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.

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

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

*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>
<thead>
<tr>
<th>Risk factor</th>
<th>Parameter</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gland texture</td>
<td>Firm</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Soft</td>
<td>2</td>
</tr>
<tr>
<td>Pathology</td>
<td>Pancreatic adenocarcinoma or pancreatitis</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Ampullary, duodenal, cystic, islet cell, etc...</td>
<td>1</td>
</tr>
<tr>
<td>Pancreatic duct diameter</td>
<td>$\geq 5, mm$</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>4, mm</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>3, mm</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>2, mm</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>$\leq 1, mm$</td>
<td>4</td>
</tr>
<tr>
<td>Intraoperative blood loss</td>
<td>$\leq 400, ml$</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>401–700, ml</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>701–1,000, ml</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>$&gt;1,000, ml$</td>
<td>3</td>
</tr>
</tbody>
</table>

**Total 0 to 10 points**

From Callery et al., *JACS*, 2013
Technique alone cannot completely prevent pancreatic leak and fistula.

Table 1 Selected trials performed to evaluate rates of POPF

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

POPF, post-operative pancreatic 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
  - Pancreaticeo-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
Disconnected body/tail

- Fistula tends to be prolonged but may close
- Ductal dilatation usual
- Pain may be problematic
- Surgery has a role
  - Pancreatico-jejunalostomy
  - 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%


<table>
<thead>
<tr>
<th>Authors, Ref. Year</th>
<th>No. of Patients</th>
<th>EUS Guidance</th>
<th>Success</th>
<th>Complications of Procedure</th>
<th>Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kozarek et al.1985</td>
<td>4</td>
<td>No</td>
<td>2/4 (50%)</td>
<td>Infection: 1; Bleeding: 1</td>
<td>Nil</td>
</tr>
<tr>
<td>Cremer et al.1989</td>
<td>33</td>
<td>No</td>
<td>Technical: 32/33 (97%); Clinical: 26/32 (82%)</td>
<td>Bleeding: 1; Infection: 1</td>
<td>4/32 (12%)</td>
</tr>
<tr>
<td>Smits et al.1995</td>
<td>17</td>
<td>No</td>
<td>10/17 (59%)</td>
<td>Bleeding: 2; Perforation: 2</td>
<td>Apnea: 1</td>
</tr>
<tr>
<td>Binmoeller et al.1995</td>
<td>24</td>
<td>No</td>
<td>Technical: 20/24 (83%); Clinical: 19/20 (95%)</td>
<td>Bleeding: 2; Gallbladder perforation: 1</td>
<td>6/19 (32%)</td>
</tr>
<tr>
<td>Sharma et al.2002</td>
<td>33</td>
<td>No</td>
<td>33/33 (100%)</td>
<td>Bleeding: 1; Infection: 3 (sten block); Perforation: 1</td>
<td>—a</td>
</tr>
<tr>
<td>Sanchez Cortes et al.2002</td>
<td>33 patients 34 attempts</td>
<td>Yes</td>
<td>Technical: 32/33 (97%); Clinical: 31/32 (97%)</td>
<td>Bleeding: 2; Pneumoperitoneum: 1</td>
<td>1/32 (3%)</td>
</tr>
<tr>
<td>Cahen et al.2005</td>
<td>54</td>
<td>No</td>
<td>36/54 (67%)</td>
<td>39%</td>
<td>—a</td>
</tr>
<tr>
<td>Kruger et al.2006</td>
<td>35</td>
<td>Yes</td>
<td>Technical: 33/35 (94%); Clinical: 29/33 (88%)</td>
<td>None</td>
<td>4/29 (14%)</td>
</tr>
<tr>
<td>Antillon et al.2006</td>
<td>33</td>
<td>Yes</td>
<td>Technical: 31/33 (94%); Clinical: 27/31 (87%)</td>
<td>Perforation: 1; Bleeding: 1</td>
<td>1/27 (4%)</td>
</tr>
<tr>
<td>Barthe et al.2008</td>
<td>41</td>
<td>Yes</td>
<td>Technical: 40/41 (98%); Clinical: 36/40 (90%)</td>
<td>Bleeding: 3; Infection: 6</td>
<td>—a</td>
</tr>
<tr>
<td>Lopes et al.2008</td>
<td>31</td>
<td>Yes</td>
<td>Technical: 31/31 (100%); Clinical: 29/31 (94%)</td>
<td>Pneumoperitoneum: 1; Peritonitis: 1</td>
<td>6/29 (21%)</td>
</tr>
<tr>
<td>Penn et al.2012</td>
<td>20 (used covered SEMS)</td>
<td>Yes</td>
<td>Technical: 20/20 (100%); Clinical: 17/20 (85%)</td>
<td>Infection: 2</td>
<td>3/17 (18%)</td>
</tr>
<tr>
<td>Shrode et al.2012</td>
<td>36</td>
<td>Not mentioned</td>
<td>27 (75%)</td>
<td>—a</td>
<td>—a</td>
</tr>
</tbody>
</table>
ERCP stenting

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

*Gastrointest Endoscopy Clin N Am 23 (2013) 863–892*
Conclusions

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

• May be contained as a pseudocyst or communicate with other organs or surfaces

• Assessment of ductal and fistula anatomy vital

• Prevent complications such as malnutrition, sepsis and bleeding

• Intervene for symptoms or complications

• EUS internal drainage preferred

• Surgery reserved for anastomotic revision and distal resection or ductal drainage