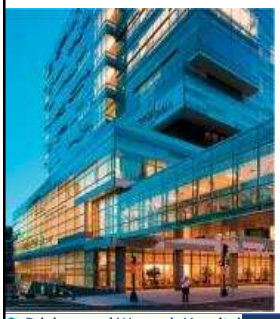
Practical Approaches to Pancreatobiliary Disease Management



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Disclosures

- Consultant for Boston Scientific, Fujifilm Medical, Fractyl

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Case 1

- 36yo female 12 weeks postpartum with mild intermittent RUQ pain since 3rd trimester who presented with severe RUQ pain.
  - Afebrile
  - ALT 742, AST 1073, T bili 2.9, Alk phos 150
  - WBC 9,000, normal lipase
  - US multiple gallstones, 6mm CBD, no intrahepatic duct dilation

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- ➢ Should pt undergo ERCP?

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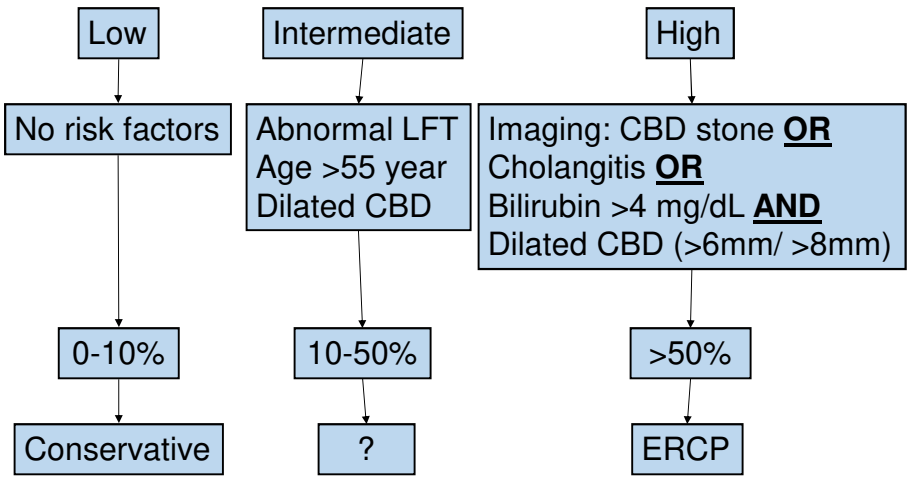
- Should pt undergo ERCP?
- What's the likelihood that the patient has a CBD stone?

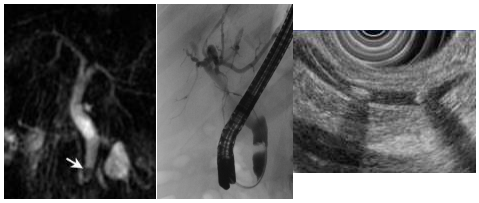
Risk of CBD Stone



Buxbaum et al. GIE 2019.

Imaging CBD Stone

Test	Sensitivity	Specificity	NPV
US	20-55%	83%	**56%**
Helical CT	40-85%	88-92%	**78%**
MRCP (no gadolinium)	85-91%	93%	**92%**
EUS	93%	96%	**96%**
ERCP	72-90%	99%	-



Approach to Intermediate Risk

EUS or MRCP or Lap CCY with IOC

Approach to Intermediate Risk

EUS or MRCP or Lap CCY with IOC

- **EUS and MRCP safer than ERCP**
- **46-60% more invasive tests avoided with EUS**
- **Limitations of MRCP:**
  - Lower sensitivity for small stones <6mm
  - 15-20% intrasphincteric CBD not seen on MRCP

Karakan et al. GIE 2009; Napoleon et al. Endoscopy 2011.

CBD Stones

- Labs: bilirubin || degree obstruction
  - Bilirubin usually 2-5, rarely >12
  - ALT/ AST can present in 1000s

Case 1

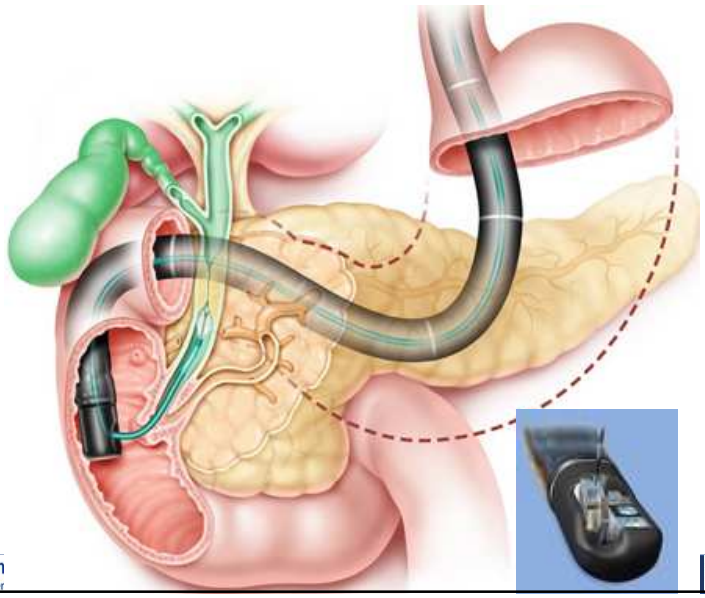
- 36yo female with RUQ pain, total bilirubin 2.9, gallstones, CBD 6mm and no intrahepatic biliary ductal dilation.
- Intermediate risk for CBD stone
- Best next step: EUS or MRCP
- MRCP: gallstones, CBD 8mm, no choledocholithiasis

Case 1

- Ongoing intermittent RUQ pain after eating
- Total bilirubin continued to rise to 6.1
- Other LFTs lower (AP 179, ALT 393, AST 173)

EUS

ERCP



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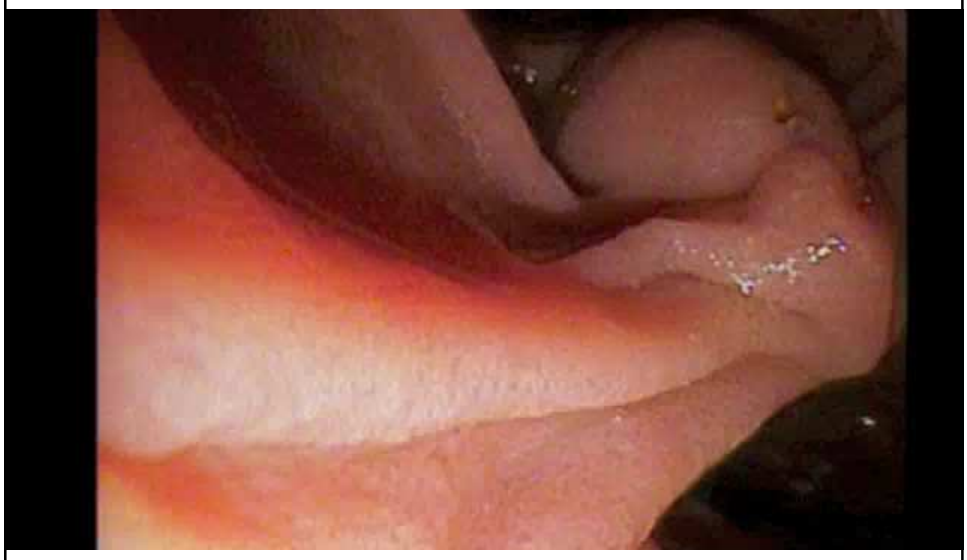

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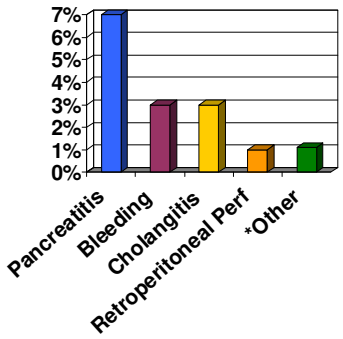
ERCP Complications

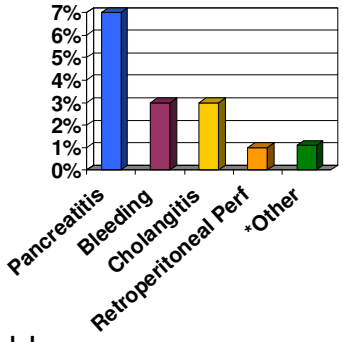
- Overall morbidity 6.9%
- Mortality 0.33%



* MDRO/CRE infection

ERCP Complications

- Overall morbidity 6.9%
- Mortality 0.33%
- Do not check amylase, lipase unless pain
- Rectal Indocin
- After sphincterotomy, hold anticoagulants ≥3 days, antiplatelets ≥7 days



* MDRO/CRE infection

After ERCP, Now What?

All should have CCY unless contraindicated

- ESGE recommends CCY within 2 weeks of ERCP
- 5-40% recurrent biliary symptoms after ERCP
- Median 3 months after ERCP
- 2/3 abdominal pain

Byrne et al. Surg Endosc 2009; Boerma et al. Lancet 2002; Lau et al. Gastro 2006; Williams et al. Gut 2017; Manes G et al. Endoscopy 2019

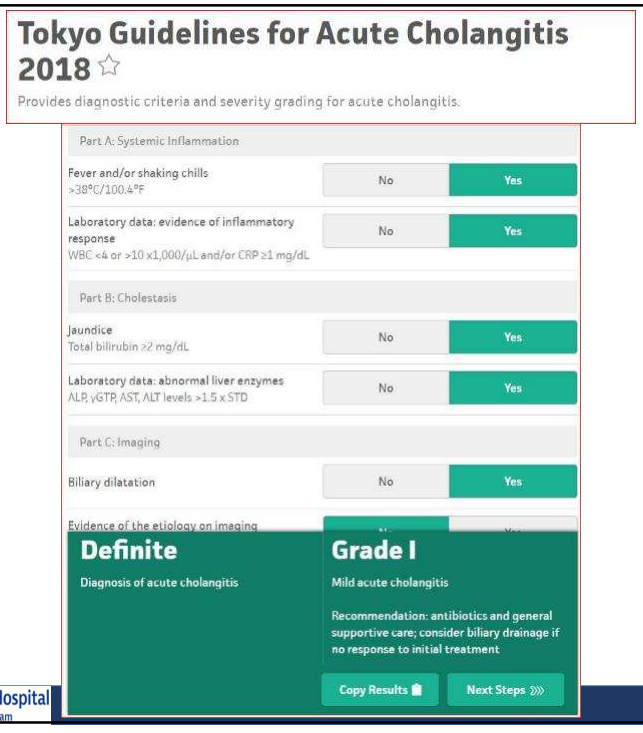
Case 2

- 45yo female with diabetes admitted with severe right upper quadrant pain.
- Temp 101, HR 90, BP 124/84
- ALT 100, AST 89, T bili 3, Alk phos 199.
- WBC 15
- Normal amylase, lipase
- Abdominal US: gallstones, CBD 8mm

- What is the likely diagnosis?

Cholangitis

- Diagnosis
  - ❖Charcot's triad (present in 22%): RUQ pain, fever, jaundice
  - ❖Reynold's pentad: Charcot's + ΔMS, hypotension
  - ❖Tokyo guidelines: Fever or elevated/depressed WBC + abnormal LFTs + abnormal imaging (biliary dilation or cause of cholangitis seen)
    - 92% sensitivity, 78% specificity



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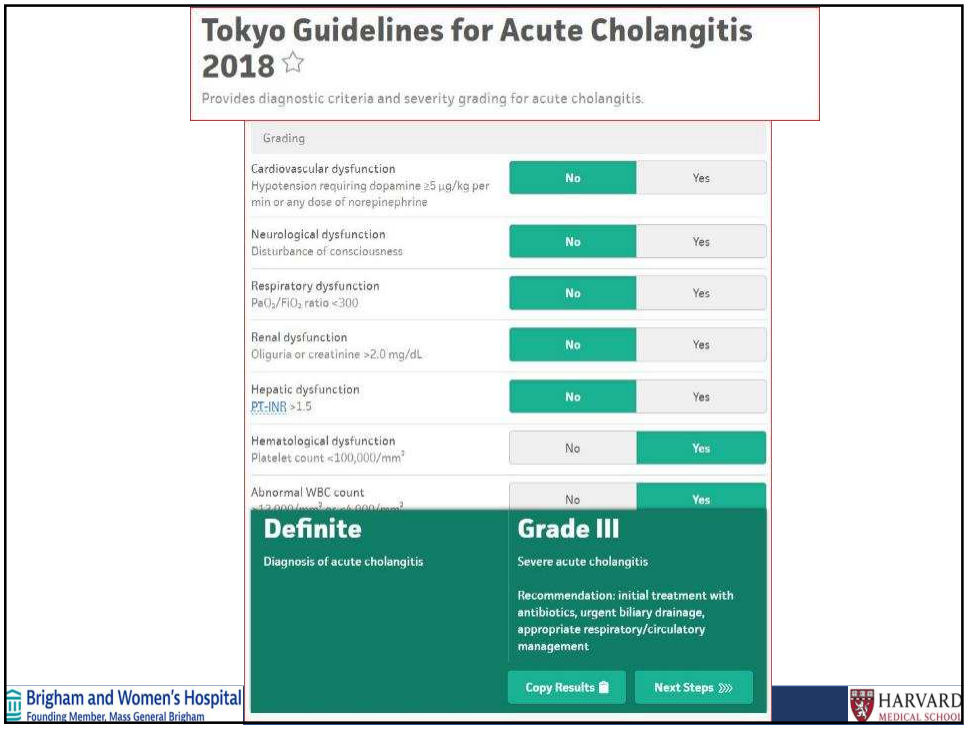


Cholangitis Management

- Initial management:
  - ❖IVF
  - ❖IV antibiotics (cover GNR and enterococcus)
    - Ampicillin + gentamicin or fluoroquinolone ± metronidazole
- 80% respond
- Eventually biliary drainage necessary
- Percutaneous drain:
  - ❖Failed ERCP
  - ❖Post-surgical anatomy
  - ❖Patient unstable and ERCP not available

Timing of ERCP

▪ *Mild, grade 1*: responds to antibiotics	*Elective*
▪ *Moderate, grade 2*: not responding but stable	*24-72h*
▪ *Severe, grade 3*: organ dysfunction	*<24h*

Transfer patient ASAP where ERCP available

Lee J. Nature Reviews GI and Hep 2009; Khashab M et al. Clin Gastro Hep 2012; Manes G et al. Endoscopy 2019; Mukai S et al. Dig Endo 2022

Case 2

- 45yo female with severe right upper quadrant pain, fever, elevated WBC, LFTs, dilated CBD.
- IV ciprofloxacin initiated
- Patient defervesced, repeat WBC 8K
- Elective ERCP

Case 3

- 53yo obese female admitted with severe epigastric pain which began last nite. Temp 98.3.
- Amylase 1000, lipase 2658
- ALT 100, AST 89, T bili 2, Alk phos 69.
- WBC 10

- What is the likely diagnosis?

Epidemiology of Acute Pancreatitis

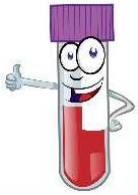
- One of top GI reasons for hospitalization in US
- >275,000 admissions annually
- $ 2.6 billion
- Incidence rising

Approach to Acute Pancreatitis

- Establish diagnosis
- Determine etiology
- Assess severity
- Treat with (moderately) aggressive IVF
- Reassess patient frequently especially during initial 24 hours of admission
- Early nutrition- use the gut!
- Refer to pancreas center for:
  - ❖Idiopathic pancreatitis
  - ❖Severe pancreatitis

Diagnosis of Acute Pancreatitis

2 of 3 criteria: Revised Atlanta



Single best imaging?

Banks et al. Gut 2013.

Diagnosis of Acute Pancreatitis

When is abdominal CT helpful?

Diagnosis of Acute Pancreatitis

When is abdominal CT helpful?

- Diagnosis unclear
- Not improving after 48-72 h
- Signs of severe pancreatitis
- Signs of local complications

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Etiology of Acute Pancreatitis

Gallstone 40-70%

Alcohol 30% (at least 50g/d)

RCT 8% v. 21% ($p<0.05$) recurrent pancreatitis over 2 yrs for two 30-min counseling (inpt + 6m later) v. 1 inpt

Etiology of Acute Pancreatitis

Smoking

	RR non-gallstone pancreatitis
Current smoking	1.8
≥ 20 pack-year	2.3
≥ 20 pack-year + ≥ 400g/ month alcohol (~1 glass wine/day)	4.1

- Current smoking > former > never

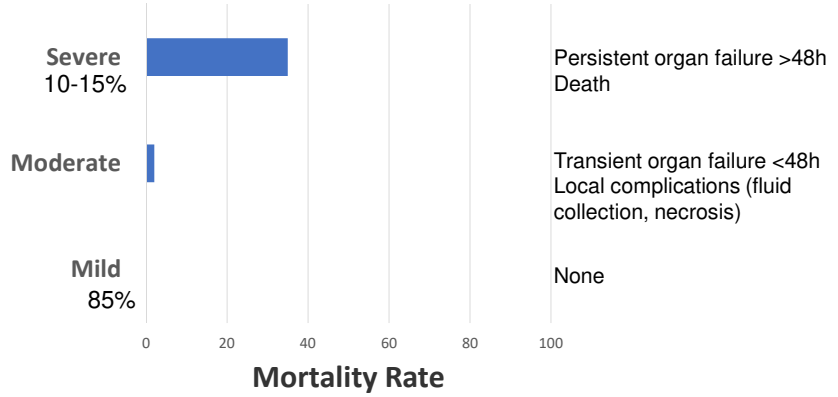
Etiology of Acute Pancreatitis

- Metabolic
  - Triglyceride >1000 mg/dL, but likely lower even >500
  - Hypercalcemia
- Structural
  - Mass, cyst (IPMN), pancreas divisum, annular pancreas, choledochal cyst, SOD
- Autoimmune (IgG4)
- Genetic/ Hereditary (mutations in PRSS1, SPINK1, CTRC, CFTR)
- ERCP
- Drug (6-MP, azathioprine, ACE-I, diuretics, ddI, valproic acid, cocaine, marijuana)
- Infection (e.g., EBV, CMV, hepatitis B, hepatitis C, HIV, ascariasis in developing countries)
- Rheumatologic disease (lupus, RA)
- Trauma
- Acute flare-up of chronic pancreatitis

Etiology Acute Pancreatitis

- Initial work-up
  - History: alcohol, smoking, ERCP, surgery, trauma, medications, history of autoimmune disorders, family history of pancreatitis
  - Labs: LFT, Ca, triglyceride (at presentation)
  - US

Severity Correlates with Mortality



Sternby et al. Annals Surgery 2019; Banks et al. Gut 2013; Van Dijk et al. Gut 2017.

Defining Organ Failure: Modified Marshall Score

- ≥2 in any system = organ failure

Organ	Score 0	1	2	3	4
Respiratory (PaO2/FiO2)	>400	301-400	201-300	101-200	≤101
Renal Cr	<1.4	1.4-1.8	1.9-3.6	3.6-4.9	>4.9
Cardiac (SBP)	>90	<90, fluid responsive	<90, not fluid responsive	<90, pH<7.3	<90, pH<7.2

Supplemental O2 (L)	Estimating FiO2%
Room air	21
2	25
4	30
6-8	40
9-10	50

Koutroumapkis E, et al. AJG 2015.

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9-10	50

Predictors of Organ Failure:

- Admit Hct ≥44
- Rising BUN 1st 24 hrs

Predictor of Mortality in Acute Pancreatitis

- Ranson, Glasgow, APACHE, BISAP

Risk Factors	Odds Ratio	
• BUN ≥20mg/dL admission	4.6	BAD
• Rise BUN ≥ 2 mg/dL in 24h	4.3	BAD

Nonsevere Acute Pancreatitis

Harmless acute pancreatitis score (HAPS):

- Normal Hct
- Normal Creatinine
- No abdominal guarding and/or rebound

99% PPV for predicting who won't develop complications due to AP

Papachristou et al. Am J Gastro 2010.

PASS Score in Acute Pancreatitis

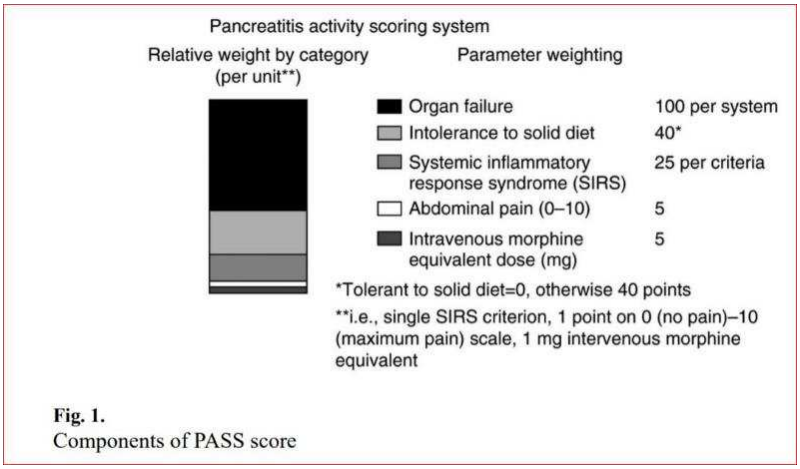


Fig. 1.
Components of PASS score

Wu B et al. AJG 2017; Buxbaum J et al. AJG 2018.

PASS Score in Acute Pancreatitis

- Admission PASS score >140 predicts moderate to severe pancreatitis
  - 65% sensitivity, specificity ~ Glasgow, Ranson
  - Associated with ICU, SIRS, local complications, longer LOS, time to nutrition
- Discharge PASS score >60 predicts early readmission and ED visit within 30d
  - 68% sensitivity, 71% specificity

Buxbaum J et al. AJG 2018.

Case 3

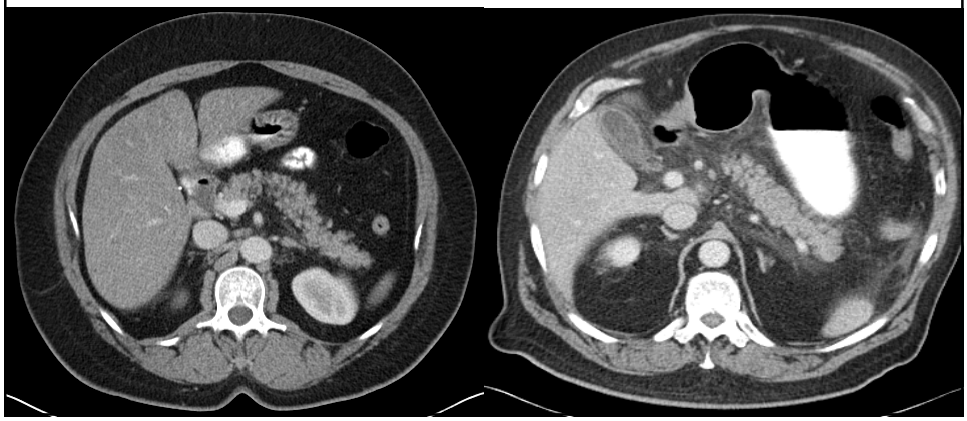
- 53yo female admitted with pancreatitis, elevated LFTs, on room air.
- BUN 12, Creatinine 0.6
- Hct 35
- PASS score=50
- Mild pancreatitis
- Low risk of mortality

Terminology

	Interstitial edematous	Necrotizing
Acute collection	Acute peripancreatic fluid collection (20-40%)	Acute necrotic collection (90-100%)
Mature collection	Pseudocyst (10% of APFC)	Walled off pancreatic necrosis (WON, ~50% ANPFC)
Sterile or infected	Infected pseudocyst	Infected necrosis

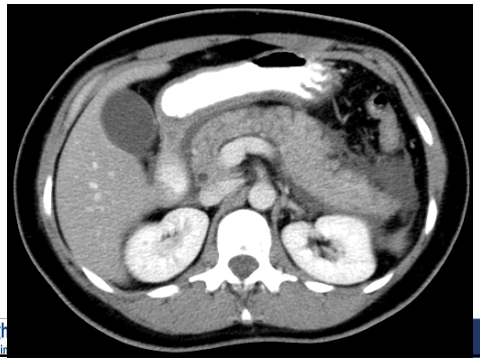
Terminology

- Interstitial pancreatitis



Terminology

- Acute peripancreatic fluid collection ~<4 weeks old



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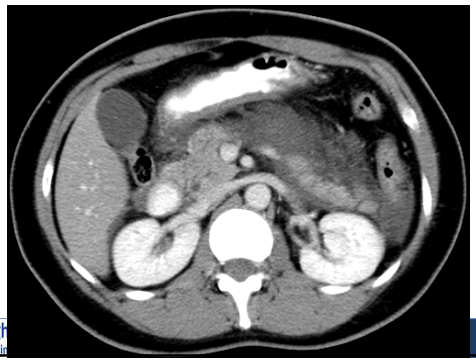

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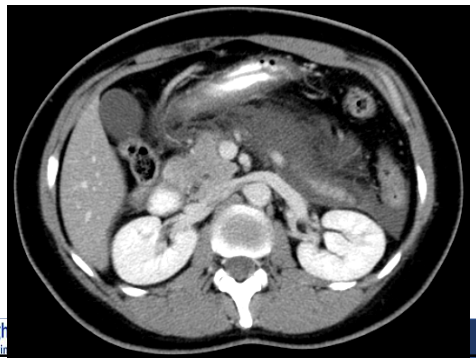
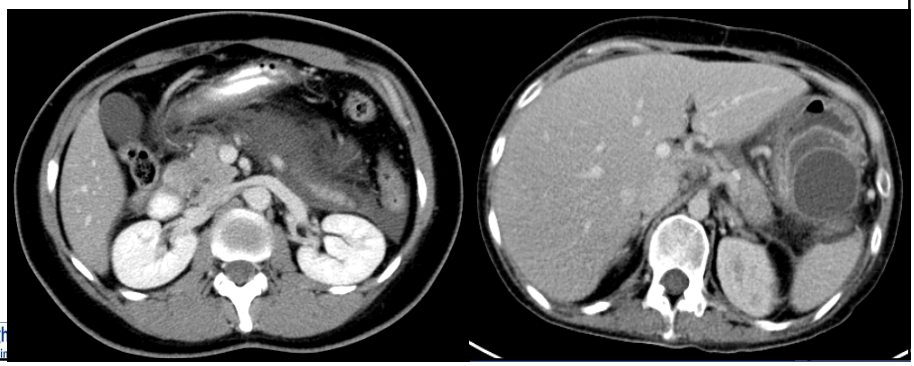


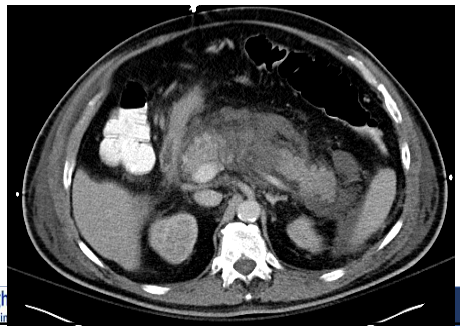
Terminology

- Acute peripancreatic fluid collection ~<4 weeks old
- Pseudocyst: walled fluid ~>4 wks after attack



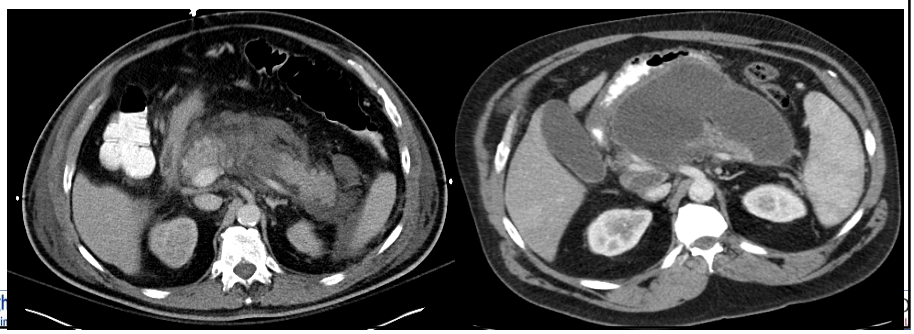
Terminology

- Necrotizing pancreatitis
  - Acute necrotic collection ~<4 weeks



Terminology

- Necrotizing pancreatitis
  - Acute necrotic collection ~<4 weeks
  - Walled-off pancreatic necrosis ~>4 weeks after attack



Initial Management

IVF

- **What type?**

  LR: decreases SIRS and severity

- **How much?**

  Goal directed IVF

Initial Management

- Randomized mild acute pancreatitis 20ml/kg bolus, 3ml/kg/hr v. 10ml/kg bolus if hypovolemic, 1.5ml/kg/hr
- Goal directed at 12 to 24h:
  - ❖Hypovolemic: repeat bolus
  - ❖Normovolemic: 1.5ml/kg/hr
  - ❖Volume overload: decrease or stop infusion

	Aggressive IVF	Moderate IVF	P value
Mod to severe pancreatitis	22%	17%	NS
Fluid overload	21%	6%	0.004

Initial Management

IVF

- Goal: decrease BUN
- Reassess patient q6-12h
- Recheck key labs (BUN, Hct) in 6-12h and adjust IVF accordingly

Case 3

- 53yo female with diabetes admitted gallstone pancreatitis.
- Admission labs:
  - BUN 12, Creatinine 0.6
  - Hct 35
- 12 hours after admission:
  - BUN 20, Creatinine 0.7
  - Hct 39
- Next step?

Case 3

- Bolus 1 liter LR as pt hypovolemic
- Recheck Hct, BUN/Cr in 6 hours, adjust IVF PRN
- Repeat Hct 35, BUN 14, Creatinine 0.7

Pain

- Try non-opioids first
  - NSAID, tramadol- no worse than opioids
  - Then opioids if needed

Machicado et al. Curr Op Gastro 2019.

Nutrition: Start within 24hrs

Early oral or enteral feed 24-48h → *Need for intervention for necrosis*

Trend towards decreased infection and organ failure

- Do not need to start with clear liquids (low fat, normal fat, soft or normal)
- NGT or NJT> TPN
- Fluid collections or elevated pancreatic enzymes not contraindication to nutrition

Tenner et al. Am J Gastro 2013; Bakker OJ et al. NEJM 2014; Crockett SD et al. Gastro 2018.

Antibiotics

- **Do not give prophylactic antibiotics**
- Cholangitis, infected necrosis, infected pseudocyst, patient decompensating: *YES*
- If concern for infection, CT-guided aspiration before antibiotics (if possible)
- Beware: false negative CT aspiration ~20-9%
- Procalcitonin may help

Abdominal Compartment Syndrome

- Abdominal compartment syndrome (ACS) = intraabdominal pressure >20 mmHg + new onset organ dysfunction
- In acute pancreatitis, 49% mortality with ACS
- Measure in severe pancreatitis with organ failure, persistent SIRS, or APACHE II ≥8; tense, distended abdomen

Van Brunschot S et al. Pancreas 2014.

Abdominal Compartment Syndrome

- Bladder pressure with bladder catheter
- NGT/rectal tube
- Optimize sedation and analgesia
- Consider muscle relaxants
- Diuretics
- Early enteral nutrition
- Percutaneous drainage of fluid
- Surgical decompression when IAH>25mmHg
- Neostigmine IM 1mg q12h; if no BM at 12h, q8h; if no BM at 24h, q6h x7 days or IAP <12mmHg

Trikudanathyan et al. Pancreatology 2014; He et al. Crit Care 2022

CCY Timing in Mild Gallstone Pancreatitis

- When should patients undergo CCY after mild acute gallstone pancreatitis?

BEFORE DISCHARGE

	Interval cholecystectomy (n=136)	Same-admission cholecystectomy (n=128)	Risk ratio (95% CI)	p value
Primary endpoint				
Mortality or readmission for gallstone-related complications	23 (17%)	6 (5%)	0·28 (0·12–0·66)	0·002
Secondary endpoints				
Readmission for gallstone-related complications				
Recurrent pancreatitis	12 (9%)	3 (2%)	0·27 (0·08–0·92)	0·03
Cholecystitis	2 (2%)	0		0·50
Choledocholithiasis needing ERCP	2 (2%)	1 (1%)	0·53 (0·05–5·79)	1·00
Gallstone colic	7 (5%)	2 (2%)	0·30 (0·06–1·43)	0·17
Mortality	0	1 (1%)		0·48
Patients reporting colics during waiting period*	62 (51%)	3 (3%)	0·06 (0·02–0·19)	<0·0001

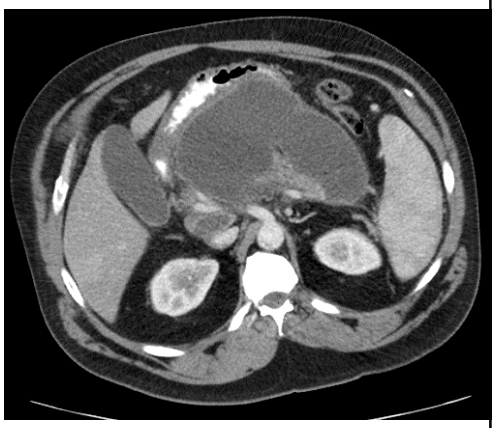
- In non-surgical pts, ERCP with sphincterotomy

Role of ERCP in Acute Gallstone Pancreatitis

- ERCP within 72hrs
  - ✓Cholangitis
  - ✓CBD stone
  - ✓Post-operative CBD stone removal
- Not indicated for severe gallstone pancreatitis
  - ✓Urgent ERCP within 24 hrs did not reduce complications or mortality compared with conservative management

Case 2

- 54yo male necrotizing gallstone pancreatitis 5 weeks ago, transiently intubated now on floor with abdominal pain and unable to eat.

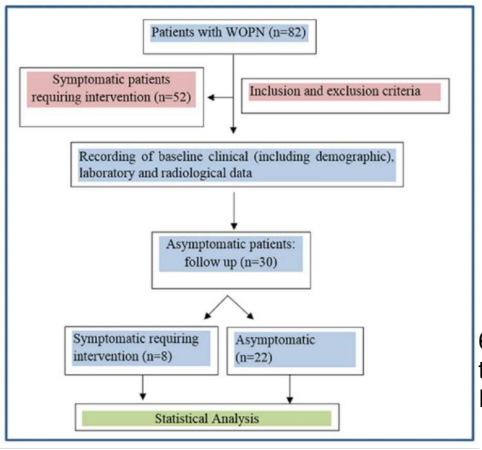


Approach to WON

- What are the management options?
  - Surgical necrosectomy
  - Radiologic percutaneous drain
  - Endoscopic necrosectomy
- Transfer patient to center with above expertise

Conservative Management WON

Prospective observational



27%
Within 1.5 months from onset
No surgery or mortality

64% smaller 7.6cm to 5.1cm
Rest no change

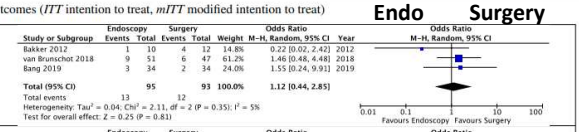
Endoscopic vs. Surgical Management of WON

RCT

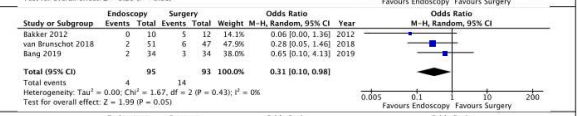
Table 3 Meta-analysis of all outcomes (*ITT* intention to treat, *mITT* modified intention to treat)

Endo Surgery

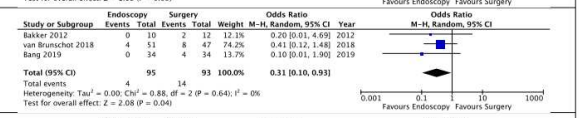
Mortality ITT



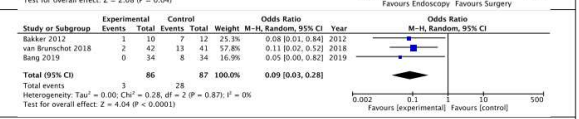
New onset multiple organ failure ITT



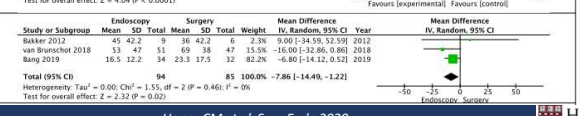
Perforation of visceral organs Enterocutaneous fistulae ITT



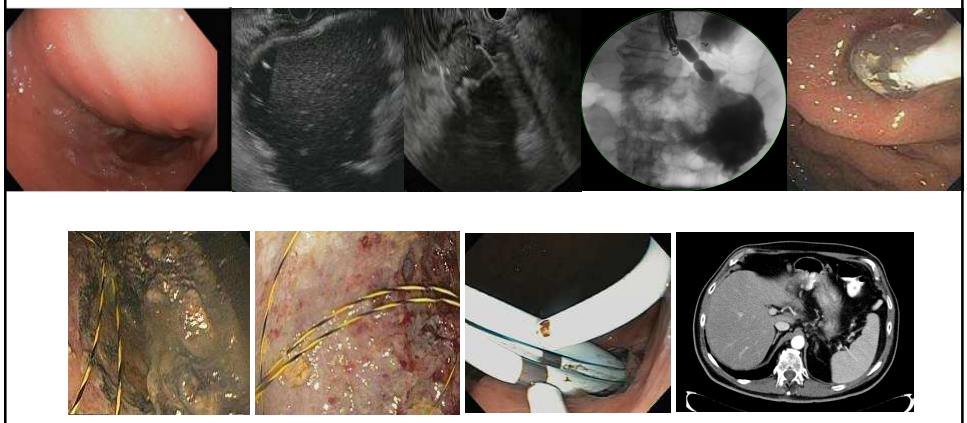
Pancreatic fistulae ITT



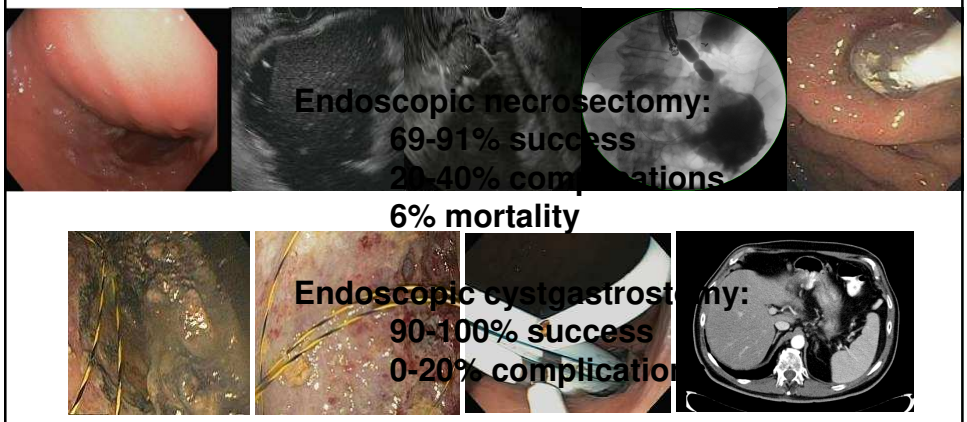
Hospital stay mITT

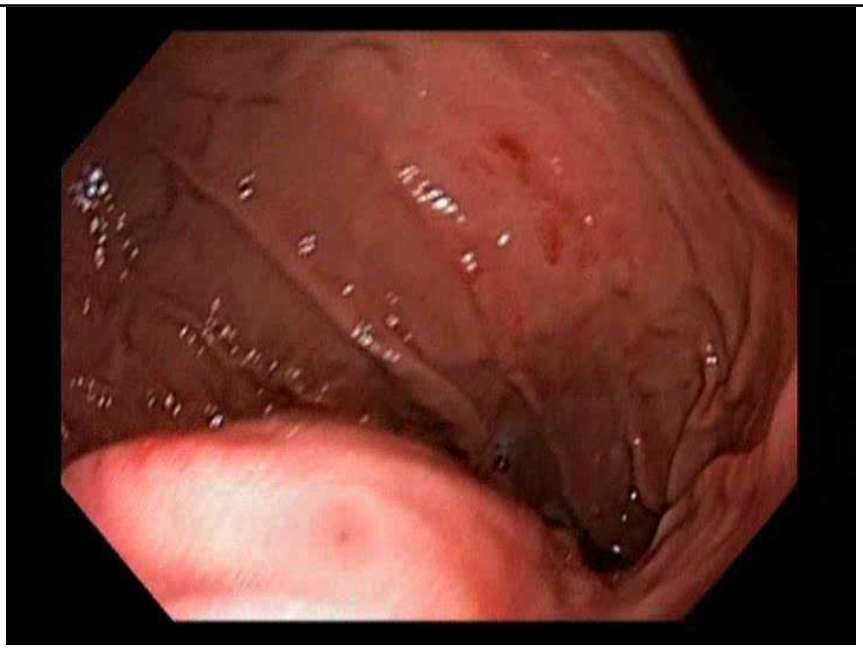


Endoscopic Necrosectomy

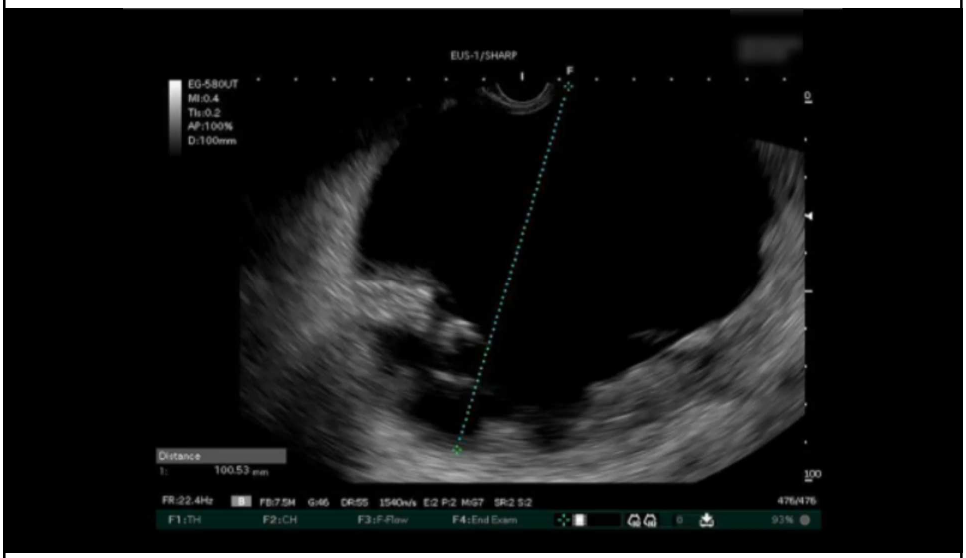


Endoscopic Necrosectomy





Courtesy Dr. Christopher Thompson



Pancreatic Necrosis/ Pseudocyst

- Decision points:
  - **Symptoms** present?
  - Necrosis/ fluid **collection mature**? (≥4 weeks)
- No symptoms: no intervention, but should be followed in pancreas center
- Symptomatic sterile or infected necrosis:
  - **Endoscopic necrosectomy (>4 wks with wall)**
  - **Radiologic percutaneous drain (<4 wks)**
  - Surgical necrosectomy
- Infected necrosis: conservative management with antibiotics until wall matures reasonable

Take Home Points

- CBD stones: intermediate probability, EUS, MRCP, IOC
- CCY after ERCP for CBD stone
- Emergent ERCP (<24h) for severe cholangitis (Tokyo)
- Early ERCP (<72h) in acute gallstone pancreatitis: cholangitis or retained CBD stone
- In acute pancreatitis, determine etiology (gallstone, Etoh, smoking)
- Moderate IVF LR in 1st 24h

Take Home Points

- Recheck BUN, Hct within 1st 24h and tailor fluids
- Start solid PO/ enteral feed within 24-48h
- Use antibiotics sparingly in acute pancreatitis
- Monitor bladder pressure in severe pancreatitis
- CCY before discharge in mild gallstone pancreatitis
- PASS score may help decrease early readmission
- Multidisciplinary approach with referral to pancreas center for severe or idiopathic pancreatitis

Thank you from Boston!