Gallstone Pancreatitis: An Evidence-Based Approach

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Tuesday, March 27, 2012

Gallstone Pancreatitis: Questions

1. What is the incidence of finding CBDS in GSP?
2. Can the course of acute GSP be altered by treating CBDS?
3. What is the best timing for LC as definitive treatment after resolution of GSP?
4. In resolving, uncomplicated pancreatitis, what is the appropriate way to detect and manage potential CBDS?

Gallstone Pancreatitis: Introduction

- Literature is difficult to interpret because of large series with heterogeneous populations
- Examine the evidence to address specific questions commonly encountered in a general surgical practice.

Gallstone Pancreatitis: Epidemiology

- Incidence
  - Acute pancreatitis 4.8 - 73.4 cases per 100,000 / year
    - Scotland: 24 cases per 100,000
    - Finland: 73 cases per 100,000
  - Gallstone pancreatitis: 35-57% of all cases
- Mortality
  - Overall for hospitalized pts with severe acute pancreatitis: 10%
GS Pancreatitis: Pathogenesis

- Eugene Opie, 1901:
  - Mechanism for pancreatitis is the gallstone
  - Post-mortem dissection of bile ducts in pancreatitis pts –
    found a GS impacted in the ampulla of Vater in a pt who died of pancreatitis – now recognized that this is an extremely rare occurrence
  - “Common channel bile reflux theory”
  - Opie E. Johns Hopkins Hosp Bull 1901; 121: 182

The causal relationship fell into question when stones in the CBD were frequently NOT found.

GS Pancreatitis: CBDs Pathogenesis

- Juan Miguel Acosta, 1974
  - Stool screened for gallstones within the first 10 days of presentation (done by surgical house staff)
    36 pts with GBS and acute pancreatitis (AP) VS.
    36 pts with GBS but no pancreatitis
  - GBS with AP: 34/36 (94.4%) had GS in stool
  - GBS without AP: 3/36 (8.3%) had GS in stool

  Found gallstones in 94% within the first 10 days of presentation

Gallstone Pancreatitis

- Kelly 1976
  - Again, screening stool for stones ...
  - Presence of GS in stool of pts with GSP was significantly more common than in pts with other forms of biliary symptoms.
  - Stones tended to appear in stool specimens as symptoms improved, suggesting that passage of the stone correlates with clinical improvement.

CBD Incidence in Gallstone Pancreatitis

- Abboud et al 1999
  - Metaanalysis
    - LR of CBD Stone with history of recent pancreatitis is 2.1
    - LR of CBD stone with history of hyperamylasemia is 1.5
CBD Incidence in Gallstone Pancreatitis

Summary

- Gallstones cause pancreatitis
- Stones frequently pass spontaneously
- Incidence of identifying calculi in the CBD decreases with time from onset of symptoms
- Clearance of stones from CBD (& subsequent finding in stool) correlates with relief of symptoms & resolution of GSP

Gallstone Pancreatitis

Treatment Options: Medical

- General conservative treatment: Bowel rest (NPO status), IVF, narcotic meds
- ± NGT suction - 4 prospective randomized trials showed no difference in outcome compared to no NGT – only use if ileus.
  - Levant. JAMA 1974; 229:51
  - Sarr. Surgery 1986; 100: 500

Gallstone Pancreatitis

Treatment Options: Medical

- No benefit from atropine or glucagon
- H2 receptor antagonist or PPI - no benefit

- Somatostatin & Octreotide - no benefit (but does have a role in fistulae)
  - D’amico. Hepatol Gastroenterol 1990; 37: 32
  - Gjorup. Surg Gynecol Obstet 1992; 175: 397

- Platelet activating factor inhibitors (Lexipafant) – no benefit
- Protease inhibitors
  - Aprotinin - no benefit
  - Gabexate mesylate - no benefit
    - Buchler. Gastroenterology 1993; 104: 1765
    - Valderama. Digestion 1992; 51: 65
  - FFP - no benefit
Gallstone Pancreatitis

Treatment Options: Medical

- TPN
  - In mild pancreatitis: no benefit
  - In severe pancreatitis: showed benefit
    - reduced complications (24% vs 96%)
    - reduced mortality (13% vs 38%)

- Total Enteral Nutrition (TEN)
  - Enteral feeds should be post ligament of Treitz (not gastric or duodenal feeding)
  - GIP / VIP / somatostatin stimulation
    - suppresses pancreatic activity while giving nutritional benefit
  - Advantages:
    - reduced cost compared to TPN or PPN
    - no associated risk of catheter line sepsis
    - prevents gut atrophy and bacterial translocation and infection
  - Disadvantages:
    - risk of proximal migration of the tube tip into the duodenum or stomach
    - patient refusal due to discomfort

Prophylactic Antibiotics

  - Imipenem n=41 vs no antibiotic n=33
  - Significant reduction in pancreatic infection
    - 12% vs 30%
    - *No change in mortality*
  - Bassi. *Gastroenterology* 1998; 115: 1513
- Overall: consider for use in severe pancreatitis!

Gallstone Pancreatitis

- Does removing CBD calculi provide benefit for acute GSP with improvement in course / resolution of inflammation?
Gallstone Pancreatitis

CBDS treatment – open surgery

Kelly 1982
- Pre-ERCP Era – open surgery
- Early treatment (<48h) had a higher mortality rate than late treatment (where incidence of CBD stones less)

Risk of laparotomy outweighed the benefit of removing the CBD stone.

- In the ERCP Era, the issue was revisited because of the perceived lower risk of the procedure.

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CBDS treatment?

Kelly et al
- Randomized controlled trial
- Ranson's score > 3: higher mortality if submitted to pancreatic surgery early in the clinical course - prior to resolution of pancreatitis

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Severity of Disease

Neoptolomos et al
- Statistically significant decrease in LOS for patients with severe pancreatitis only who were offered urgent ERCP + ES, if a stone was found and removed
- Trend for lower incidence of complications and mortality in the severe group who underwent urgent intervention.
- When the patients with a biliary tract indication for ERCP are removed, there is no significant difference between early and late treatment.
- Also demonstrated that there is no increased risk of complications from the ERCP itself.

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CBD Stones

Fan et al.
- Also found a non-significant trend of decreased mortality in severe pancreatitis for patients who had urgent intervention.
- When gallstone pancreatitis subgroup is analyzed, the only benefit is seen in patients with a biliary tract indication for ERCP.
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CBD Stones

- Folsch et al
  - 238 Patients with no biliary obstruction randomized to early ERCP (126) or later ERCP if biliary symptoms presented (112)
    - 58 patients in early group had a stone present, which was removed
    - 22 patients in observation group developed a biliary indication for ERCP → 13 had CBD stone
  - Early group had more respiratory failure (p<0.03)
  - Overall mortality within three months was 11% in the early group, 6% in the observation group (NSS)
  - A policy of early ERCP / ES does not benefit patients with acute pancreatitis without biliary indication
  - Did not stratify mild vs. severe pancreatitis

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CBD Stones

- Acosta and Pelligrini
  - JACS, August 1997
  - Experimental and clinical evidence that duration of stone impaction correlates with the severity of pancreatitis
  - Major complications of pancreatitis were rare if the stone passed in <48 hours

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CBD Stones

- Borie et al
  - Systematic review
  - Surgical Endoscopy Aug 2003
  - When biliary indications are excluded, the complication rates are no different with or without ERCP
  - There is no evidence to support ES in severe pancreatitis if calculi are not present

Gallstone Pancreatitis

CBD Stone Treatment

- The literature is confusing because of heterogeneous populations with differing indications for ERCP
- Without concern for CBDs, there is NO proof the early ERCP/ES improves the course of pancreatitis in a stable patient
- Probable benefit in pts with severe pancreatitis who are deteriorating
No studies relating to patients with pancreatitis alone.

Mickley and Reisman
- In patients with known or clinically suspected CBD stones, clinical symptoms develop in 100% patients in 5 years.

Mills et al.
- Review of 8 series
  - Average incidence of CBDS = 2.5%
  - In pts without IOC, 0.03 to 0.8% will present later with symptomatic stones
- Rec: always to investigate (IOC) and treat potential CBD stones in GSP patients as early as possible following resolution of pancreatitis.

In resolving, uncomplicated pancreatitis, what is the most appropriate management of suspected CBD stones?

There are no studies specific to the gallstone pancreatitis population
- Extrapolate from the general CBD stone literature
- Debate: pre-op ERCP vs. planned IOC, and intraop or postop stone removal by various methods
Managing Potential CBD Stones

- **Open Surgery Era Evidence**
- *Voluminous literature*
- Four randomized trials
  - All favoured one stage OC/IOC/OCBDE over pre op ERCP and OC
  - Neoptolemos and Carr-Loke
    - 55 preop ERCP 3.6% mortality
    - 59 one stage surgery = 1.7% mortality

- **Laparoscopic Era Evidence**
  - Sees et al
    - LC/OCBDE shorter LOS than preop ERCP/LC → ERCP pancreatitis
  - Cuschieri et al
    - European Collaborative Trial
      - LC/IOC +/- LCBDE superior to pre op ERCP/LC
    - Also Rhodes et al., Sourakis et al.

- **T se, Barkun et al**
  - Decision analysis model
    - High risk = Pre op ERCP
      - Criteria: (>80% likelihood CBD stone)
    - Medium risk (includes history of pancreatitis) = LC/IOC
      - Stone removal if identified (via LCBDE, post op ERCP or OCBDE)
    - Low risk = no imaging of duct
  - Also: Urbach et al (2001)
Showed that ERCP/S+LC and LC+LCBDE were both:
- highly effective in detecting and removing common bile duct stones
- equivalent in overall cost and patient acceptance
- Overall duration of hospitalization was shorter for LC+LCBDE.
- A single surgical procedure for common bile duct stone disease is feasible, cost-effective, and ultimately should be made available for most patients.

Timing for LC after GSP
- What is the best timing for LC as definitive treatment after an episode of gallstone pancreatitis?

Timing of LC after GSP
- Osbourne / Tandelli
  - BJS, ~1960
  - Recommended OC prior to hospital discharge because early risk of recurrent pancreatitis
- Kelly 1988
  - RCT OC <= 3 days after onset vs. >= 3 days but before discharge
  - Higher mortality (3.3% vs. 0%) and morbidity (48 vs. 11.3%) with early surgery
Best Timing for LC after GSP

- Uhl et al.
  - Surgical Endoscopy 1999
  - Reviewed 5 case series:
    - Recurrent pancreatitis in 29 – 63% if discharged without cholecystectomy

Barkun et al. 1994
- 35 patients pre-laparoscopic era
  - Average time to surgery (OC) 9.9 days
  - Complications while waiting for surgery = 0
- 58 patients - early laparoscopic era – wait for surgery
  - Average time to surgery (LC) 39.3 days
  - Complications while waiting:
    - 1x cholangitis
    - 2x acute cholecystitis
    - 3x recurrent pancreatitis
- Recommended LC during index hospitalization, as early as possible after stabilization and resolution of GSP

Surgery: Risk of Conversion

- Borie et al.
  - Review of 5 LC case series
  - Early operation and >3 Ranson’s criteria were associated with increased conversion rate

Pelligrini
- AJS (vol 165) -- 1994
- NIH Consensus conference
- Optimum time 5-6 days following onset of pancreatitis
**Best Timing for LC after GSP**

- Discharge without cholecystectomy results in a significant rate of complications, including recurrent GSP, while waiting.
- LC on the same admission does not result in a significant increased conversion rate if performed once the pancreatitis has resolved.
- Rec: LC with IOC should be carried out during index hospitalization just prior to d/c as soon as the pancreatitis has resolved.

**Gallstone Pancreatitis Summary**

- Gallstones cause pancreatitis, & frequently pass spontaneously.
- Incidence of identifying CBD calculi decreases with time from onset of symptoms.
- Spontaneous clearance of stones from CBD correlates with relief of symptoms.

**Gallstone Pancreatitis Summary**

- If there is no suspicion for biliary cause, early ERCP/ES does not improve the course of pancreatitis in a stable patient.
- There may be benefit to ERCP in pts with severe pancreatitis who are deteriorating.

**Gallstone Pancreatitis Summary**

- History of pancreatitis has a positive predictive value of between 2 - 8% for presence of CBDS.
- No evidence to support pre-operative ERCP in patients with a history of pancreatitis.
- High likelihood that this CBD stone will cause future morbidity.
Gallstone Pancreatitis Summary

- LC with IOC should be done during IH for GSP once resolved.
- Discharge without LC results in a significant rate of complications while waiting for OP LC.
- LC during index hospitalization does not result in a significant increased conversion rate if performed once inflammatory process has resolved.

Gallstone Pancreatitis Summary

- LC is better protection than ES.
- ES is viable option in patients in whom the surgical risk outweighs the increased protection of LC.

Gallstone Pancreatitis Summary

- We should investigate and treat potential CBD stones in GSP whenever possible after resolution of pancreatitis.
- IOC should be done during IHLC.
- Decision for LCBDE or post op ERCP (or OCBDE) if CBDS found will depend on local expertise.
- All general surgeons should learn LCBDE to offer pts optimal care.

Mahalo