Minimizing Adverse Events During ERCP

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Objectives

• Identify adverse events associated with ERCP

• Understand the risk factors for developing ERCP-related adverse events

• Discuss strategies to minimize risk, improve diagnosis, and manage ERCP-related adverse events
Major Complications

- Pancreatitis
- Perforation
- Bleeding
- Infection
- Cardio-pulmonary (anesthesia)

Post-ERCP Pancreatitis

- Reported range: 1% to 40%
- Typical ~ 5%

- Definition
  - New or worsened abdominal pain
  - Amylase > 3x ULN at more than 24 hrs post-ERCP
    - Mild: 2-3 days in hospital
    - Moderate: 4-10 days
    - Severe: > 10 days; pseudocyst, or intervention; ICU

Mechanisms of PEP

- Mechanical
- Chemical
- Hydrostatic
- Enzymatic
- Microbiologic
- Thermal injury

Risk Factors for Post-ERCP Pancreatitis (Multivariate Analyses)

Definite*:  
- Suspected sphincter of Oddi dysfunction
- Young age
- Normal bilirubin
- History of post-ERCP pancreatitis
- Difficult or failed cannulation
- Pancreatic duct injection
- Pancreatic guidewire placement
- Pancreatic tissue sampling by biopsy
- Pancreatic sphincterotomy (especially minor papilla)
- Balloon dilation of intact biliary sphincter
- Precut sphincterotomy

Maybe*:  
- Female sex
- Acinarization
- Absence of common bile duct stone
- Lower ERCP case volume
- Trainee involvement

No*:  
- Small common bile duct diameter
- Sphincter of Oddi manometry
- Biliary sphincterotomy


* Significant by multivariate analysis in most studies.
* Significant by univariate analysis only in most studies.
* Not significant by multivariate analysis in any study.
Evaluating Predictors & Interventions in Sphincter of Oddi Dysfunction (EPISOD)

- RCT
- Multicenter
- Type 3 SOD
- Sham vs Sphincterotomy

1 year follow-up success
- Sham group: 36%*
- Sphincterotomy group: 22%

Cotton PB et al. JAMA 2014.

Protective Factors

Chronic Pancreatitis  Pancreatic Cancer
Preventing PEP

- Appropriate use of ERCP
- Patient selection
- Techniques
- Pharmacologic
- Experience

Non-ERCP Evaluation

MRCP

EUS
Procedure-Related Risk Factors

- Papillary trauma

- Pancreatic manipulation
  - Contrast injection
  - Acinarization
  - Pancreatic sphincterotomy
    - Major papilla
    - Minor papilla

- “Difficult cannulation”

- Pre-cut papillotomy
Timing of Precut Papillotomy

<table>
<thead>
<tr>
<th>Study</th>
<th>OR (95% CI)</th>
<th>EPC</th>
<th>PA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tang, 2005</td>
<td>0.93 (0.13, 6.98)</td>
<td>2/32</td>
<td>2/30</td>
</tr>
<tr>
<td>Zhou, 2006</td>
<td>0.56 (0.06, 5.59)</td>
<td>1/43</td>
<td>2/48</td>
</tr>
<tr>
<td>De Weerth, 2006</td>
<td>0.75 (0.17, 3.36)</td>
<td>3/145</td>
<td>4/146</td>
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<tr>
<td>Klajbien, 2008</td>
<td>0.70 (0.12, 4.13)</td>
<td>2/106</td>
<td>3/112</td>
</tr>
<tr>
<td>Menez, 2008</td>
<td>0.22 (0.07, 0.67)</td>
<td>2/80</td>
<td>11/78</td>
</tr>
<tr>
<td>Cennamo, 2009</td>
<td>0.56 (0.10, 3.23)</td>
<td>1/36</td>
<td>6/110</td>
</tr>
<tr>
<td></td>
<td>0.47 (0.24, 0.91)</td>
<td>1/442</td>
<td>28/524</td>
</tr>
</tbody>
</table>

Fig 1: Forest plot of the six RCTs that compared post-endoscopic retrograde cholangiopancreatograpy (ERCP) pancreatic rates of the early precut implementation and of persistent attempts by the standard approach. Post-ERCP pancreatitis developed in 2.5% of patients (11 out of 442) randomized to the early precut group and in 5.3% of patients (28 out of 524) randomized to the persistent attempts group. The pooled analysis yielded an OR of 0.47 (95% CI 0.24–0.91), EPC, early precut group; PA, persistent attempts group.

Early precut papillotomy associated with a LOWER risk of PEP


Wire-Guided Cannulation

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Events Total</th>
<th>Control Total</th>
<th>OR (95% CI)</th>
<th>EPC</th>
<th>PA</th>
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<tbody>
<tr>
<td>Maintenance studies</td>
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<tr>
<td>Sawa 2004 [54]</td>
<td>6 100</td>
<td>8 100</td>
<td>2.6 0.06 (0.00-1.15)</td>
<td>2/32</td>
<td>2/30</td>
</tr>
<tr>
<td>Apostolidis 2005 [50]</td>
<td>1 67</td>
<td>6 63</td>
<td>0.16 (0.02-1.27)</td>
<td>2/32</td>
<td>2/30</td>
</tr>
<tr>
<td>Mongioianni 2007 [55]</td>
<td>2 100</td>
<td>6 100</td>
<td>0.33 (0.07-1.25)</td>
<td>2/32</td>
<td>2/30</td>
</tr>
<tr>
<td>Aries 2007 [47]</td>
<td>5 150</td>
<td>18 150</td>
<td>0.29 (0.15-0.73)</td>
<td>2/32</td>
<td>2/30</td>
</tr>
<tr>
<td>Lee 2009 [53]</td>
<td>3 150</td>
<td>17 150</td>
<td>0.18 (0.05-0.59)</td>
<td>2/32</td>
<td>2/30</td>
</tr>
<tr>
<td>Total events</td>
<td>11 607</td>
<td>55 607</td>
<td>0.33 (0.13-0.84)</td>
<td>2/32</td>
<td>2/30</td>
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<tr>
<td>Crosswire studies</td>
<td></td>
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<tr>
<td>Gough 2007 [40]</td>
<td>4 241</td>
<td>6 235</td>
<td>0.47 (0.13-1.63)</td>
<td>2/32</td>
<td>2/30</td>
</tr>
<tr>
<td>Bayley 2008 [46]</td>
<td>16 215</td>
<td>13 215</td>
<td>1.23 (0.63-2.26)</td>
<td>2/32</td>
<td>2/30</td>
</tr>
<tr>
<td>Katoh 2000 [38]</td>
<td>9 167</td>
<td>13 165</td>
<td>0.68 (0.21-2.00)</td>
<td>2/32</td>
<td>2/30</td>
</tr>
<tr>
<td>Kogoe 2010 [52]</td>
<td>10 163</td>
<td>18 159</td>
<td>0.99 (0.42-2.28)</td>
<td>2/32</td>
<td>2/30</td>
</tr>
<tr>
<td>Mongioianni 2011 [56]</td>
<td>2 46</td>
<td>4 42</td>
<td>0.46 (0.09-2.37)</td>
<td>2/32</td>
<td>2/30</td>
</tr>
<tr>
<td>Nardelli 2011 [57]</td>
<td>2 86</td>
<td>5 86</td>
<td>0.49 (0.08-2.01)</td>
<td>2/32</td>
<td>2/30</td>
</tr>
<tr>
<td>Kowalski 2012 [55]</td>
<td>8 199</td>
<td>6 201</td>
<td>1.53 (0.40-5.81)</td>
<td>2/32</td>
<td>2/30</td>
</tr>
<tr>
<td>Total events</td>
<td>1117</td>
<td>57 1063</td>
<td>0.85 (0.58-1.23)</td>
<td>2/32</td>
<td>2/30</td>
</tr>
</tbody>
</table>

Fig 2: Meta-analysis of post-endoscopic retrograde cholangiopancreatography pancreatitis among trials comparing guide wire-assisted vs. contrast-guided cannulation techniques. CI, confidence interval. *p* obtained using Mantel–Haenszel random effects model.
Balloon Sphincteroplasty

- Meta-Analysis
- 8 RCT, 1108 pts

<table>
<thead>
<tr>
<th></th>
<th>Balloon Dilation</th>
<th>Sphincterotomy</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Success</td>
<td>94.3%</td>
<td>96.5%</td>
<td>NS</td>
</tr>
<tr>
<td>Need for Mechanical Litho</td>
<td>20.9%</td>
<td>14.8%</td>
<td>0.014</td>
</tr>
<tr>
<td>Overall Compl</td>
<td>10.5%</td>
<td>10.3%</td>
<td>NS</td>
</tr>
<tr>
<td>Bleeding</td>
<td>0%</td>
<td>2.0%</td>
<td>0.001</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>7.4%</td>
<td>4.3%</td>
<td>0.05</td>
</tr>
</tbody>
</table>


Prophylactic Pancreatic Stents

- 14 RCT
- 1541 pts
  - 760 PD stent
  - 781 control
- OR 0.39

Rectal Indomethacin

- 602 pts
  - 295 Indo
  - 307 placebo
- 82% suspected SOD
- Pancreatic stent
  - 9.7% vs 16.1% (p=.04)
- No stent
  - 6.3% vs 20.6% (p=.049)


This is NOT a substitution for pancreatic stenting

- Prophylactic placement of a pancreatic duct stent is still considered the standard of care for reducing the risk of PEP in high-risk patients
- Ongoing trials
Perforation

- Relatively rare (< 1%)

- Location
  - Intestinal lumen
  - Peri-ampullary
  - Ductal perforation

- Risk factors
  - Luminal stricture
  - Diverticulum
  - Sphincterotomy
  - Stricture dilation
  - SOD pts

Luminal Perforation
Perforation Management

• Recognition is key

• CT abdomen preferred over Abd x-ray

• Management

<table>
<thead>
<tr>
<th>Location</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Luminal perforation</td>
<td>Endoscopic clips, sutures</td>
</tr>
<tr>
<td>Peri-ampullary</td>
<td>Clips, trans-papillary stent</td>
</tr>
<tr>
<td>Ductal</td>
<td>Trans-papillary stent</td>
</tr>
</tbody>
</table>

– NG tube, IVF, IV antibiotics
– Early surgical evaluation

Bleeding

• Low incidence ~ 1%

• Most common risk factor = sphincterotomy
  – Immediate
  – Delayed up to 14 days

• Risk factors for sphincterotomy bleeding
  – Coagulopathy
  – Anticoagulation
  – Cholangitis
  – Bleeding during the sphincterotomy
  – Lower ERCP case volume
Minimize Bleeding Risk

- Correct coagulopathy
- Discontinue anticoagulants
- Avoid unnecessary sphincterotomies
- “Stent & run” when cholangitic
- Use blended current on electrosurgical generator
- Balloon sphincteroplasty
  - Increased risk of post-ERCP pancreatitis
  - Safer if combined with “mini” sphincterotomy first


Infection

- Cholangitis
  - Injection/contamination of biliary tree but NO drainage
- High risk scenarios
  - Primary sclerosing cholangitis
  - Hilar biliary obstruction
  - Unsuccessful drainage of injected liver segments
  - Removal of multiple and/or large bile duct stones
Minimize Infection Risk

- **Pre-procedure**
  - Broad-spectrum IV ABX (gram neg)
  - Careful review of imaging
    - MRCP a must in hilar strictures, PSC
  - Patient selection

- **Intra-procedure**
  - Minimal contrast injection
  - Selective wire-guided cannulation of desired ductal system
  - Drain (stent) any segment in which contrast was injected

- **Post-procedure**
  - Interventional radiology consultation
  - Repeat ERCP
  - Continue ABX (PO or IV)

Endoscopist Experience

- **Complexity and risk of ERCP**
  - 20x more likely to have a complication vs colonoscopy

- **Major source of medical lawsuits**
  - 59 cases
    - 30/59 cases for post-ERCP pancreatitis (6 deaths)
    - “Poor indication” was the allegation in 80% cases

- **Volume:** > 1 sphincterotomy/week vs < 1/week
  - Complication rate: 8.4% vs 11.1% (p = 0.03)
  - Severe complications: 0.9% vs 2.3% (p = 0.01)

1Cotton P. GIE 2006.
Summary

- ERCP associated with serious adverse events

- Risk factors
  - Patient-related
  - Procedure-related

- Patient selection is key

- Incorporate evidence-based techniques

- Individual case volume, experience, outcomes should be evaluated on ongoing basis