Strategies to minimize complications of ERCP

John G. Lee, MD | February 22, 2019
Disclosure

Cook Endoscopy

Advanced Sterilization Products
Common complications of ERCP

• Pancreatitis
• Bleeding
• Infection
• Perforation
• Cardiopulmonary
• Death

ASGE Guideline 2012
Only absolute way to eliminate the risk of ERCP...

- Anything related to SOD
  - No evidence for ‘type III’
  - No evidence for causing pancreatitis
  - Indefensible indication for ERCP

- Most diagnostic ERCP

“ERCP is most dangerous to those who need it the least...”
Incidence, severity, and mortality of post-ERCP pancreatitis: a systematic review by using randomized, controlled trials

- Over all incidence was 9.7% with mortality of 0.7%
  - Mild in 5.7%
  - Moderate in 2.6%
  - Severe in 0.5%

- Incidence in ‘high risk’ patients was 14.7%

- Incidence in North America was 13%
  - Europe was 8.4%
  - Asian 9.9%

- Incidence before 2000 was 7.7%

- Incidence after 2000 was 10%

GIE 2015;81:143-149
## Independent risk factors for post-ERCP pancreatitis identified with multivariable analysis

<table>
<thead>
<tr>
<th><strong>Patient-related risk factors</strong></th>
<th><strong>Odds Ratio</strong> (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior post-ERCP pancreatitis</td>
<td>8.7 (3.2-23.86)</td>
</tr>
<tr>
<td>Female sex</td>
<td>3.5 (1.1-10.6)</td>
</tr>
<tr>
<td>Previous recurrent pancreatitis</td>
<td>2.46 (1.93-3.12)</td>
</tr>
<tr>
<td>Suspected sphincter of Oddi dysfunction</td>
<td>1.91 (1.37-2.65)</td>
</tr>
<tr>
<td>Younger patient age (&lt;40 years old)</td>
<td>1.8 (1.27-2.59)</td>
</tr>
<tr>
<td>30 vs 70 years old</td>
<td>2.14 (1.41-3.25)</td>
</tr>
<tr>
<td>Absence of chronic pancreatitis</td>
<td>1.87 (1.003.48)</td>
</tr>
<tr>
<td>Normal serum bilirubin</td>
<td>1.89 (1.22-2.93)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Procedure-related risk factors</strong></th>
<th><strong>Odds Ratio</strong> (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficult cannulation (&gt;10 minutes)</td>
<td>1.76 (1.13-2.74)</td>
</tr>
<tr>
<td>Repetitive pancreatic guidewire</td>
<td>2.77 (1.79-4.30)</td>
</tr>
<tr>
<td>cannulation</td>
<td></td>
</tr>
<tr>
<td>Pancreatic injection</td>
<td>2.2 (1.60-3.01)</td>
</tr>
<tr>
<td>Pancreatic sphincterotomy</td>
<td>3.07 (1.64-5.75)</td>
</tr>
<tr>
<td>Endoscopic papillary large-balloon</td>
<td>4.51 (1.51-13.46)</td>
</tr>
<tr>
<td>dilation of an intact sphincter</td>
<td></td>
</tr>
</tbody>
</table>

**Risk is additive!**

Endoscopy, 46 (2014), pp. 799-815
Strategies to minimize risk of pancreatitis besides patient selection

• Hydration

• Medication

• Endoscopy technique
  • Pancreatic stenting
  • Guidewire cannulation
  • Early precut
Aggressive hydration with lactated ringsers

- Aggressive hydration with lactated Ringer's solution reduces pancreatitis after endoscopic retrograde cholangiopancreatography
  - 0% versus 17% post ERCP pancreatitis

- Aggressive hydration with Lactated Ringer's solution as the prophylactic intervention for postendoscopic retrograde cholangiopancreatography pancreatitis: A randomized controlled double-blind clinical trial
  - 5.3% versus 22.7% ($P = 0.002$) post ERCP pancreatitis

- 3ml/kg/h during and after ERCP x 8 hours + 20ml/kg bolus post procedure

- Data are weak but no reason not to use it
Indomethacin

### A Post-ERCP Pancreatitis

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Indomethacin</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Post-ERCP Pancreatitis</td>
<td>16.9</td>
<td>9.2</td>
</tr>
<tr>
<td>Moderate or Severe Post-ERCP Pancreatitis</td>
<td>8.8</td>
<td>4.4</td>
</tr>
</tbody>
</table>

### B Adverse Events

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Indomethacin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal Bleeding</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>

**Indomethacin** 50mg x 2

- Appears to work, especially in high risk
- No harm, so why not?
  - Contraindication – anaphylaxis, pregnancy

<table>
<thead>
<tr>
<th>Condition</th>
<th>Patients with PEP</th>
<th>% Relative Risk Reduction (Indomethacin vs. Placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatic Stent Placement – no. (%)</td>
<td>8 (50)</td>
<td>-28%</td>
</tr>
<tr>
<td>Suspected Sphincter of Oddi Dysfunction – no. (%)</td>
<td>1 (6)</td>
<td>+33%</td>
</tr>
<tr>
<td>History of Post-ERCP Pancreatitis</td>
<td>2 (13)</td>
<td>-21%</td>
</tr>
<tr>
<td>Difficult Cannulation</td>
<td>6 (38)</td>
<td>+16%</td>
</tr>
<tr>
<td>Wire Cannulation of Pancreatic Duct – no. (%)</td>
<td>13 (81)</td>
<td>-21%</td>
</tr>
<tr>
<td>Pancreatography – no. (%)</td>
<td>8 (50)</td>
<td>+32%</td>
</tr>
<tr>
<td>Pancreatic Acinarization – no. (%)</td>
<td>2 (13)</td>
<td>NA</td>
</tr>
<tr>
<td>Therapeutic Biliary Sphincterotomy – no. (%)</td>
<td>7 (44)</td>
<td>-39%</td>
</tr>
<tr>
<td>Therapeutic Pancreatic Sphincterotomy – no. (%)</td>
<td>2 (13)</td>
<td>+52%</td>
</tr>
<tr>
<td>Balloon Dilation of Biliary Sphincter – no. (%)</td>
<td>0 (0)</td>
<td>NA</td>
</tr>
<tr>
<td>Trainee Involvement in ERCP – no. (%)</td>
<td>12 (75)</td>
<td>-3%</td>
</tr>
</tbody>
</table>


Lactated Ringer's solution in combination with rectal indomethacin for prevention of post-ERCP pancreatitis and readmission: a prospective randomized, double-blinded, placebo-controlled trial

- Double blinded PCT
- But high pancreatitis rate
- But still makes sense

GIE, 2017 (85), 1005–1013

- What about aggressive intra and post procedure hydration?
- Beware of increased serum lactate level
- No reason not to use LR + indomethacin
Updated meta-analysis of pancreatic stent placement in preventing post-endoscopic retrograde cholangiopancreatography pancreatitis
The risk of post-ERCP pancreatitis and the protective effect of rectal indomethacin in cases of attempted but unsuccessful prophylactic pancreatic stent placement

- Not randomized; intent to stent unclear in a retrospective review
- Why was pancreatitis so common after failed stent?
  - Excessive attempt (‘beating up’ the papilla);
  - Intrinsically high risk patients in Indiana, i.e., so called SOD patients?
- Indomethacin is possibly protective after failed stenting
  - *So place PD stent only if ‘easy’*
Guidewire-assisted cannulation of the common bile duct for the prevention of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis

- Higher selective cannulation rate (RR 1.07, 95% CI 1.00 to 1.15)
- Less precut sphincterotomy (RR 0.75; 95% CI, 0.60-0.95)
  - But no difference in studies that allowed cross over
- Really no reason not to use guidewire cannulation

Cochrane Database of Systematic Reviews 2012, Issue 12.
Cannulation technique after PD is accessed first

- Maintain wire in PD
- Cut towards the biliary orifice
  - Look for bile
- Place 5fr x 5cm fall out stent using sphincterotome as pusher
- Reattempt cannulation towards the biliary orifice

- Earlier precut needle knife sphincterotomy for access
  - Repeat next day if still unable to access after precut
- Alternative cannulation techniques
  - EUS guided rendezvous
  - EUS choledochoduodenostomy
  - Percutaneous approach
Early Precut Sphincterotomy Does Not Increase Risk During Endoscopic Retrograde Cholangiopancreatography in Patients With Difficult Biliary Access: A Meta-analysis of Randomized Controlled Trials

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Early precut</th>
<th>Standard</th>
<th>Risk ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
</tr>
<tr>
<td>4.1.1 Studies with fellows involved</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tang 2005</td>
<td>2</td>
<td>32</td>
<td>2</td>
</tr>
<tr>
<td>Swan 2013</td>
<td>8</td>
<td>39</td>
<td>6</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>71</td>
<td>64</td>
<td>1</td>
</tr>
<tr>
<td>Total events</td>
<td>10</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = .00, Chi^2 = .04, df = 1 (P = .84); I^2 = 0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect Z = .25 (P = .81)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| 4.1.2 Studies with no fellows involved |
| Zhou 2006                      | 1            | 43       | 2                | 48             | 9.9%  | 0.56 [0.05, 5.94] | 2006  |
| Cennamo 2009                  | 1            | 36       | 6                | 110            | 12.4% | 0.51 [0.06, 4.09] | 2009  |
| Manes 2009                    | 2            | 77       | 11               | 74             | 22.2% | 0.17 [0.04, 0.76] | 2009  |
| Subtotal (95% CI)             | 156          | 232      | 1                | 232            | 44.5% | 0.29 [0.10, 0.86] |       |
| Total events                  | 4            | 19       |                  |                |       |                   |       |
| Heterogeneity: Tau^2 = .00, Chi^2 = 1.04, df = 2 (P = .60); I^2 = 0% |
| Test for overall effect Z = 2.24 (P = .03) |

| Total (95% CI)                | 227          | 296      | 100.00%          | 0.62 [0.28, 1.36] |
| Total events                  | 14           | 27       |                  |                |
| Heterogeneity: Tau^2 = .15, Chi^2 = 4.91, df = 4 (P = .30); I^2 = 19% |
| Test for overall effect Z = 1.19 (P = .23) |
| Test for subgroup differences: Chi^2 = 3.62, df = 1 (P = .06); I^2 = 72.4% |

- Highly variable definition of difficult cannulation – almost impossible to prove...
  - 5-12 minute attempt or >2-4 PD cannulation
- Early precut is probably better if it can be done ‘safely’
Strategies to minimize risk of pancreatitis

- Crystal clear indications
- Do everything with low to no risk
  - Hydration with LR
  - PR indomethacin
  - Guidewire cannulation
- PD stent if easy
- Consider early precut for access
Complications of endoscopic biliary sphincterotomy – significant risk factors for post sphincterotomy bleeding

- Coagulopathy (OR 3.32; \( P < .001 \))
- Active cholangitis (OR 2.59; \( P < .001 \))
- Anticoagulant therapy within 3 days after ERCP (OR 5.11; \( P < .001 \))
- Endoscopist case volume ≤1 per week (OR 2.17; \( P = .002 \))
- Any observed bleeding during the procedure (OR 1.74; \( P = .004 \))

NEJM 1996;335, 909-918
Bleeding risk

- Assume high risk
  - Unrecognized coagulopathy and importance of bleeding history
  - Exceptions – prior sphincterotomy or stent change
- Cardiology / Neurology / anticoagulation clinic when in doubt
- Warfarin
  - Hold 3-5 days, +/- check INR, restart immediately to 2-3 days
- DOAC
  - Dabigatran (Pradaxa), rivaroxaban (Xarelto), apixaban (Eliquis), edoxaban (Savaysal)
    - Hold 48 hours, restart immediately to 3 days
- Antiplatelet therapy
  - Usually continue aspirin / NSAID
  - Usually hold P2Y₁₂ e.g., ticlopidine (Ticlid), clopidogrel (Plavix), prasugrel (Effient), ticagrelor (Brilinta) for 5-14 days; continue aspirin if on dual therapy
Decreasing bleeding risk

- Don’t cut unless necessary
- Blended / microprocessor controlled cutting might be better than pure cutting current
- Do not cut with too much wire
- Do not tent too much
Minimizing infection risk

- Meticulous reprocessing
- Use of sterile accessories whenever possible including water, water bottle, tubing etc.
- Prophylactic antibiotics not recommended except for
  - Post OLT patient
  - Incomplete drainage
    - Retained stones / sludge
    - Over filling of complex hilar strictures
Risk of infection with hilar stricture

- MRCP first
- Inject only if absolutely necessary
- Always inject proximal to stricture
- Inject each side separately and only after wire access in contralateral side
Risk factors for perforation

- Surgically altered anatomy
- Recent surgery
- Stricture / cancer
- Old age – cervical spur
- Difficult cannulation
- Sphincterotomy
- Large balloon dilation
- Barotrauma
- Stiff wires, plastic stents, metal stent / introducer
Perforation

- I – limit dilation, cervical spur
- II – cut between 11 – 1 O’clock, cut and dilate
- III – hydrophilic guidewire, wire lock
- IV – CO2, water

Immediate recognition is key!
- Strange air shadow / control film
- Difficulty insufflating
- Hemodynamic instability
- Crepitus, tense abdomen
- Pain

Table 1. Classification of iatrogenic Duodenal Perforations during Endoscopic Retrograde Cholangiopancreatography

<table>
<thead>
<tr>
<th>Reference</th>
<th>Type and definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stapfer et al.¹</td>
<td>Type I, lateral or medial duodenal wall perforation, endoscope related</td>
</tr>
<tr>
<td></td>
<td>Type II, periampullary perforations, sphincterotomy related</td>
</tr>
<tr>
<td></td>
<td>Type III, ductal or duodenal perforations due to endoscopic instruments</td>
</tr>
<tr>
<td></td>
<td>Type IV, guidewire-related perforation with presence of retroperitoneal air at X-ray</td>
</tr>
<tr>
<td>Howard et al.²</td>
<td>Group I, guidewire perforation</td>
</tr>
<tr>
<td></td>
<td>Group II, periampullary perforation</td>
</tr>
<tr>
<td></td>
<td>Group III, duodenal perforation</td>
</tr>
<tr>
<td>Enns et al.³</td>
<td>Esophageal, gastric, and duodenal perforation</td>
</tr>
<tr>
<td></td>
<td>Sphincterotomy-related perforation</td>
</tr>
<tr>
<td></td>
<td>Guidewire-related perforation</td>
</tr>
</tbody>
</table>
ASGE recommendations

1. Use techniques that reduce the risk of pancreatitis (i.e., wire-guided cannulation, prophylactic pancreatic duct stenting). ☐☐☐☐

2. Pancreatic duct stenting in high-risk individuals. ☐☐☐☐

3. Follow FDA recommendations for duodenoscope reprocessing. ☐☐☐☐

4. Early precut for difficult biliary cannulation when expertise is available. ☐☐☐○

5. Rectal nonsteroidal anti-inflammatory drugs (NSAIDS). ☐☐☐○

6. No large balloon dilation (EPLBD) of an intact sphincter. ☐☐☐○

7. Sphincterotomy only when absolutely indicated. ☐☐☐○

8. Use microprocessor-controlled generator with mixed current. ☐☐☐○
ASGE recommendations

9. Antibiotic prophylaxis for OLT patients and possible incomplete biliary drainage; continue afterwards for incomplete biliary drainage. ⊕⊕⊕○

10. Insufficient evidence that rectal NSAIDs + PD stenting is better than either technique alone for prevention of post-ERCP pancreatitis in high-risk individuals. ⊕⊕○○

11. Rectal indomethacin may reduce the risk and severity of post-ERCP pancreatitis in average-risk individuals. ⊕⊕○○

12. Non operative management for type II, III, IV perforations from ERCP without peritonitis or SIRS. ⊕⊕○○

13. No premedication in patients with food or IV contrast allergies. ⊕⊕○○


GIE 2017;85: 32-47