بسم الله الرحمن الرحيم

Management of Gallstone Pancreatitis A Review

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- Introduction and importance
- Discussion and Observations
  - Pathophysiology
  - Assessment and diagnosis
  - Treatment
  - Identification and Management of Suspected CBD stones
  - Prognosis
- Conclusions
- References

Introduction and importance

- Prevalence of gallstone: 10-15% in adults in developed countries; increasing.
- Incidence of Acute Pancreatitis in US: 40 per 100,000
- 50% of cases attributable to GSP (Gallstone Pancreatitis)
- 80% of Acute Pancreatitis are mild and self-limited.
- Moderately severe and severe AP: 30% mortality and sequelae: pseudocyst, pancreatic insufficiency, multiorgan failure, and necrosis, requiring interventions.

Discussion and Observations

- Pathophysiology

Early 1900, Opie, 2 hypotheses:

1. direct obstruction of pancreatic duct and impaired pancreatic outflow >>> Acute Pancreatitis

2. common channel theory: obstruction at the ampulla of Vater >>> biliary reflux into the pancreatic duct >>> Acute Pancreatitis

Discussion and Observations

- Pathophysiology

Subsequent researchers:

Impairment of flow from the pancreatic duct
(NOT biliary reflux) >>> AP

Acosta and Ledesma, 1974: Passage of gallstones in the stool of patients with Gallstone Pancreatitis >>> symptomatic and biochemical improvement >>>> pancreatic duct obstruction is transient.

Discussion and Observations

- Pathophysiology

More recent studies:

Small gallstones (<5mm), a large cystic duct (>5mm), and multiple gallstones (>20) >>> higher risk of gallstone pancreatitis with transient obstruction of common bile duct.

Discussion and Observations

- Pathophysiology

- Gallstone is small enough to pass cystic duct, yet large enough to obstruct the CBD, then because of its relatively small size, obstruction is transient.

- Transient obstruction >>> low prevalence of concomitant cholangitis and obstructive jaundice >>> rarely ERCP is indicated and most patients will likely experience recurrent episodes of pancreatitis without prompt cholecystectomy.

Discussion and Observations

- Assessment and Diagnosis

Diagnosis:

1) Abdominal Pain +

2) Elevated pancreatic enzyme levels (lipase or amylase) greater than 3 times the upper limit of normal +

3) identified gallstones or gallbladder sludge (microlithiasis)

Discussion and Observations

- Assessment and Diagnosis

Determine Pancreatitis severity by Scoring systems.

Table 1. Common Scoring Systems to Assess Severity of Gallstone Pancreatitis

Scoring system	Comments	Variables included
Modified Ranson criteria	Predicts risk of mortality based on initial and 48-h laboratory values. Requires 48 h for full assessment.	Age; WBC count; glucose, AST, LDH, and calcium levels; change in hematocrit; change in BUN level; base deficit; and fluid sequestration
Acute Physiologic Assessment and Chronic Health Evaluation II	Estimates disease severity for patients in the intensive care unit. Includes age, chronic disease status, and 12 acute physiologic barriers, making it cumbersome to calculate.	Age; chronic health status; WBC count; temperature; heart rate; respiratory rate; mean arterial pressure; pH, sodium, potassium, creatinine, hematocrit, and bicarbonate levels; Glasgow Coma Scale; and FiO_2
Bedside Index for Severity in Acute Pancreatitis	Predicts risk of mortality using 5 variables from the first 24 h of hospitalization.	Age, BUN level, mental status, SIRS criteria, and presence of pleural effusion
Revised Atlanta classification	Grades acute pancreatitis as mild, moderately severe, or severe based on the presence of organ failure and local or systemic complications.	Presence of organ failure, local and/or systemic complications
CT severity index	Grades severity based on extent of pancreatic inflammation and/or necrosis on CT.	CT findings of pancreatic inflammation, fluid collections, and/or necrosis
Glasgow-Imrie criteria	Predicts severity of pancreatitis based on 8 variables at 48 h after admission. Requires 48 h for full assessment.	Age; WBC count; $Pa0_2$; and calcium, BUN, LDH, albumin, and glucose levels

Abbreviations: AST, aspartate aminotransferase; BUN, blood urea nitrogen; CT, computed tomography; FiO_2, fraction of inspired oxygen; LDH, lactate dehydrogenase; $Pa0_2$, arterial oxygen pressure; SIRS, systemic inflammatory response syndrome; WBC, white blood cell.

Discussion and Observations

- Assessment and Diagnosis

- No consensus on which scoring systems is best.
- BISAP and revised Atlanta classification can be used within 24 hours to determine if gallstone pancreatitis is mild.
- APACHE II and Ranson criteria: accurate but burdensome to calculate.
- Regardless of system used, determine severity.

Discussion and Observations

- Treatment: Aggressive or Moderate fluid resuscitation

- Aggressive fluid resuscitation: 20 cc/kg followed by 3 cc/kg/hour
- Moderate fluid resuscitation: 10cc/kg followed by 1.5cc/kg/hour

2023 meta-analysis: aggressive resuscitation association with increased risk of fluid-related complications.

Promising strategy: Goal directed/Moderate fluid therapy

Discussion and Observations

- Treatment: Antibiotics

- The most recent and generally better designed studies do not support the use of prophylactic antibiotics to reduce the frequency of pancreatic infectious complications, surgical intervention, and death.

Discussion and Observations

- Treatment: PO or NPO?

- Its no longer acceptable to “rest the pancreas” by avoiding enteral nutrition.
- Nutritional support can be started 4-6 hours after admission after fluid resuscitation.
- Early initiation of PO nutrition (within 24 hours of admission) is not superior to delaying an oral diet until 72 hours.

Discussion and Observations

- Treatment: PO or NPO?

- If not tolerated over 48 to 72 hours, Nasogastric tube feeding can be started and increased in step-wise fashion over 2-3 days.
- The tube can be advanced to jejunum, by endoscopy or fluoroscopy, if there is feeding intolerance.

Discussion and Observations

- Treatment: PO or NPO?

- Parenteral nutrition: more expensive, riskier, not more effective than enteral nutrition, and should *only* be offered if the patient's calculated nutritional requirements cannot be achieved by the enteral route.

Discussion and Observations

- Timing of Cholecystectomy for mild GSP

- Timing of cholecystectomy for acute GSP = Balancing the risk of intraoperative complications with the risk of recurrence.
- Mild pancreatitis >>> risk of recurrence is more than intraoperative complications.

Discussion and Observations

- Timing of Cholecystectomy for mild GSP

- PONCHO trial: multicenter RCT, compared same-admission vs interval cholecystectomy >>> same-admission cholecystectomy reduced mortality or readmission for gallstone-related complications.
- While trials suggest that patients with mild pancreatitis can undergo early (within 24-28 hours of admission) cholecystectomy, the exact timing remains unresolved.

Discussion and Observations

- Timing of Cholecystectomy for mild GSP

- While trials suggest that patients with mild pancreatitis can undergo early (within 24-28 hours of admission) cholecystectomy, the exact timing remains unresolved.
- Concern surrounding the accuracy of severity determination before 12-24 hours >>> doubts in widespread consensus about early cholecystectomy.

Discussion and Observations

- Timing of Cholecystectomy for mild GSP

Table 2. Prospective RCTs and Inclusion Criteria for EC

Prospective RCT	Inclusion criteria	Timing of EC	Outcomes in mild pancreatitis
Kelly and Wagner,[35] 1988	Ranson criteria: ≤3 (mild pancreatitis) Ranson criteria: >3 (severe pancreatitis)	Within 48 h of admission	EC had minimal effect on outcomes in patients with ≤3 Ranson criteria.
Aboulian et al,[36] 2010	Ranson criteria: ≤3 Absence of acute cholangitis and significant hypovolemia Low suspicion for retained CBD stones	Within 48 h of admission	EC resulted in decreased length of stay with no effects on technical difficulty or perioperative complication rates.
Mueck et al,[38] 2019	BISAP score of 0-2 No evidence of organ failure or local or systemic complications	Within 24 h of admission	EC was associated with reduced rates of ERCP; decreased time to surgery; decreased 30-d length of stay, including readmission; and no difference in raw rates of complications.
Riquelme et al,[37] 2020	Mild pancreatitis according to revised Atlanta classification Meeting no SIRS criteria	Within 48-72 h of admission	EC was associated with reduced length of stay and no difference in perioperative complications.

Abbreviations: BISAP, Bedside Index for Severity in Acute Pancreatitis; CBD, common bile duct; EC, early cholecystectomy; ERCP, endoscopic retrograde cholangiopancreatography; RCT, randomized clinical trial; SIRS, systemic inflammatory response syndrome.

Discussion and Observations

- Timing of Cholecystectomy for Moderately Severe or Severe GSP

  - Risk of intraoperative complications is more than recurrency of biliary events within 8-10 weeks of discharge >>> Cholecystectomy in moderately severe and severe pancreatitis should be delayed.
  - Further studies needed to determine optimal timing of surgery.

Discussion and Observations

- Timing of Cholecystectomy for Moderately Severe or Severe GSP

Table 3. EC vs DC for Moderately Severe or Severe Pancreatitis

Study	Inclusion criteria	Definition of EC	Outcomes in moderate or severe pancreatitis
Kelly and Wagner,[35] 1988	Ranson criteria: >3	<48 h After admission	EC was associated with increase in rates of morbidity and mortality.
Tang et al,[43] 1995	Ranson criteria: ≥3	<1 wk After admission	EC was associated with increase in operative complications, rate of conversion, and longer postoperative stays.
Nealon et al,[44] 2004	Ranson criteria: >5 Presence of peripancreatic fluid collections on CT	Before resolution of pseudocyst or established persistence of pseudocyst at 6 wk	EC was associated with increased rates of sepsis, infected necrosis, morbidity, reoperation, readmission, and prolonged hospital length of stay.
Hallensleben et al,[45] 2022	Severe and moderately severe acute biliary pancreatitis according to the revised Atlanta classification CT severity index score ≥3	<10 wk After discharge	Risk of complications of cholecystectomy (including infected necrosis) did not decrease significantly over time.
Di Martino et al,[46] 2023	Severe and moderately severe acute biliary pancreatitis according to the revised Atlanta classification	≤14 d After admission	EC was associated with higher mortality, morbidity, and infections compared with DC.

Abbreviations: CT, computed tomography; DC, delayed cholecystectomy; EC, early cholecystectomy.

Discussion and Observations

- Identification and management of Suspected CBD stones

- Severity of pancreatitis is associated with length of ampulla obstruction.
- Urgent ERCP is indicated for acute GSP with concomitant cholangitis or obstructive jaundice. (total Bilirubin>4mg/dl)

Discussion and Observations

- Identification and management of Suspected CBD stones

- Any increase in amylase, lipase, total bilirubin, ALK-P, AST, ALT between 1 to 2 days of hospitalization, with Positive Predictive value of 31% and Negative predictive value of 92% for persistent CBD stones.
- Chang et al: total bilirubin>1.35 mg/dl on day 2 has sensitivity of 90.5% and specificity of 63% (best predictor of persistent CBD stone)

Discussion and Observations

- Identification and management of Suspected CBD stones

- Chang et al randomized patients without cholangitis or obstructive jaundice with at least 1 finding suspicious of persistent CBD stone in 2 groups:

1. Preoperative ERCP
2. Intraoperative cholangiography (IOC) followed by selective postoperative ERCP if needed.

Group 2: shorter hospital stay, decreased costs, no increase in combined treatment failure rate, and reduction in ERCP use.

Discussion and Observations

- Identification and management of Suspected CBD stones

- In addition to lab data, MRCP is useful for persistent CBD stone evaluation. (Sen=92% Spec=97%)
- However, monitoring lab data and MRCP will delay treatment.

Discussion and Observations

- Identification and management of Suspected CBD stones

One multicenter RCT compared 2 group of patients:

1. MRCP followed by ERCP if needed
2. IOC followed by ERCP if needed

- Result: group 2 was associated with shorter length of stay, higher stone detection rate, and no differences between costs and complications.

Discussion and Observations

- Identification and management of Suspected CBD stones

- Thus, preoperative MRCP may *not* be necessary to evaluate for CBD stone if cholangitis or biliary obstruction has been ruled out.

Discussion and Observations

- Intraoperative Evaluation and Management of Suspected CBD Stones

- Instead of preop MRCP or ERCP, IOC can determine CBD stone.
- If CBD stone is confirmed by IOC, several options exist:

1. Laparoscopic CBD exploration (trans-cystic or trans-choledochal)
2. Intraoperative ERCP
3. Postoperative ERCP

- Laparoscopic exploration is associated with decreased hospital length of stay, with no difference in efficacy, morbidity, or mortality.

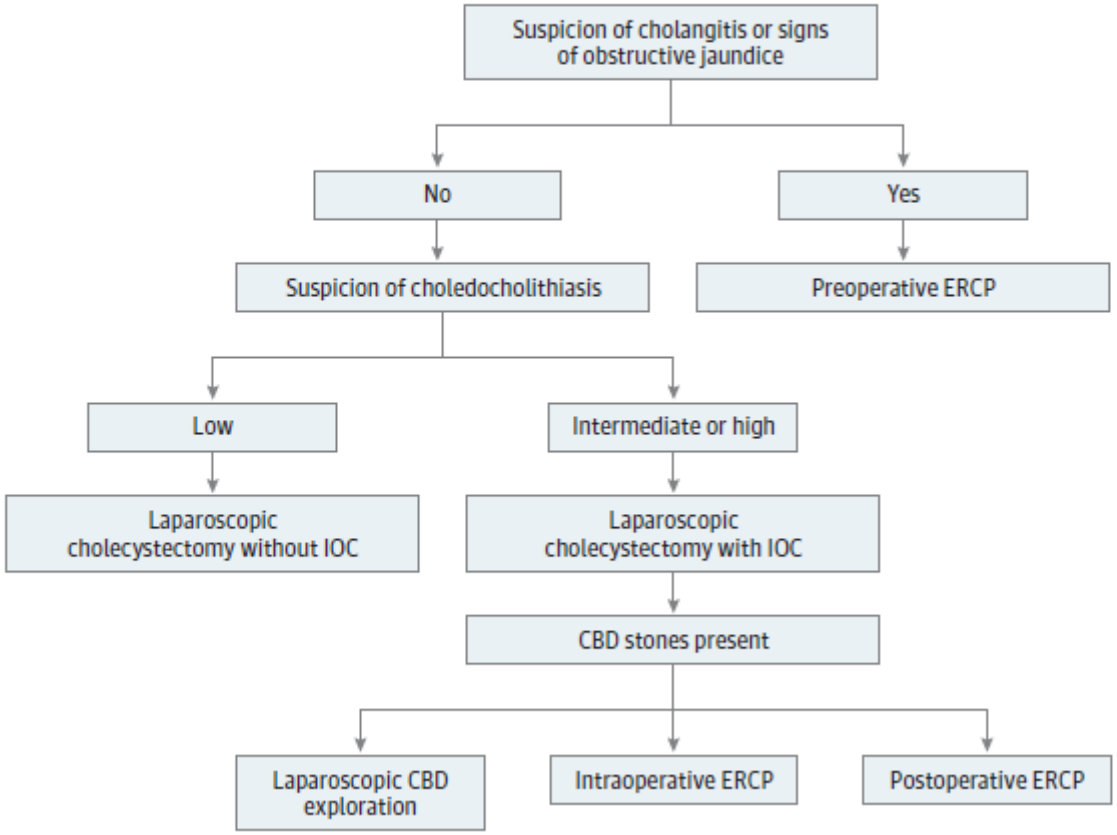
Discussion and Observations

- Intraoperative Evaluation and Management of Suspected CBD Stones

- However, several RCTs and a systematic review of RCTs have questioned the routine use of IOC.
- Johnson and Walsh followed 300 patients with GSP for almost 4 years: no difference in the rate of recurrent pancreatitis or biliary complications between those who underwent IOC and those who did not.
- Role of routine IOC in patients with GSP and normalizing bilirubin level remains unclear.

Discussion and Observations

Figure. Evaluation and Management of Retained Gallstones in Gallstone Pancreatitis



CBD indicates common bile duct; ERCP, endoscopic retrograde cholangiopancreatography; and IOC, intraoperative cholangiography.

Discussion and Observations

- Prognosis: Mild GSP

- most patients have resolution of symptoms
- Early cholecystectomy is well tolerated and associated with fewer long-term complications and decreased recurrence.

Discussion and Observations

- Prognosis: Moderately severe or severe GSP

- Significantly increased morbidity and mortality, with sequelae: pseudocysts, pancreatic insufficiency, multiorgan failure, and necrosis.

Discussion and Observations

- Conclusions

- Gallstone pancreatitis is a clinical challenge, with treatment dependent on disease severity, which can be difficult to assess and predict.
- *Early cholecystectomy for mild GSP is more important than anything else.*
- Further research is needed to determine best management practices for moderately severe and severe pancreatitis.

Discussion and Observations

- 10 key points and recommendations for gallstone pancreatitis

Box. Ten Key Points and Recommendations for Gallstone Pancreatitis

Gallstone pancreatitis is associated with gallstones that are small and numerous in quantity. This lends itself to transient obstruction of the ampulla, as most stones pass in the bowel.[8-11]

There is a tendency for recurrent episodes of pancreatitis without prompt cholecystectomy.[14]

The small stone size and the transient nature of the obstruction make associated cholangitis rare.[12-14] Thus, ERCP is rarely needed in the absence of persistent biliary obstruction.[15,16]

There is value in assessing the severity of pancreatitis at admission to help evaluate prognosis and guide management, including the timing of cholecystectomy. Severe pancreatitis generally declares itself within 24-48 hours. Given that no scoring system has shown consistent superiority or inferiority, the choice of which to use can be based on clinician preference.[17-22]

Aggressive fluid hydration is unnecessary and may be detrimental.[23-25]

In patients with mild pancreatitis, cholecystectomy should be performed during the index hospitalization.[27-30] Several randomized clinical trials support cholecystectomy within 48 hours of admission.[35-37,39-42] Prior to proceeding, a reevaluation of the patient 12 hours after admission may be of benefit.[38]

Discussion and Observations

- 10 key points and recommendations for gallstone pancreatitis

For patients with severe pancreatitis, cholecystectomy should be delayed, although the length of delay is uncertain.[35,43-48] For those with moderately severe pancreatitis, further studies are needed to determine optimal timing of surgery.

Early preoperative ERCP is indicated when concomitant cholangitis is suspected or in the presence of obstructive jaundice (total bilirubin level, >4 mg/dL). In the absence of these indications, the benefit of preoperative ERCP is uncertain.[16,52-55]

Although persisting CBD stones can be identified by trending laboratory results and/or MRCP, using these strategies may delay definitive care and increase the use of unnecessary preoperative ERCP.[56,57,62] Performing an IOC instead may shorten hospital stay.[58,61]

Further studies are needed to determine whether routine IOC is necessary in patients with mild gallstone pancreatitis and normalizing bilirubin level.[70-74]

Abbreviations: CBD, common bile duct; ERCP, endoscopic retrograde cholangiopancreatography; IOC, intraoperative cholangiography; MRCP, magnetic resonance cholangiopancreatography.

SI conversion: To convert bilirubin to micromoles per liter, multiply by 17.104.

Discussion and Observations

- References

1. Andersen, Dana K, et al. *Schwartz's Principles of Surgery*. 11th ed., New York, Mcgraw-Hill, 2019.
2. McDermott J, Kao LS, Keeley JA, Nahmias J, de Virgilio C. Management of Gallstone Pancreatitis: A Review. JAMA Surg. 2024 Jul 1;159(7):818-825. doi: 10.1001/jamasurg.2023.8111. PMID: 38691369.

با سپاس از توجه شما