Acute Pancreatitis: Improving the Outcomes

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Disclosures

• Royalty for chapters in UpToDate – 2006

• Consultant for Cacimedica, Breach Candy

• Full time or near full time clinician for over 32 years

• Started treating acute pancreatitis for as many years
Important Outcomes

- Death
- Persistent organ failure (> 48 hrs)
- Intensive care need and length of stay
- Length of stay
- Interventions for necrosis
- Vascular and other complications
- Recurrences
- Endocrine, exocrine insufficiency

What Is the Big Deal About Acute Pancreatitis?

- 275000 discharges of AP in 2009. Commonest GI hospital discharge diagnosis
- 30% increase from 2000 but mortality 1%
- 2.7 billion $ in health care costs in 2009

Gastroenterology 2012;143:1179
Yadav D, Vege SS, Chari ST. GI Epidemiology 2014:306
Limitations of Atlanta Classification

- Many!
  
  *(Vege SS, Chari ST. Time to revisit Atlanta classification. Gastroenterology 2005;1133-5)*

- Led to a symposium in DDW 2006 at LA

- Resulted in International working group to revise the classification

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Moderately Severe AP; A New Category.
*(Vege SS et al. AJG 2009;104:710)*

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<th>Structural Alterations</th>
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<th>Moderate</th>
<th>Severe</th>
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<td>Local complications</td>
<td>Interstitial or Necrotizing</td>
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*Talukdar R, Clemens M, Vege SS. Validation of MSAP Pancreas 2012;41:306*
Phases of Acute Pancreatitis

• **First phase** - 1-2 weeks (Systemic inflammation dominant feature. Responsible for deaths and organ failure. No correlation with morphology at this stage)

• **Second phase** – After 1-2 weeks. Morphology of pancreatic and peri-pancreatic areas determines morbidity. Infection more common
New Nomenclature of Pancreatic Fluid Collections

Acute necrotic collections (Peri ± pancreatic necrosis) 4 – 6 wks Walled-off necrosis

Acute peri-pancreatic fluid collections (Resolve mostly) 4 - 6 wks Pseudocyst (very rare)

Acute Peripancreatic Fluid Collections

Acute Fluid Collection
Psuedocyst with Wall and Outside the Pancreas

Acute Necrotic Collection
Pancreatic and Peri-pancreatic Necrosis
Walled-off Pancreatic Necrosis (WON)

Sterile vs Infected Necrosis

- Sterile does not need intervention usually
- Presence of gas bubbles diagnostic of infection
- FNA not necessary, clinical and imaging features of infection sufficient. If no response intervention anyway!
- FNA may be needed in patients without clear clinical picture of sepsis but not improving over time
When, why and how do patients with acute pancreatitis die? A large experience of 910 direct (not transfer), consecutive admissions in recent years. (Yang A, Vege SS. Abstract DDW 2014)

• 24% deaths in 72 hrs, 80% deaths in 2 weeks
• Most patients with AP die due to persistent organ failure in 2 weeks
• Subsequent deaths due to infected necrosis rare
• To lessen mortality need to improve persistent OF early on. Find a drug!!

ACG Practice Guidelines for AP

IAP/APA Evidence-based Guidelines Pancreatology 2013;13:e1

Up-To-Date Vege SS

Ask Mayo Expert Vege SS
1. Diagnosis of AP

- Two of the following 3 must be present:
  
  1. Abdominal pain consistent with AP
  2. Amylase or lipase $\geq 3$ times the ULN
  3. Imaging consistent with AP

Be aware of at least 5 lipase systems with ULN ranging from 50 – 300 units!!

2. Role of Imaging in AP

- CT reserved for unclear diagnosis or no improvement in first 48 – 72 hrs. Not for all
- US indicated in all on day 1
- MRI, EUS rarely needed at presentation
**3. Identifying the Cause**

**Gallstones and Microlithiasis**

- Gallstones + alcohol >60% of cases
- ALT $\uparrow$ 3× UNL has >90% PPV for biliary cause
- 3-fold $\uparrow$ALT, no stones on US: Think of microlithiasis. Go for MRCP or EUS
- **But** if liver tests normal, cause of AP may be not gallstones

(Vege SS et al, Surgery 2012;151:199)
Acute Pancreatitis Due to Medications

- Only Badalov class 1 & 2 (positive challenge and consistent interval) need to be given importance
- Preferably started in the preceding 6 months
- One could never be very sure of a medication as the culprit; be on the lookout for other causes

Other Causes

- Be sure of TG as the cause only if > 1000 mg/dL
- Repeat TG and Ca after the attack subsides
- Don’t forget cancer in pts > 50 yrs. 2% of AP due to cancer, 2% of cancers present with AP
- AIP rare cause of AP
- Main duct and side branch IPMN
  
  (Venkatesh PG, Vege SS. J Clin Gastroenterol 2011;45:755)
- Younger pts with idiopathic AP – Genes!!
4. Current Status of Predictors of Severity

- Not superior to expert clinical judgment
- Positive predictive value ~50%
- High negative predictive value for mortality, but one can predict that any way!!
- SIRS as good as any
- Patient risk factors, SIRS, persistent SIRS and organ failure, BUN, hematocrit during Rx
- Urgent need for new predictors (ANN, machine learning tools and others)

Systemic Inflammatory Response Syndrome (SIRS) Score

- SIRS defined by \( \geq 2 \) of the following:
  - Pulse > 90 /min
  - Resp > 20 / min or PaCO2 < 32 mm Hg
  - Temp > 38 or < 36° C
  - WBC count > 12,000 or < 4,000 / mm3
Treatment

6. Intravenous Fluid Therapy

- Trikudanathan G, Navneethan U, Vege SS. Pancreas 2012;41:827
Intravenous Fluid Therapy

- 5-10 ml/kg/hr or 250-350 ml/hr depending on clinical status
- Lactated ringer may be preferred to normal saline (acidosis activates trpsinogen, makes acinar cells susceptible to necrosis)
- Compartment syndrome and more intubations with mortality recent concerns
- Not of benefit beyond 24 – 48 hrs

7. Failure to Recognize Acute Compartment Syndrome (ACS)

- Thought to be rare but recent reports 20-50% of AP (bladder pressure > 20 mm HG)
- Due to increase in aggressive iv hydration?
- Look at CT Round belly sign
  Enhancing bowel loops
- Monitor bladder pressures in those with CT findings and those with established SAP in ICU (intubated)
**Treatment of Acute Compartment Syndrome**

- Conservative mostly
- NG suction, less fluids, rectal tube
- Metoclopramide, sedation, neuromuscular blockade
- Intervention – percutaneous drainage of ascites, collections, rarely laparastomy
8. Prophylactic Antibiotics

• No role

• May have a role in subgroup of necrosis and persistent organ failure (Vege SS. UpToDate)

9. ERCP for Biliary Pancreatitis

• Urgent (≤24 hrs) only if cholangitis present

• In high risk patients w/o cholangitis – pre-ERCP MRCP or EUS to confirm CBD stones

• Elective before cholecystectomy
10. Oral Feeding in Acute Pancreatitis

- “Gut resting” passe. “Gut rousing” current concept
- If no significant ileus, vomiting, oral feeds as tolerated
- No need to wait for pain and enzymes to come down
- GI mucosa needs nutrition for integrity
- Can start with low fat solids

(4 RCTs and recent cohort study)

11. Nutritional Support in SAP – When and How

- Usually between 3-5 days, when diagnosis of SAP is secure
- Early (during the first day) is under study
- No TPN
- 3 RCTs – nasogastric and nasojejunal no difference
- RCT NG vs NPO in mild AP - ↓ opiates, ↑ gut function
Second Phase

- Infection – pancreatic, extra-pancreatic
- Intervention for collections
- Vascular and surrounding organ complications

Infection in AP

- More common after 1st week
- Pancreatic and peri-pancreatic – infected necrosis
- UTI, pulmonary, other
- Fungal infections in pancreas outcomes same as bacterial
  
  (Vege SS, et al. Amer J Gastroenterol 2009;104:2065)

- Prophylactic antifungals for those on abx not needed
  
  (Trikudanathan G, Vege SS. Amer J Gastroenterol 2011;106:1188)
Walled-off Necrosis (WON)

• ~15-20% of AP develop necrosis pancreatic and or peripancreatic
• 4-6 weeks later, they develop wall and become WON
• CT may misclassify them as “pseudocyst” if debris not seen
• May be sterile (70%) or infected

Interventions for Necrotizing Pancreatitis

Summary of a Multidisciplinary Consensus Conference

Martin L. Freeman, MD,* Jens Werner, MD; Hjalmar C. van Santvoort, MD, PhD,‡
Todd H. Baron, MD,§ Marc G. Besselink, MD, PhD,|| John A. Windsor, MD,^ Karen D. Horvath, MD,^ Electric vSonnenberg, MD,** Thomas L. Bollen, MD,†† Santhi Swaroop Vege, MD,§ and An International Multidisciplinary Panel of Speakers and Moderators‡‡

(Pancreas 2012;41:1176–1194)
11. Do Not Intervene Early!

- Preferably 4 weeks for a mature wall formation (less mortality, technically easier, less organ resection)

- Based on 1 RCT (surgery) and few good prospective studies (Strong rec)

- Emphasized in both recent guidelines (ACG, IAP/APA)

  - Am J Surg 1997;173:71,
  - Gastroenterology 2011;141:1254,
  - Arch Surg 2007;142:1194,
  - Arch Surg 2010;145:817

12. WON : Indications for Intervention

- ~60% conservative treatment
- Most infected necrosis patients
- Sterile necrosis if:
  - Gastroduodenal
  - Biliary
  - Colonic
    - “Persistently unwell”
  - Disconnected duct with collections
Options to Treat WON

- Percutaneous catheter drainage (PCD)
- Endoscopic transluminal drainage (ETD)
- Endoscopic transluminal necrosectomy (ETN)
- Sinus tract endoscopy (nephroscope or flex endoscope)
- Video assisted retroperitoneal debridement (VARD)
- Laparoscopic (retro, trans peritoneal, transgastric)
- Open necrosectomy (infrequent now)
- Medical (antibiotics)

13. WON : What Intervention?

- Open surgery very rare now (high mortality, morbidity, level 1 evidence)
- Small group with antibiotics ± PCD (stable infected necrosis)
- PCD commonest world wide and 40% don’t need any other modality
- ETD, ETN becoming more common
- Laparoscopy, while has advantages, not picked up
- Step-up favored (PCD or ETD) followed by VARD or ETN
- Hybrid methods (endoscopic and ercutaneous) may become the future
14. WON : Where Should Interventions Be Done?

- Necrotizing pancreatitis, specially if interventions required, needs **specialist center**
- **Specialist center** – High volume, multidisciplinary team (IR, ERCP, surgeon, gastroenterologist 24/7)
- **High volume** > 118/yr (Gastroenterology 2009;137:1995)

Vascular Complications of Acute Pancreatitis

- Necrosis and bleeding from duodenum, colon
- Thrombosis of splenic, portal and/or superior mesenteric veins
  
  Harris S, Vege SS. Pancreas 2013;42:1251

- Splenic artery pseudo-aneurysms with bleeding
15. Pseudoaneurysms

- Recognize in necrotizing pancreatitis
- Don’t wait for bleeding
- IR embolization after diagnosis
16. Splanchnic Venous Thrombosis

- Anti-coagulate if:
  - Acute during clinical course of necrosis
  - If extending into portal system with increasing liver tests
  - SMV extension
  - Incidental with collaterals no need for A/C

Pancreatic (Peri) Necrosis Consensus

- Try not to intervene till ~ 4 weeks
- Delay, drain and debride (minimally invasive route)
- Conservative treatment with ABX in selected group of stable patients with infected necrosis
- Minimally invasive intervention preferred to open surgery
- Know the available expertise at your center
- When in doubt, refer!
Future

• Better methods of prediction
• Quality metrics
• We need a drug
• Pentoxifylline? (Vege SS, et al RCT abstract Gastroenterology May 2013)
• Bigger trial currently awaiting funding by NIH