New Endoscopic Treatments for Pancreatitis and Its Complications

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Goals

- Review role of endoscopy in acute pancreatitis
- Endoscopic interventions in Chronic pancreatitis
  - ERCP procedures
  - EUS
  - Combined procedures
- Pseudocysts
- Prevention of Post ERCP pancreatitis
Indications for Pancreatic stenting

- Prophylactic: major papilla to prevent pancreatitis either from excessive manipulation during cannulation or following therapeutic procedure like ampullectomy, pancreatic sphincterotomy, or in high risk patients (SOD, prior PEP); also in minor papilla following therapeutics in pancreas divisum
- Seal a fistula
- Relieve obstruction: stricture (inflammatory, fibrotic, neoplastic, stone)

Indiana Group: Smaller is better for prophylaxis

- Retrospective review of 2447 ERCP's over a 6 year period comparing rate of post ERCP pancreatitis, spontaneous stent migration, and stent related sequelae of 3, 4, 5, & 6 F stents
- Found smaller unflanged stents more effective than 5-6 F stents in preventing post ERCP pancreatitis, with less stent induced ductal changes and less need for endoscopic removal

Indiana patients

- Suspected SOD (represented 75+% of pancreatitis group), pancreas divisum undergoing therapy, and needle knife sphincterotomy
- Historical control of 5&6F stents

Mayo Group

- Prospective study of patients at high risk for post ERCP pancreatitis
- Randomized to 5F 3cm unflanged stent (n=116) or a 3 F 8cm long unflanged stent (n=133)
- After 14 days the spontaneous dislodgement rate was 98% for 5F stents vs 88% for 3F (P=.0001). No significant difference in PEP (9% in 5F, 14% in 3F)
- Placement failure in 11 of 133 of 3F vs 0 in 5F (P=.0003)

Chahal P, Clin Gastroenterol Hepatol 2009;8:834-9
Michigan Study

- Randomized trial of 3F vs 5F single pigtail Zimmon stent without internal flange; either 6 or 5 cm
- Looked at spontaneous passage, pancreatitis, and difficulty of placement
- Found spontaneous passage to be equal at 2 weeks (66.7% in 5F; 75.8% in 3F; P=0.439)
- PEP rates did not differ
- Procedures in 3F required 20% more wires, took longer, were more difficult, and nearly 20% in 3 F group required crossover to 5 F due to difficulty placing

Zolotarevsky E, Endoscopy 2011;43:325-330

What about 4F?

- Restrospective look from Columbia U; 179 prophylactic PD stents over 14 month period
- Used Hobbs either 4F pigtail vs 4 F short straight stent no side holes
- PEP in 3.7% long stent vs 13.6% short
- Spontaneous dislodgement in 95.4% in long vs 81.8% in short (p=0.007)

Iqbal S, Dig Dis Sci 2011;56:260-265
Overall Picture: Prophylactic PD Stents

• Prophylactic Pancreatic stents are an effective way to reduce PEP in high risk patients
• Smaller stents (3F) may cause less ductal injury; but prospective trials have found no difference in frequency of PEP between 3 F vs 5F: but in 3 F you have higher wire utilization and greater failure rate

Randomized Trial of Rectal Indomethacin to Prevent Post-ERCP Pancreatitis

• Multicenter, randomized, placebo-controlled, double-blind clinical trial single dose of 50 mg rectal indomethacin or placebo immediately post procedure
• 602 patients, 82% clinical suspicion of SOD
• Primary outcome post ERCP pancreatitis; defined as new abdominal pain, elevation in enzymes to > 3X’s NI 24 hours post, and hospitalization for at least 2 nights
Rectal Indomethacin

- Post-ERCP pancreatitis developed in 27 of 295 patients in indomethacin group (9.2%)
- Developed in 52 of 307 patients in placebo group (16.9%)  \( P=0.005 \)
- Moderate-severe pancreatitis developed in 13 patients (4.4%) in indomethacin group; 27 patients in placebo group (8.8%)  \( P=0.03 \)
- Conclusion: rectal indomethacin significantly reduced incidence of post-ERCP pancreatitis

Elmunzer JB, NEJM 2012;366:1414-22

Pancreatic Endoscopic interventions

- Stricture management
- Stone removal
- Seal leaks
- Drainage: ductal and fluid collections
- Pain management
- Complication management
Non Invasive Imaging Studies

- Multidetector CT scanning; pancreatic neoplasm diagnosis and staging, identification of pancreatic fluid collections, necrosis, and vascular lesions
- MRI/MRCP; visualization of both biliary and pancreatic ductal anatomy, as well as parenchymal disease

Acute Pancreatitis

- Inflammatory condition of the pancreas characterized by abdominal pain, typically with radiation to the back, with elevated pancreatic enzymes (amylase, lipase)
- 75% of cases in US secondary to gallstones or alcohol
- Little role for endoscopy early unless suspicion of cholangitis
- May be helpful in non resolving pancreatitis, especially if concerned for a pancreatic fistula
ERCP in Acute Gallstone Pancreatitis

- Performed within 24 hours if there is associated cholangitis (Fan ST, NEJM 1993:328)
- Performed within 72 hours in those with high suspicion of CBD stone (imaging of persistent dilated duct or obvious stone, jaundice, non resolving liver tests)
- Low or moderate risk can be evaluated with alternative imaging

Smoldering Pancreatitis

- Syndrome in patients recovering from acute pancreatitis of unremitting pain, food intolerance, persistent elevation of pancreatic enzyme levels, and pancreatic and peri-pancreatic inflammation
- May be consequence of functional pancreatic duct obstruction
- Respond to stenting

Varadarajulu S, GIE 2003;58:438-441
Chronic Pancreatitis

- Permanent and irreversible damage to pancreas characterized by histologic evidence of:
  - chronic inflammation
  - fibrosis
  - destruction of exocrine (acinar cell) and endocrine (islets of Langerhans) issue

May be asymptomatic over long time periods (can be found in 5% autopsies)
- Fibrotic mass, calcifications
- Pancreatic Insufficiency with or without pain
EUS in Chronic Pancreatitis

• High resolution images of ductal structures (hyperechoic walls, dilatation, stones, side branch abnormalities) and parenchyma (lobularity, hyperechoic foci and strands, cysts)

Complications of chronic pancreatitis

• Duodenal obstruction
• Stricture of Bile duct
• Pancreatic Ascites
• Pleural Effusion
• Splenic Vein Thrombosis
• Pseudoaneurysm
• Pseudocyst
• Pancreatic Cancer
Endoscopic therapy for Chronic Pancreatitis

- Done to relieve pain
- In the absence of specific complications the primary aim is relieving outflow obstruction whether secondary to stones or stricture
- Second line endoscopic therapy would be EUS guided celiac block

Therapeutic EUS Uses

- Celiac plexus block/neurolysis
- Pseudocyst drainage
- Pancreatic-biliary access
- Other therapy: Injections, fiducials
- Abscess drainage
PD stricture

PD Fistula
Pancreatic Stones

Extracorporeal Lithotripsy

- Fluoroscopic imaging of densely calcified stones
- Commonly practiced in Europe
- Complete or partial relief of symptoms in ~80% of patients

Tandan M, Indian J Gastroenterol 2010;29:143-148
Stone extraction post ECL

Pancreas divisum
Endoscopic Rx in Chronic Pancreatitis

- Data analyzed on 146 patients followed in longstanding pancreatitis study; 71 of whom had endoscopic Rx at UPMC
- ET associated with high rate of technical success (60/71 cases, 85%)
- Clinical success in 50% of patients with symptoms; with surgery successful in 50% of those not responding (4.8 yr f/u)
- Symptoms respond in only 31% of medically treated patients

Endoscopic Stent Therapy

- 5 year follow-up of 19 consecutive patients with intermittent pain attacks and severe chronic pancreatitis by pancreatogram
- 6 of 19 with stricture, 13 with strictures and stones
- Treated with endoscopic sphincterotomy, dilatation of the PD and stent placement, followed by subsequent ERP 4 weeks later, then at 3 months
- Successful intervention in 17 patients
- 57% of patients exhibited long term benefit at 5 years


FCSEMS for PD strictures in CP

- 10 patients with painful CP and refractory pancreatic strictures treated over a 5 month period with FCSEMS
- With stents in place 9 patients experienced pain relief (one morphine addicted patient persisted)
- Following stent removal diameter of stricture increased from 3.5 mm to 5.8 mm
- After 19.8 month f/u 9 no longer had chronic pain, none required surgery

Glacino C, Endoscopy 2012;44:874-877
Celiac Plexus Block in CP

- Prospective study from Gress suggesting benefit based on decreased pain score in 55%
- Benefit generally of short duration persisting beyond 12 weeks in 26% of patients
- Steroid with anesthetic, not neurolysis

Gress F, Am J Gastroenterol 2001;96:409-416

Disconnected Duct Syndrome (DDS)

- Generally follows an episode of acute necrotizing pancreatitis resulting in a completely transected pancreatic duct not communicating with functional upstream pancreatic tissue
Rendezvous techniques to manage DDS

- Report on 15 patients with DDS and external pancreatic fistulas treated with combined endoscopic and percutaneous techniques at expert center with avoidance of surgery
- Median number of procedures was 1, with median procedure time of 65 Minutes

Irani S. GIE 2012;76:586-593

Pancreatic Cysts

- Not all pancreatic cysts are cystic neoplasms
  - Up to 80%-90% are pseudocysts
  - Approximately 10% are cystic pancreatic tumors
  - Other cysts account for the remainder of cysts seen within the pancreas (e.g., retention cysts, duplication cysts, parasitic cysts, etc)
- Cystic tumors account for only 1% of primary pancreatic neoplasms
- Increasingly recognized due to widespread use of high-resolution imaging of the chest and abdomen
## Cyst Fluid Evaluation

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<th>Amylase</th>
<th>Cytology</th>
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<td>High</td>
<td>Histiocytes</td>
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<td>Low</td>
<td>Low</td>
<td>Neg</td>
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<td>Low</td>
<td>Columnar Mucinous Cells</td>
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<tr>
<td>IPMN</td>
<td>High</td>
<td>High</td>
<td>Columnar Mucinous Cells</td>
</tr>
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## Pseudocyst

- A collection of pancreatic juice enclosed by a non-epithelialized wall
- Requires ≥4 weeks to form
- Contain little or no solid debris
- May be acute or chronic
Is it a Pseudocyst?

- Is there a definite history of acute or chronic pancreatitis?
- If recent acute pancreatitis, was it severe?
- Is there a previous imaging study (CT)?
Pseudocyst Drainage: EUS

Pancreatic Cyst

- 58 yo wm non drinker with presumed gallstone pancreatitis 3 months earlier with CT documented development of symptomatic pancreatic pseudocyst
Pig tailed stents

Pseudocysts: When to intervene

- Symptom driven
  - pain
  - compression - GOO
  - ascites/effusion
- Infection
- Progressive enlargement
- NOT size alone
Endoscopic necrosectomy

Necrosectomy
Overview Of Endoscopic Management

- Endoscopy plays a critical role in the evaluation and management of pancreatic disorders
- Provides symptom relief in chronic pancreatitis
- Differentiation and management of cystic lesions
- Increasing therapeutic applications are being explored with huge potential for significant impacts on patient care