomosis)	187	13 (6.7%) Grade B/C	
Kleespies, 2009	Duct-to-mucosa PJ	90	12 (13%)	Fewer POPF with use of Blumgart anastomosis
	PJ	82	13 (16%)	
Topal, 2013	PG	167	13 (8%)	PG decreases POPF rate
	PJ	162	33 (19.8%)	
Winter, 2006	Pancreatic duct stent	58	Hard pancreas 1.7%, soft pancreas 21.1%	No difference in POPF rates
	No stent	63	Hard pancreas 4.8%, soft pancreas 10.7%	
Poon, 2007	External pancreatic duct stent	60	4 (6.7%)	External stent decreases POPF
	No stent	60	12 (20%)	
Diener, 2011	Stapled distal pancreatectomy	175	32%	No difference in POPF rates
	Hand-sewn distal pancreatectomy	177	28%	
Yeo, 2000	Octreotide	104	11 (9%)	No difference in POPF rates
	No octreotide	107	10 (11%)	
Allen, 2014	Pasireotide	152	9%	Pasireotide decrease POPF rates
	No pasireotide	148	21%	

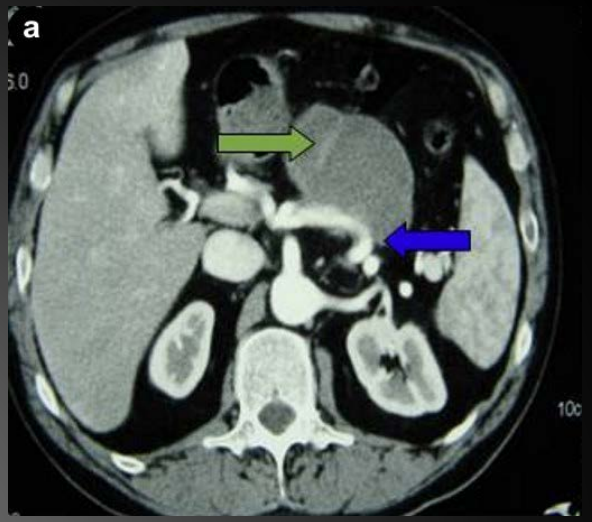
POPF, post-operative pancreatic fistula.

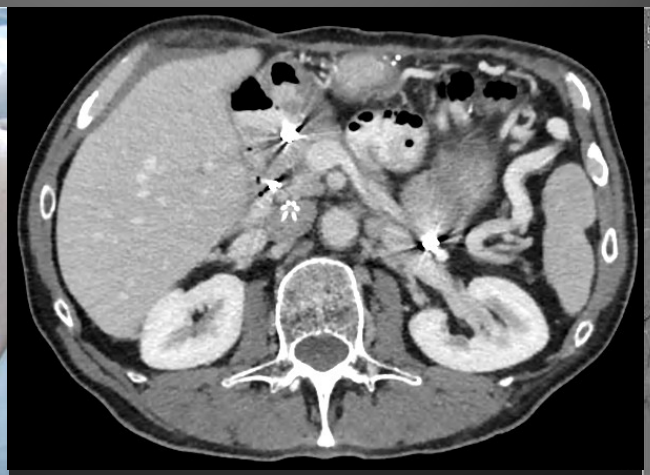
Technique alone cannot completely prevent pancreatic leak and fistula

Consequences of PF

- Sepsis
- Bleeding
- Malnutrition
- Diarrhoea
- Skin excoriation
- Mortality 5-28%

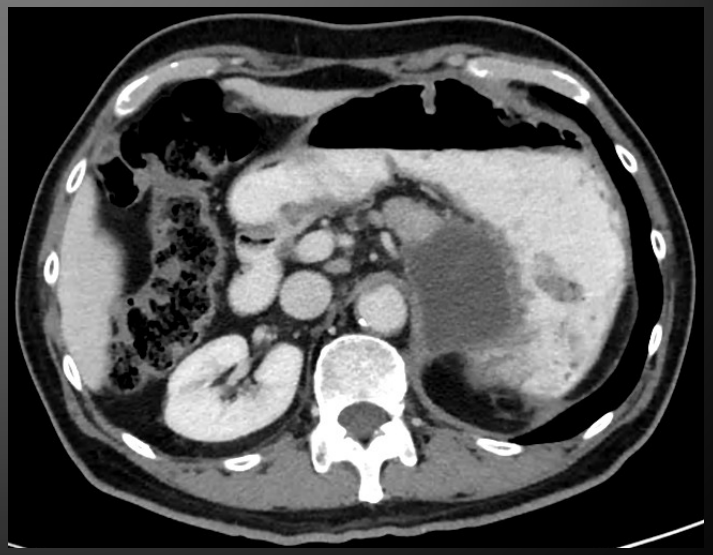






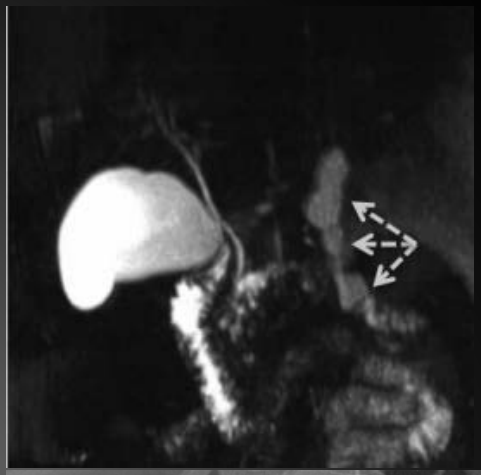
Indicators of PF

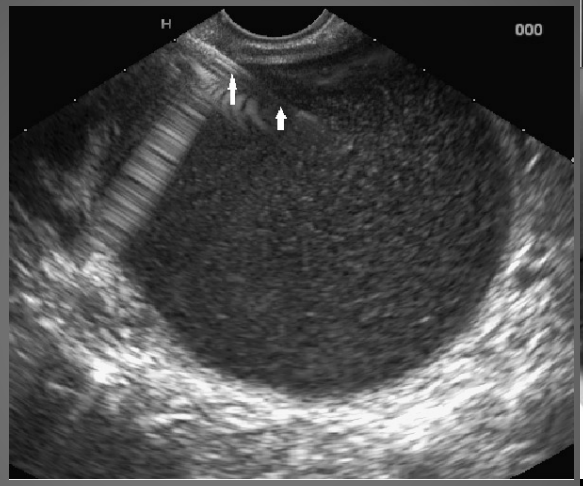
- Drain fluid high in amylase
- Collections post surgery, pancreatitis, trauma
- Ascites, pleural effusion
- Diarrhoea post pancreatitis, surgery, intervention
- Signs of sepsis



Diagnostic modalities

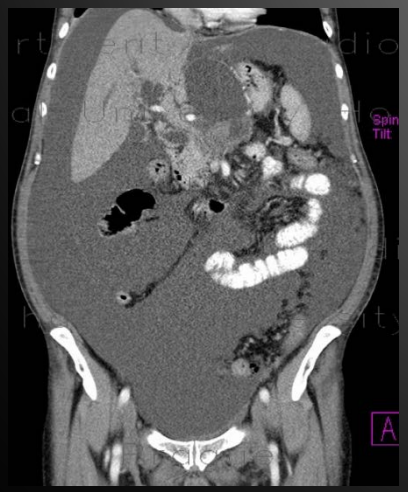
- Sonar
- CT
- MRI and MRCP
- EUS
- ERCP
- Sinogram and fistulogram





Confirmation of PF

- Fluid with high amylase content
  - External fistula
  - Sampling of peri-pancreatic fluid collections
  - Ascites or pleural effusion
- Contrast study showing pancreatic ductal communication

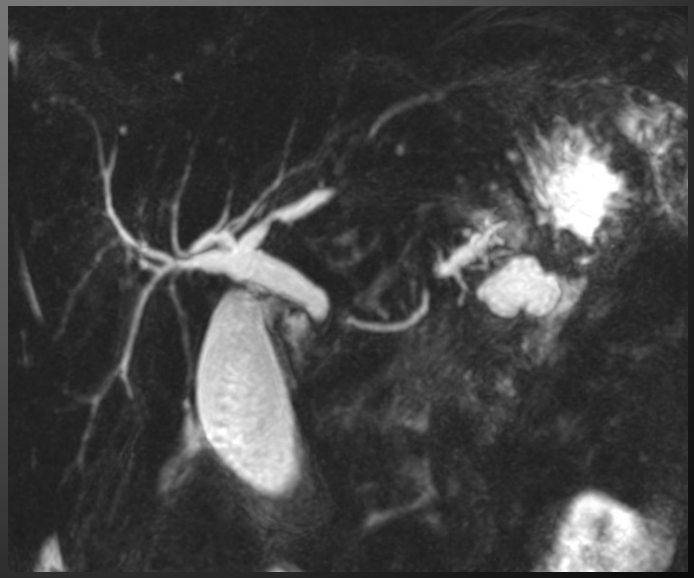


Initial management

- Control sepsis
  - Drain collections
    - Percutaneous
    - EUS drainage into stomach or duodenum
  - Appropriate antibiotics
- Control fistula
- Nutritional support
  - Enteral feeding if possible
  - Correct electrolytes, protein
- Stoma care for cutaneous fistulae

Pancreatic duct and fistula anatomy

- Site of leakage
- Strictures
- Duct continuity
- Ductal disconnection



Management options

- Somatostatin analogues
- Glue injection
- External drainage
- Endoscopic
  - Transpapillary drain/stent
  - EUS or endoscopic internal drainage into stomach or duodenum
- Surgery
  - Surgical reconstruction
  - Surgical resection
  - Surgical cyst drainage

Principles of management

- Allow time for spontaneous closure
- Use minimally invasive treatment if possible
- Avoid loss of pancreatic parenchyma
- Disconnected pancreatic tissue may require surgical intervention
  - Pancreatico-jejunostomy
  - Resection

70% to 82% of pancreatic fistulae will close spontaneously without the need for definitive intervention

Somatostatin analogues

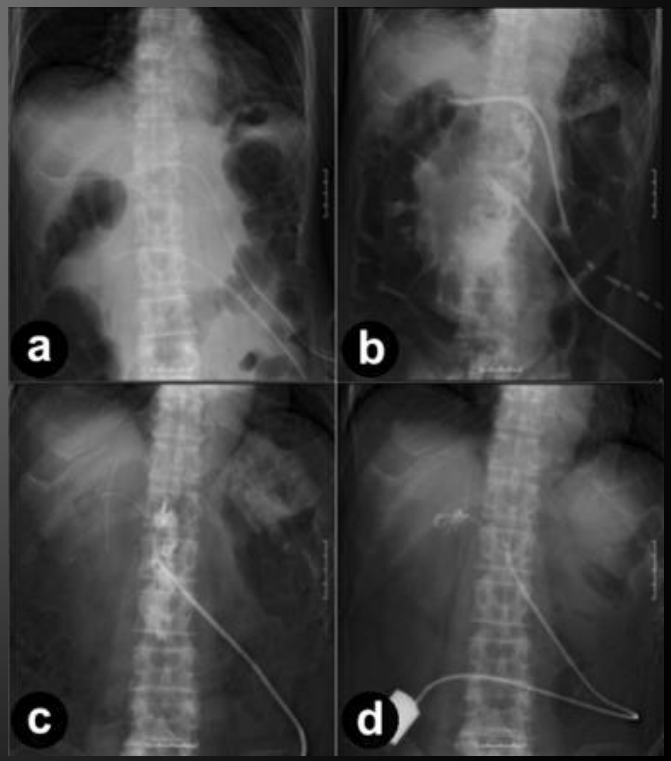
- Inhibit pancreatic exocrine, biliary, and small bowel secretions
- Somatostatin analogues reduce fistula output
- No solid evidence that somatostatin analogues result in a higher closure rate of POPF compared with other treatments

Gans et al BJS 2012

Routine use not indicated

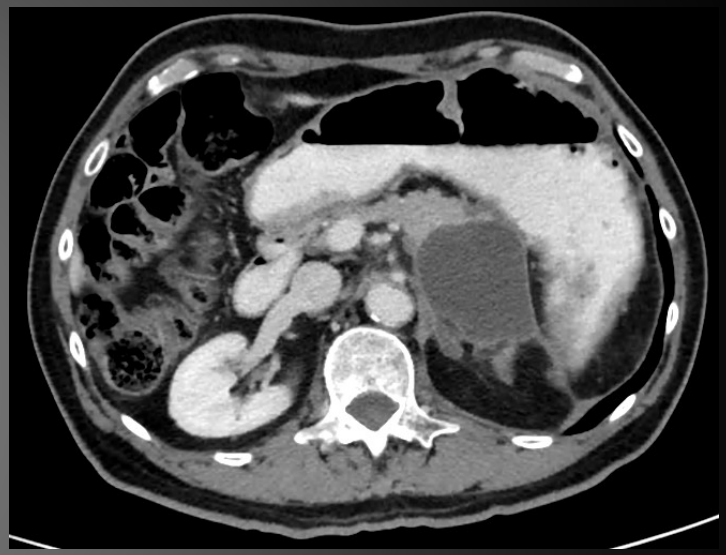
Glues

- Limited data
- Can be considered in very specific cases with low output
- Not generally recommended



Clinical scenarios

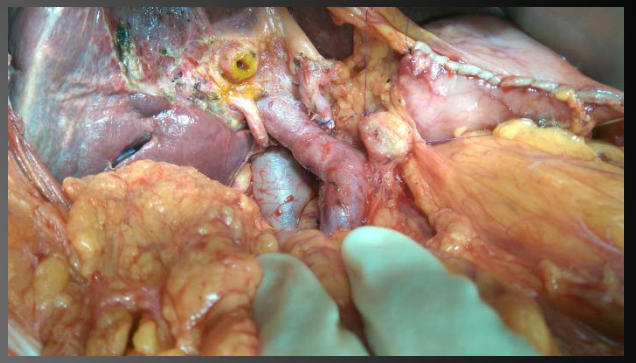
- Anastomotic fistula/leak
  - Whipple
  - Pancreatico-jejunostomy (Frey, etc)
- Stump leak post distal pancreatectomy
- Post pancreatitis fistula
- Disconnected body/tail
- Trauma

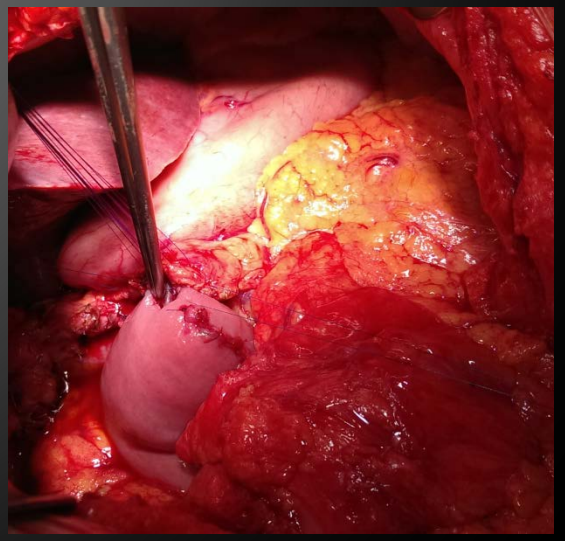


Anastomotic leaks

- Ensure that fistula is controlled
- Wait
- Wait some more
- Wait even more
- Surgical reconstruction after 3-4 months
- ?? Completion pancreatectomy
  - Early
  - Late

  Not recommended



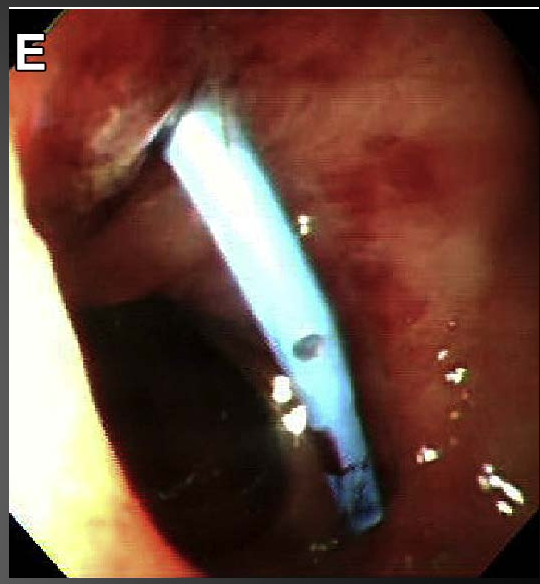


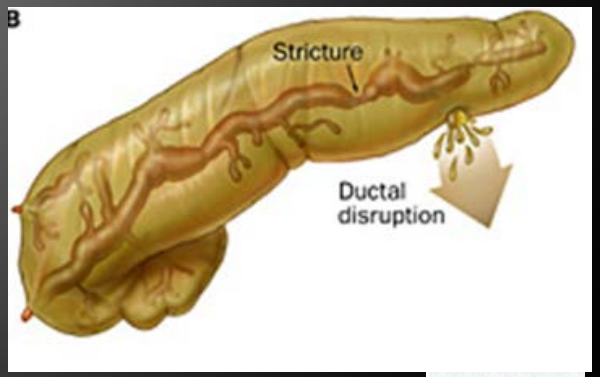
Stump leaks

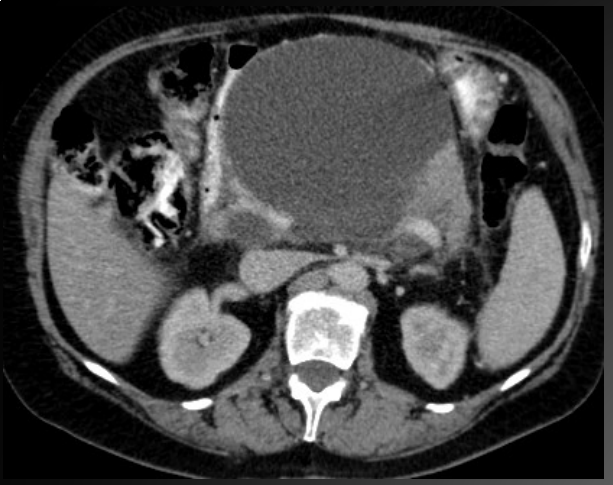
- Most will close spontaneously if no downstream obstruction
- Intervention not always required
- Control sepsis by drainage
  - Internal EUS guided cyst-gastrostomy or cyst-duodenostomy (preferred)
  - ERCP and sphincterotomy w/wo pancreatic stent
  - External
- Surgery not indicated

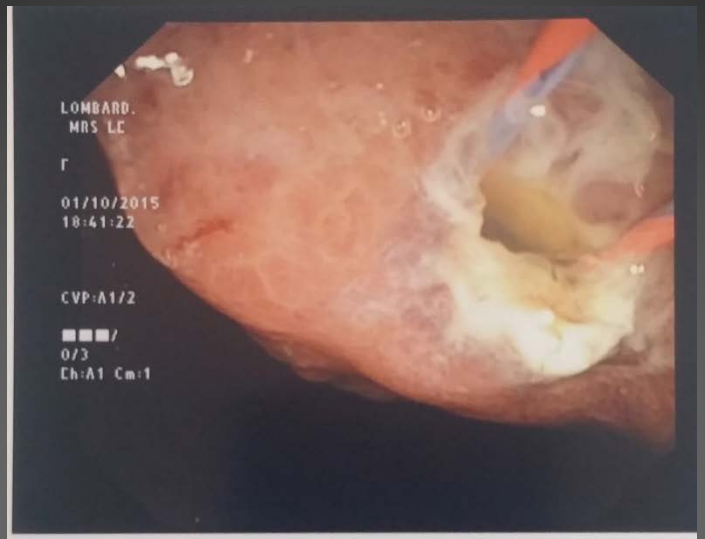
Post pancreatitis collection/fistula

- Intervene for symptomatic or complicated collections
- EUS guided internal drainage if possible
- Assess ductal continuity / stricture
- ERCP stenting if
  - duct in continuity and side-branch leak present
  - ductal stricture can be traversed
- External drainage if endoscopic drainage not possible (trans-gastric or retroperitoneal)
- Surgical cyst-drainage seldom indicated





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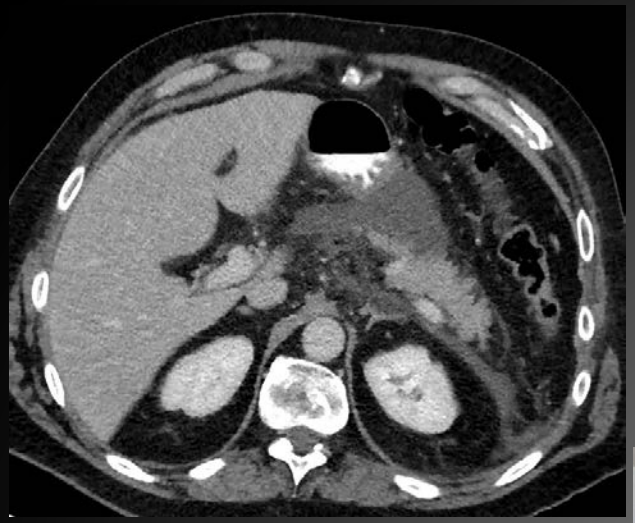

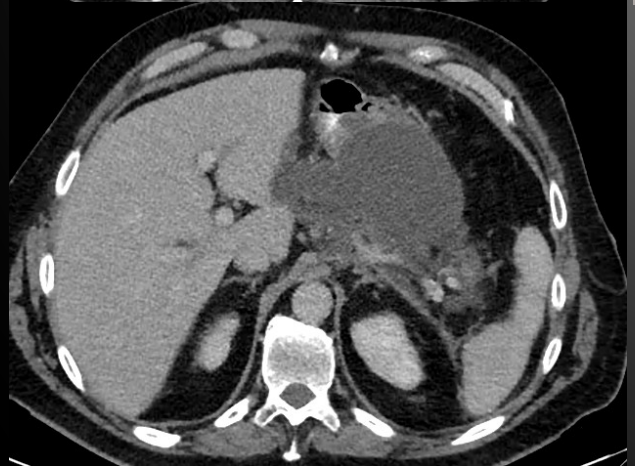

HANAROSTENT® Biliary Flap Lasso (CCC)

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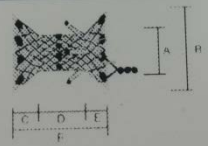
SPECIFICATION



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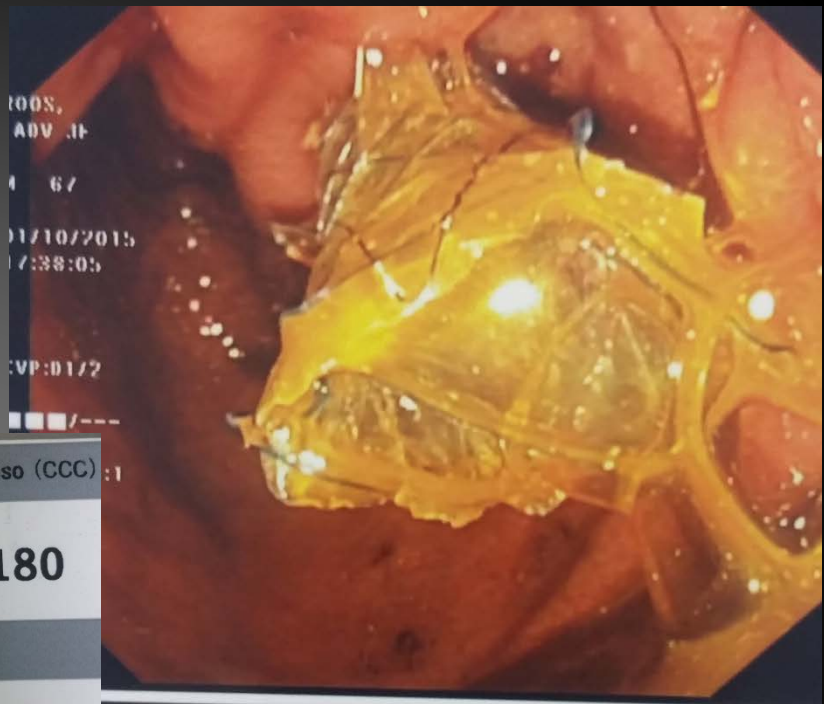
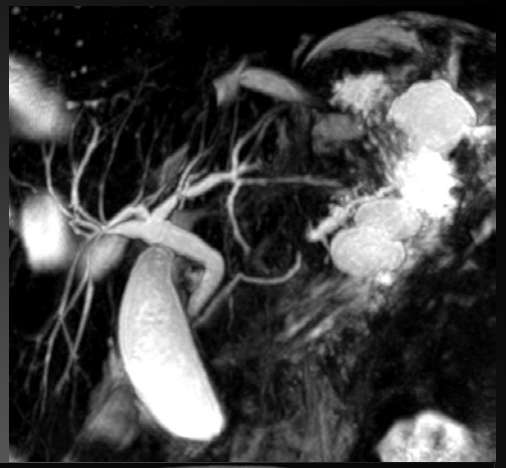
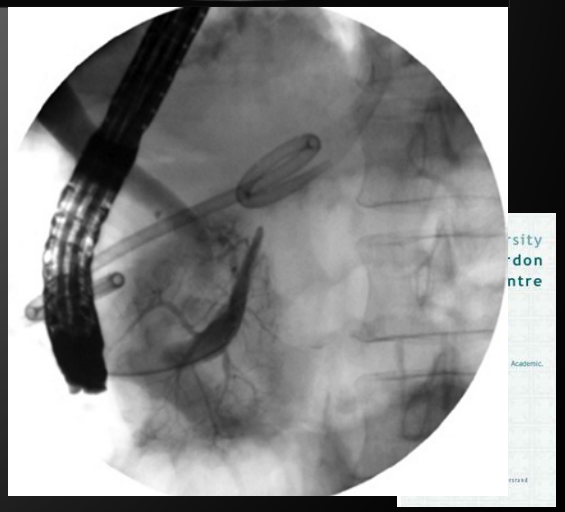


Disconnected body/tail

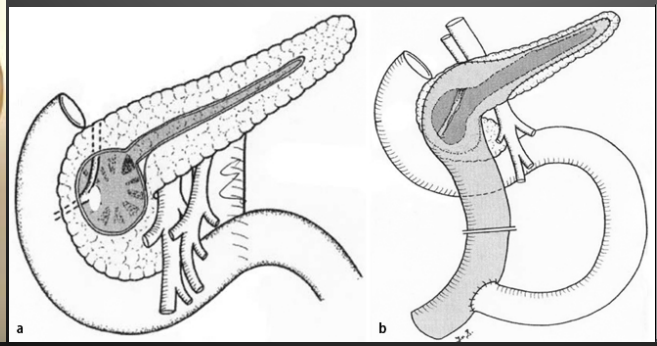
- Fistula tends to be prolonged but may close
- Ductal dilatation usual
- Pain may be problematic
- Surgery has a role
  - Pancreatico-jejunostomy
  - Distal pancreatectomy

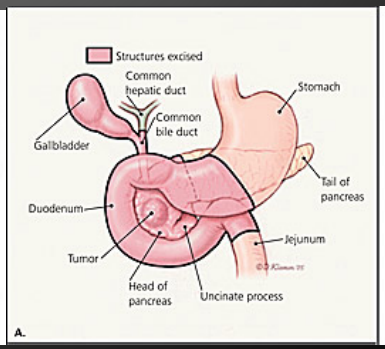


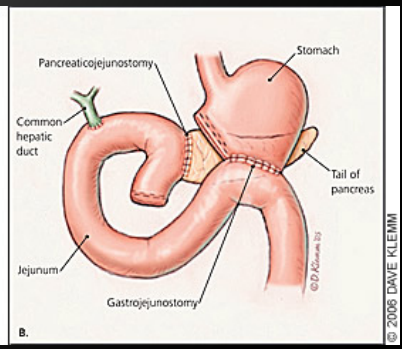


Traumatic injuries

- Ductal anatomy is main determinant
- Drainage to control collections
- EUS internal drainage for collections
- Disconnected body/tail may require surgery
- Complex head injury may require Whipple







Endoscopic drainage

- Physiological
- Success rate 50-100%
- Recurrence rate 0-32%

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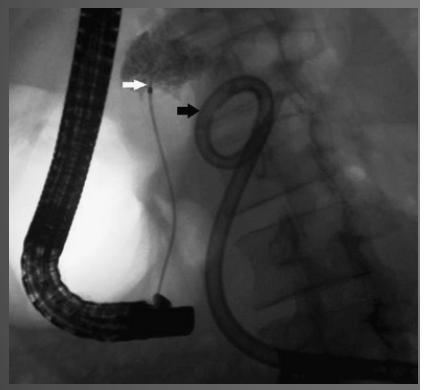

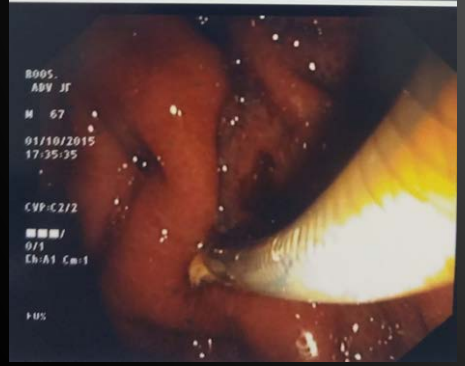

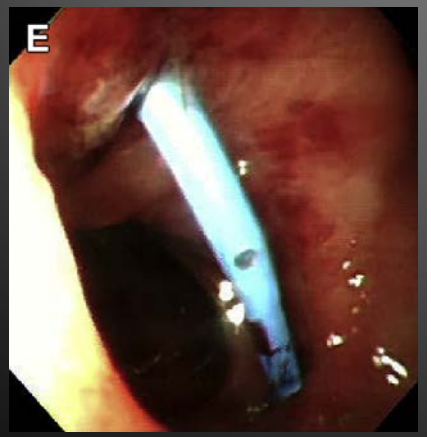

Table 1
Selected studies on endoscopic transmural drainage alone of pancreatic pseudocysts (studies in which results of endoscopic transmural drainage alone are given separately)

Authors,[Ref.] Year	No. of Patients	EUS Guidance	Success	Complications of Procedure	Recurrence
Kozarek et al,[50] 1985	4	No	2/4 (50%)	Infection: 1 Bleeding: 1	Nil
Cremer et al,[54] 1989	33	No	Technical: 32/33 (97%) Clinical: 26/32 (82%)	Bleeding: 1 Infection: 1	4/32 (12%)
Smits et al,[55] 1995	17	No	10/17 (59%)	Bleeding: 2 Perforation: 2 Apnea: 1	—[a]
Binmoeller et al,[52] 1995	24	No	Technical: 20/24 (83%) Clinical: 19/20 (95%)	Bleeding: 2 Gallbladder perforation: 1	6/19 (32%)
Sharma et al,[56] 2002	33	No	33/33 (100%)	Bleeding: 1 Infection: 3 (stent block) Perforation: 1	—[a]
Sanchez Cortes et al,[60] 2002	33 patients 34 attempts	Yes	Technical: 32/33 (97%) Clinical: 31/32 (97%)	Bleeding: 2 Pneumoperitoneum: 1	1/32 (3%)
Cahen et al,[47] 2005	54	No	36/54 (67%)	39%	—[a]
Krüger et al,[53] 2006	35	Yes	Technical: 33/35 (94%) Clinical: 29/33 (88%)	None	4/29 (14%)
Antillon et al,[58] 2006	33	Yes	Technical: 31/33 (94%) Clinical: 27/31 (87%)	Perforation: 1 Bleeding: 1	1/27 (4%)
Barthet et al,[51] 2008	41	Yes	Technical: 40/41 (98%) Clinical: 36/40 (90%)	Bleeding: 3 Infection: 6	—[a]
Lopes et al,[57] 2008	31	Yes	Technical: 31/31 (100%) Clinical: 29/31 (94%)	Pneumoperitoneum: 1 Peritonitis: 1	6/29 (21%)
Penn et al,[59] 2012	20 (used covered SEMS)	Yes	Technical: 20/20 (100%) Clinical: 17/20 (85%)	Infection: 2	3/17 (18%)
Shrode et al,[49] 2012	36	Not mentioned	27 (75%)	—[a]	—[a]

ERCP stenting

- Success rate 72-100%
- Recurrence rate 0-40%
- Risk of late ductal stricture

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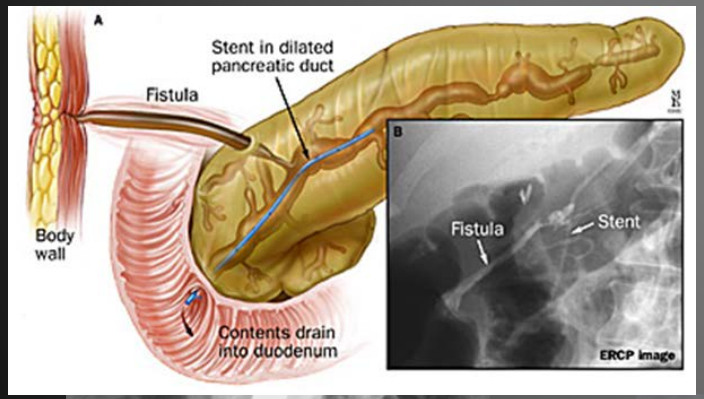
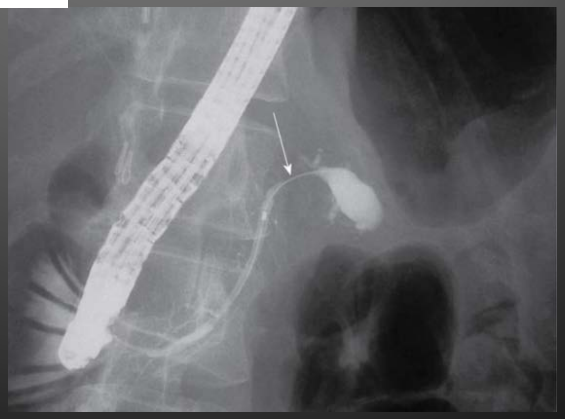


Table 3
Selected studies on endoscopic transpapillary drainage for pancreatic ascites and effusion (studies in which results of endoscopic drainage in patients with pancreatic ascites/effusion are given separately)

Authors,[Ref.] Year	No. of Patients	Success	Complication	Recurrence
Kozarek et al,[73] 1994	4	4/4 (100%) Percutaneous drain in 2	Stent-induced ductal changes: 2	None
Bracher et al,[71] 1999	8	Technical: 8/8 (100%) Clinical: 8/8 (100%) metal stent in 1 patient	None	None
Chebli et al,[72] 2004	11 (4 treated endoscopically)	4/4 (100%)	None	None
Varadarajulu et al,[1] 2005	20	Separate figures for ascites only not given	Separate figures for ascites/ effusion only not given	Separate figures for ascites only not given
Halttunen et al,[80] 2005	25	23/25 (2%)	Separate figures for ascites/effusion only not given	None
Bhasin et al,[68] 2006	10	10/10 (100%)	NPD block: 1 Infection: 1	None
Pai et al,[74] 2009	28	Technical: 27/28 (96%) Clinical: 26/27 (96%)	Severe pain: 2 Fever: 5	None
Kurumboor et al,[75] 2009	11	Technical: 9/11 (82%) Clinical: 5/9 (55%)	Infection: 3	None; recurrent pain in 2
Shrode et al,[49] 2012	3	Separate figures for ascites only not given	Separate figures for ascites/ effusion only not given	Separate figures for ascites only not given



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Conclusions

- Pancreatic fistula implies ductal injury with leakage of amylase-rich fluid

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- EUS internal drainage preferred
- Surgery reserved for anastomotic revision and distal resection or ductal drainage