Practical Approaches to Pancreatobiliary Disease Management

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Disclosures

I have no disclosures to make.

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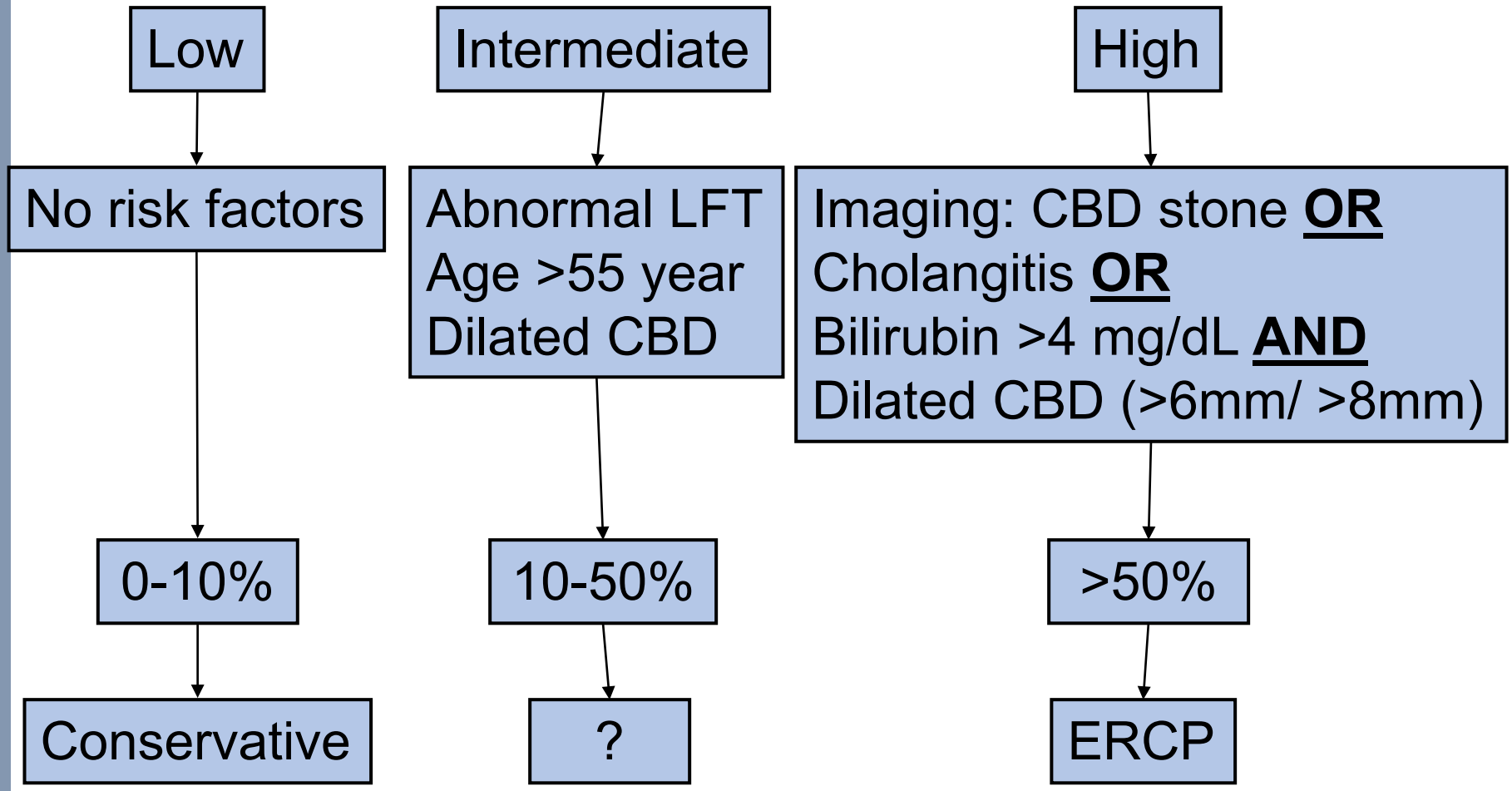
- Should pt undergo ERCP?
- What's the likelihood that the patient has a CBD stone?

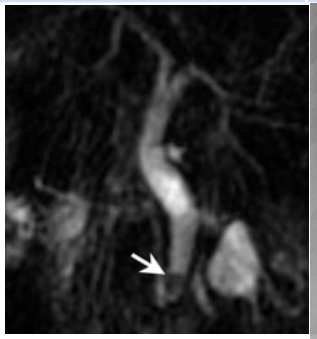
Risk of CBD Stone

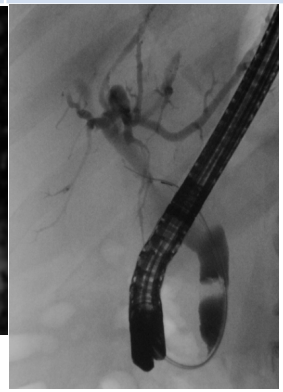


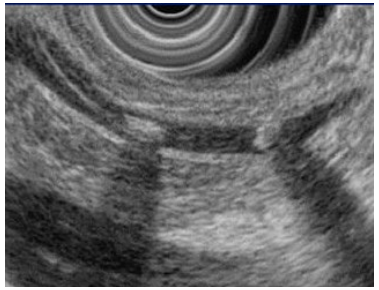
Buxbaum et al. GIE 2019.

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%	-







Gurusamy KS et al. Cochrane 2015.

Approach to Intermediate Risk

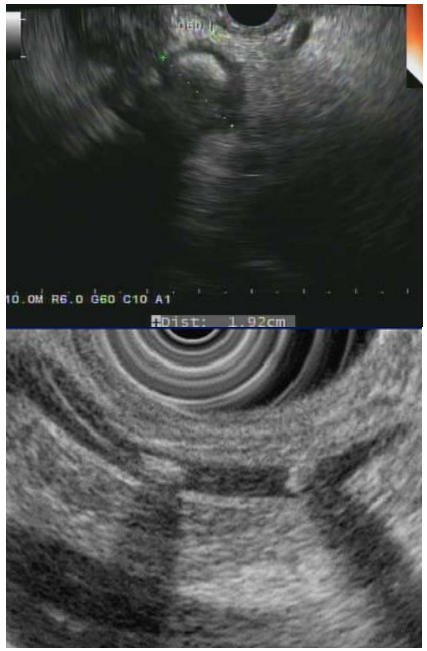
EUS or MRCP or Lap CCY with IOC

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

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

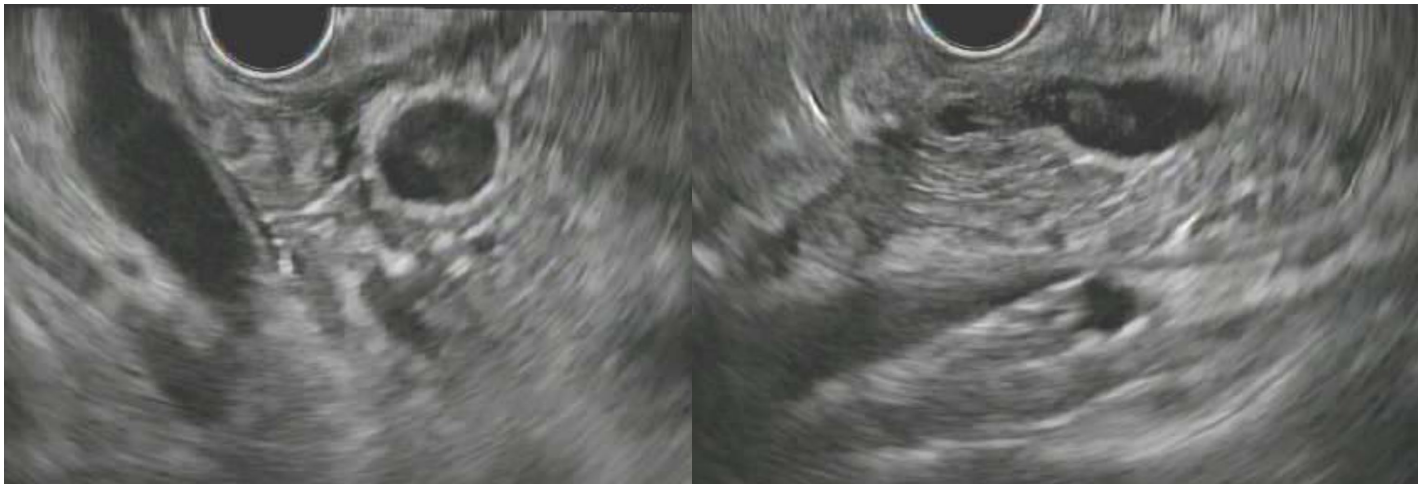
- 36yo female with RUQ pain, total bilirubin 2.9, gallstones, CBD 6mm and no intrahepatic biliary ductal dilation.
- Intermediate risk for CBD stone
- Best next step: EUS or MRCP

- MRCP: gallstones, CBD 8mm, no choledocholithiasis

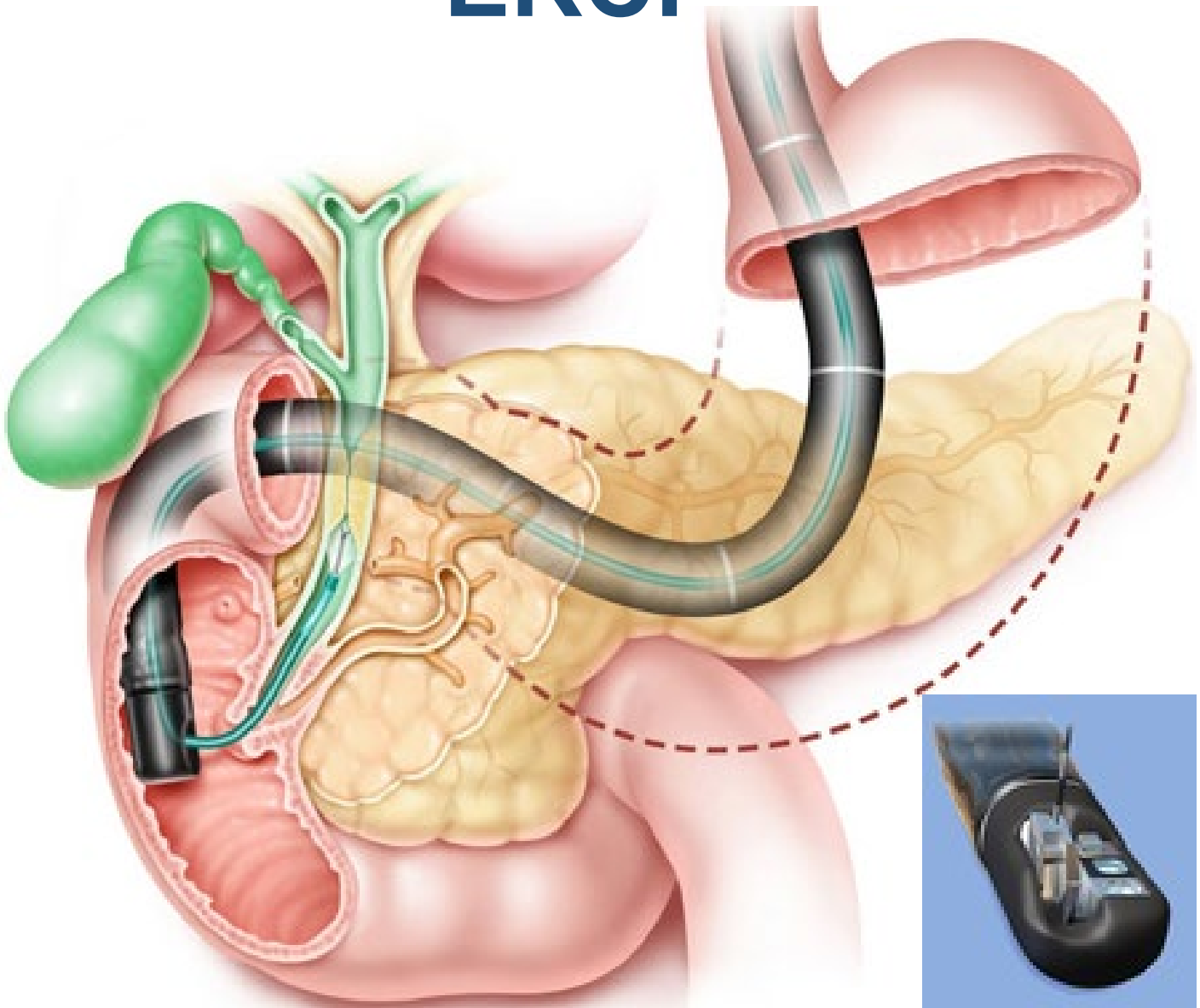
Case 1

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

EUS

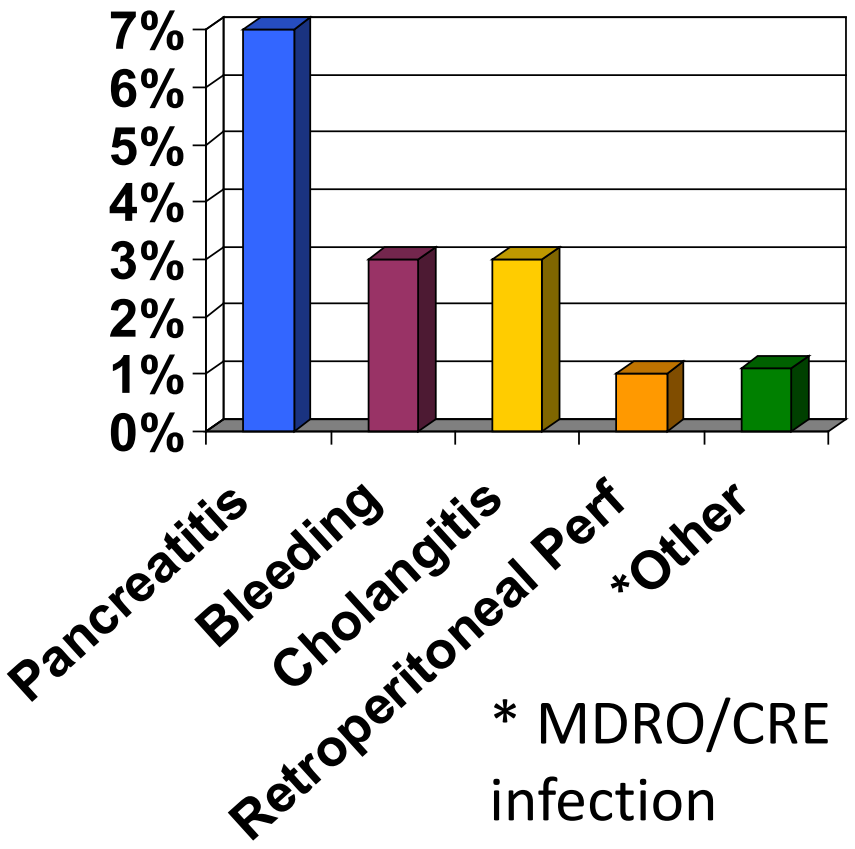


ERCP



ERCP Complications

- Overall morbidity 6.9%
- Mortality 0.33%

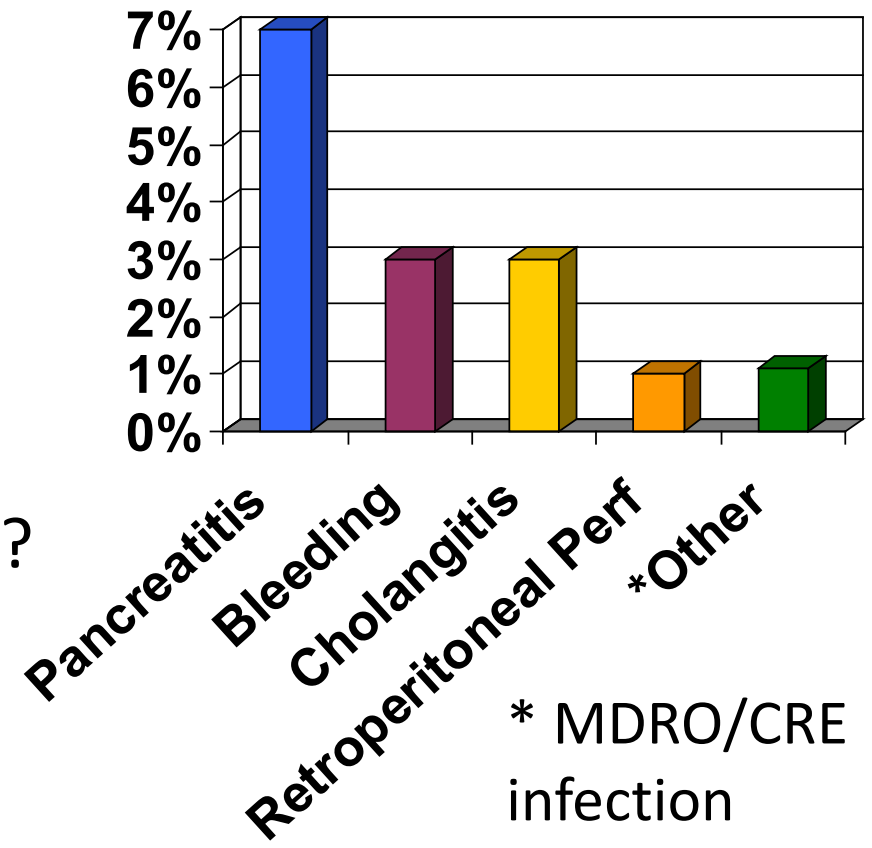


* MDRO/CRE infection

Luo et al. Lancet 2016.

ERCP Complications

- Overall morbidity 6.9%
- Mortality 0.33%
- <u>Do not check amylase, lipase unless pain</u>
- Rectal Indocin: pre-all ERCP?
- After sphincterotomy, hold anticoagulants ≥3 days, antiplatelets ≥7 days



* MDRO/CRE infection

Luo et al. Lancet 2016.

After ERCP, Now What?

All should have CCY unless contraindicated

- 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.

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

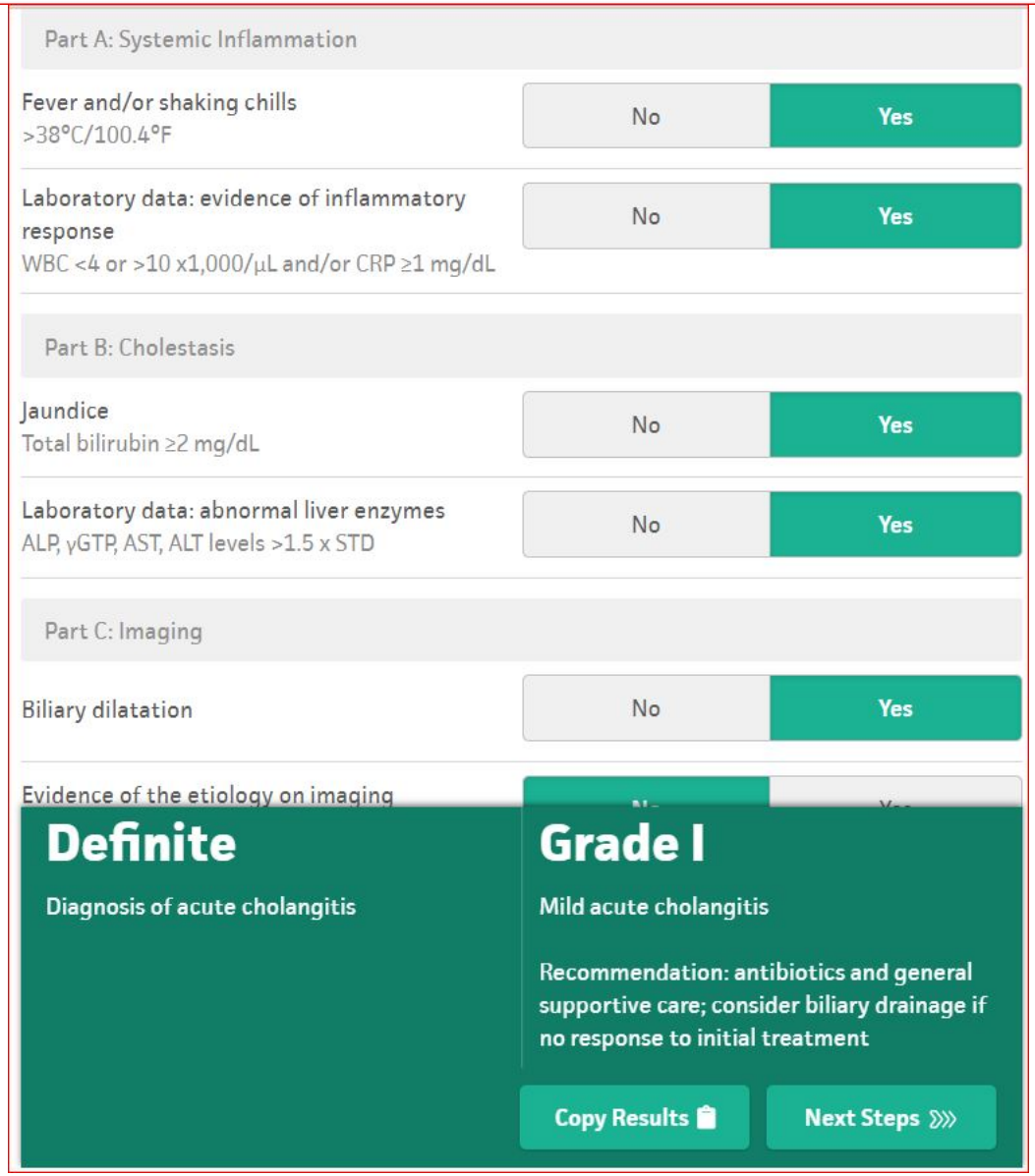
- What is the likely diagnosis?

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

Tokyo Guidelines for Acute Cholangitis 2018 ☆

Provides diagnostic criteria and severity grading for acute cholangitis.



Tokyo Guidelines for Acute Cholangitis 2018 ☆

Provides diagnostic criteria and severity grading for acute cholangitis.

Grading

Cardiovascular dysfunction Hypotension requiring dopamine ≥5 μg/kg per min or any dose of norepinephrine	**No**	Yes
Neurological dysfunction Disturbance of consciousness	**No**	Yes
Respiratory dysfunction PaO_2/FiO_2 ratio <300	**No**	Yes
Renal dysfunction Oliguria or creatinine >2.0 mg/dL	**No**	Yes
Hepatic dysfunction PT-INR >1.5	**No**	Yes
Hematological dysfunction Platelet count <100,000/mm^3	No	**Yes**
Abnormal WBC count >12,000/mm^3 or <4,000/mm^3	No	**Yes**

Definite

Diagnosis of acute cholangitis

Grade III

Severe acute cholangitis

Recommendation: initial treatment with antibiotics, urgent biliary drainage, appropriate respiratory/circulatory management

Copy Results

Next Steps

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

Emergent (<24hr) vs. elective (24-72h) from admission?

- *Mild, grade 1*: responds to antibiotics — *Elective*
- *Moderate, grade 2*: not responding but stable — *Elective*
- *Severe, grade 3*: organ dysfunction — *Emergent*

Transfer patient ASAP where ERCP available

Lee J. Nature Reviews GI and Hep 2009.
Khashab M et al. Clin Gastro Hep 2012.

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

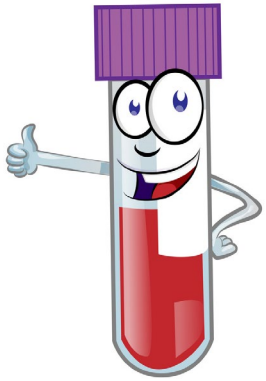
- One of top GI reasons for hospitalization in US
- >275,000 admissions annually
- $ 2.6 billion
- Incidence rising

Approach to Acute Pancreatitis

- Establish diagnosis
- Determine etiology
- Assess severity
- Treat with aggressive IVF
- Reassess patient frequently especially during initial 24 hours of admission
- 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

Etiology of Acute Pancreatitis

Gallstone 40-70%

- CCY before discharge in mild cases

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

Crockett SD et al. Gastro 2018.

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

Azodi et al. Gut 2012.
Aune et al. Pancreatology 2019.

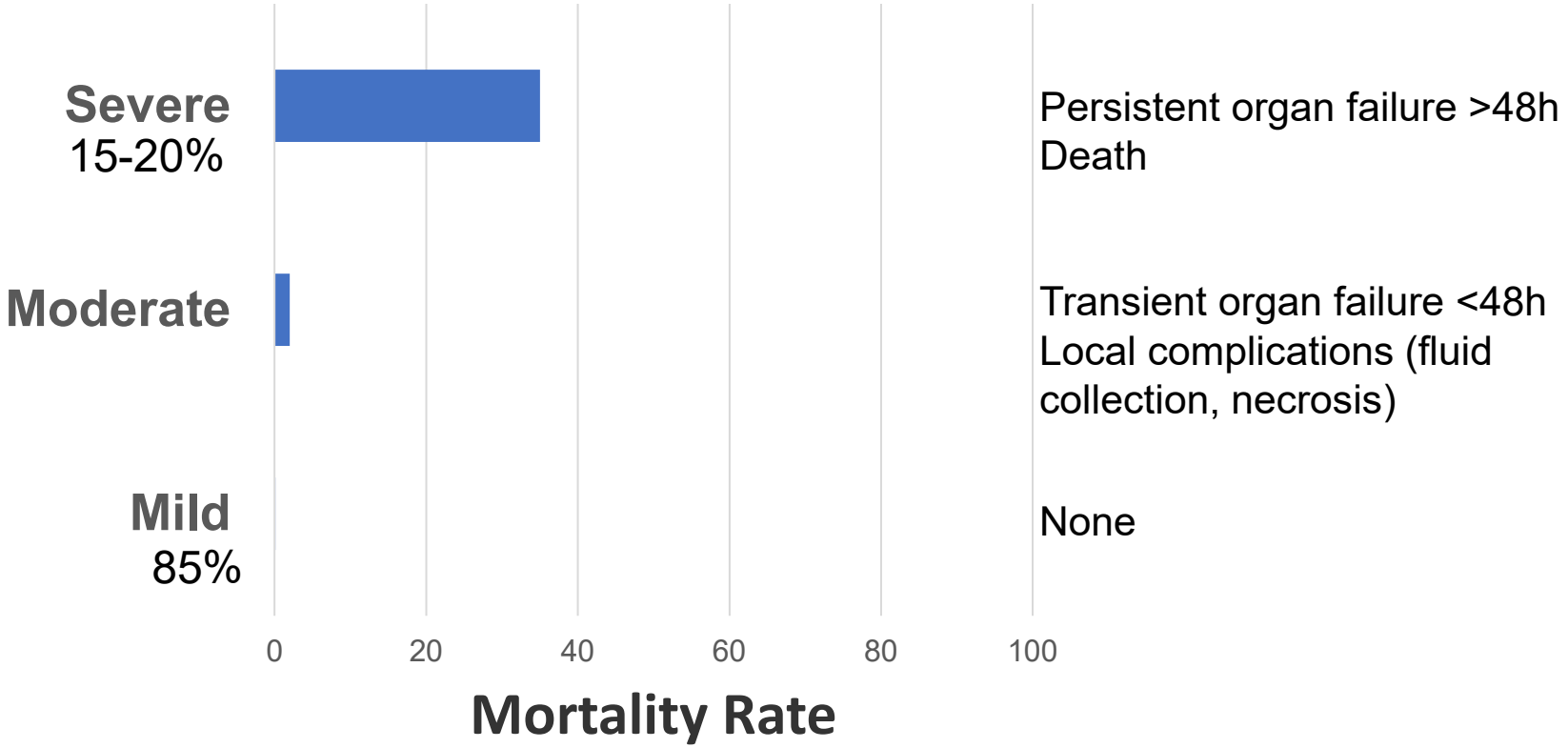
Etiology of Acute Pancreatitis

- Metabolic
  - Triglyceride >1000 mg/dL
  - 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 of 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
  - In pts >40, check for pancreatic mass

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

Koutroumapkis E, et al. AJG 2015.

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

Wu et al. Arch Int Med 2011.

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

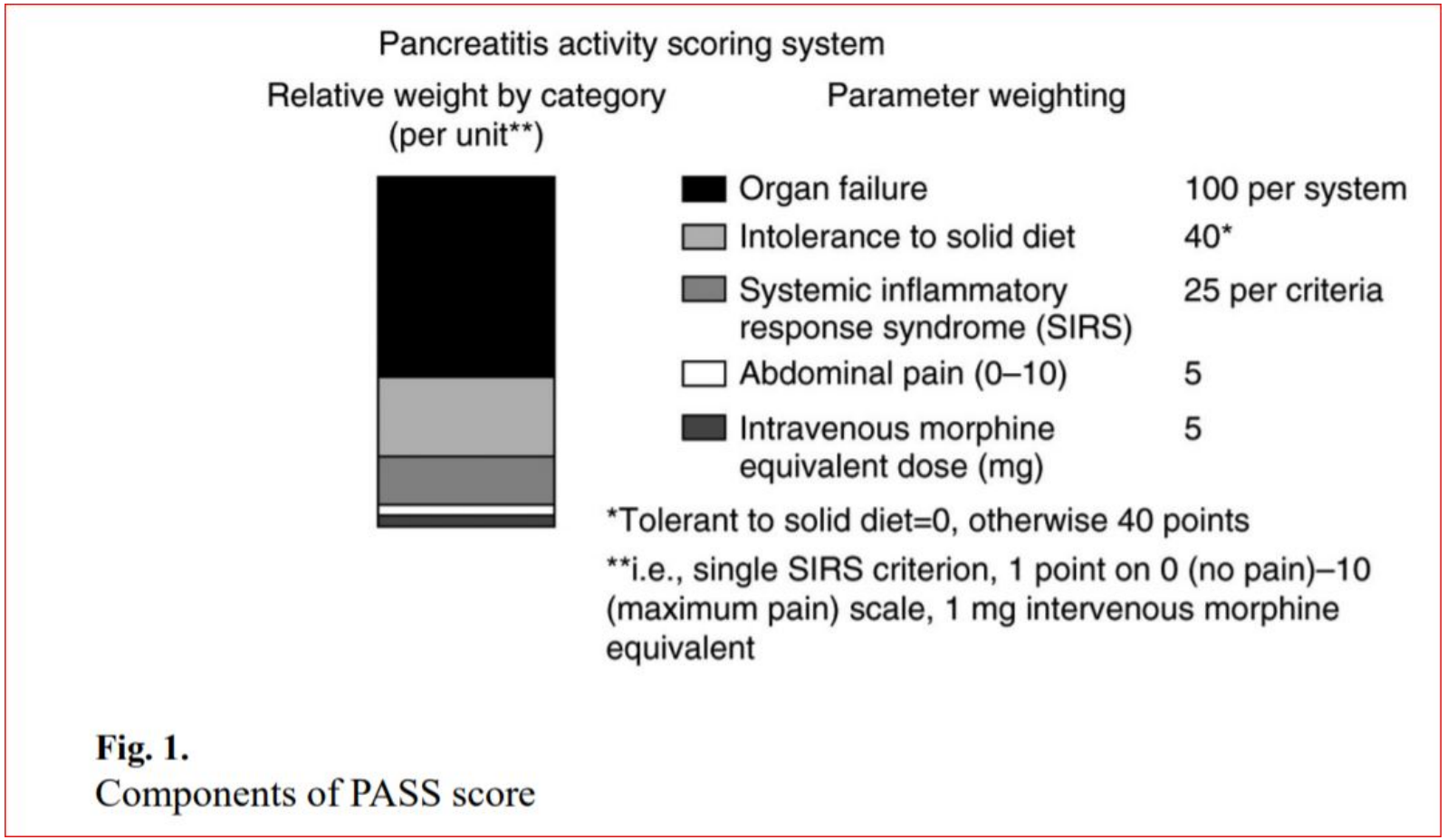


Fig. 1.
Components of PASS score

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

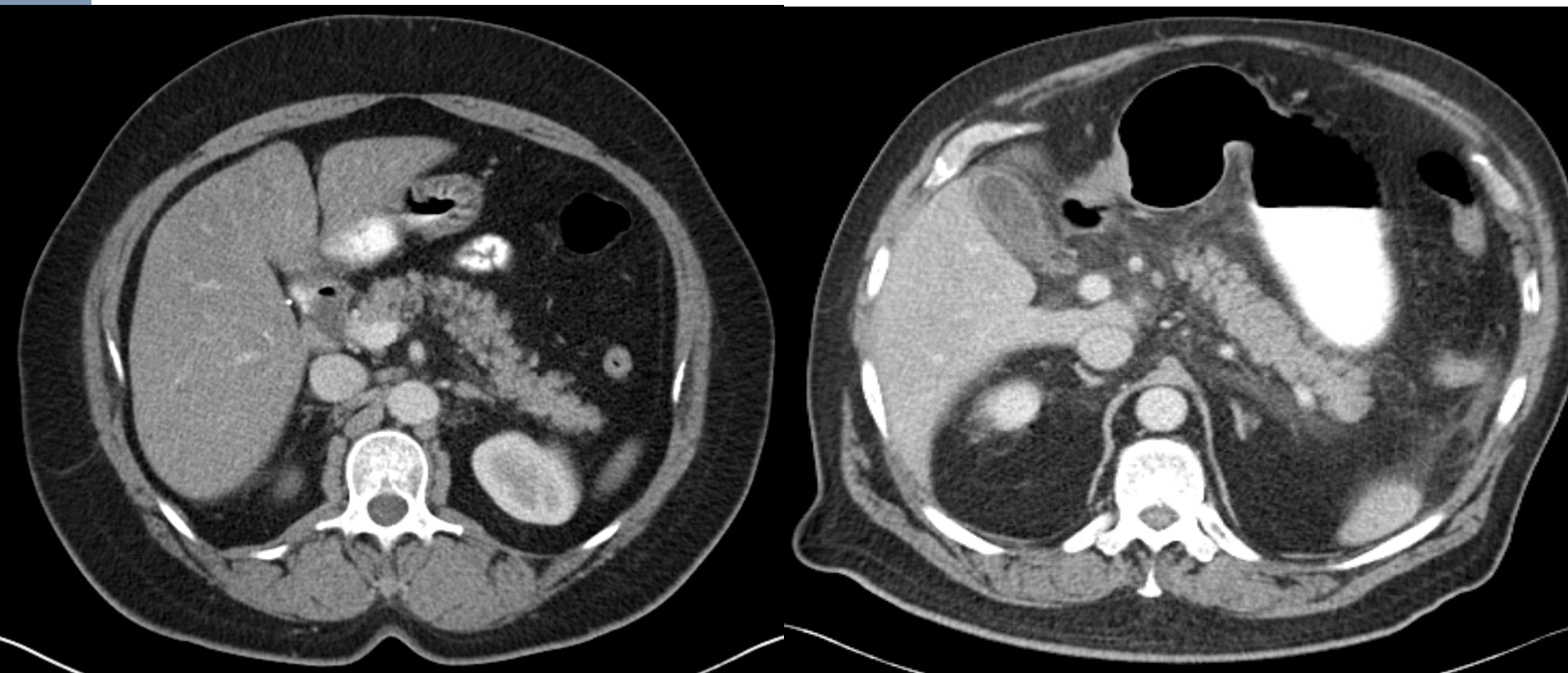
- Mild pancreatitis
- Low risk of mortality

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

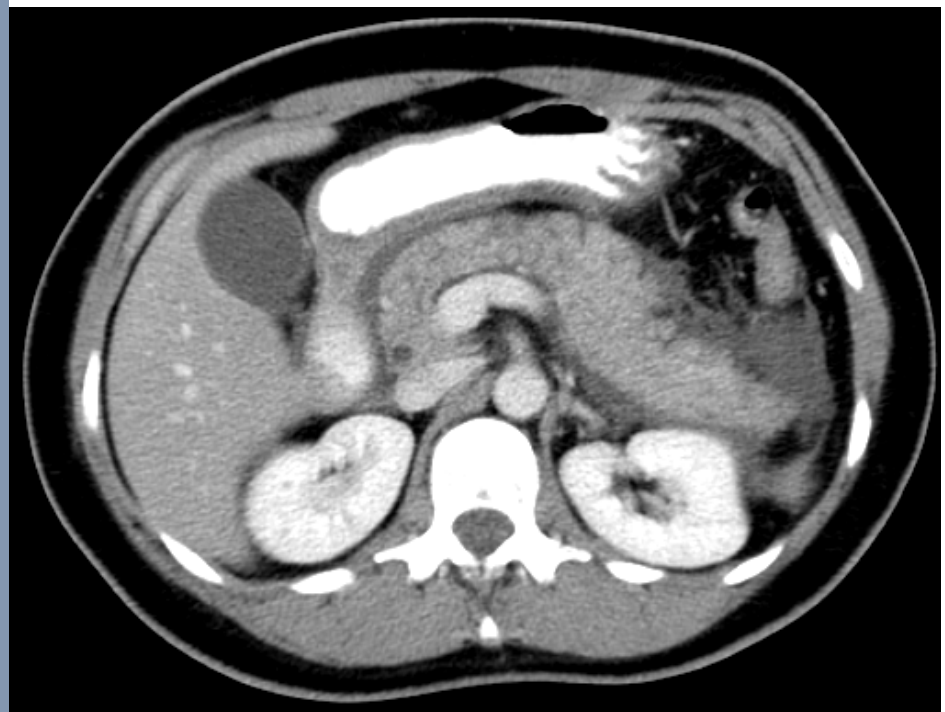
Terminology

- Interstitial pancreatitis



Terminology

- Acute peripancreatic fluid collection ~<4 weeks old



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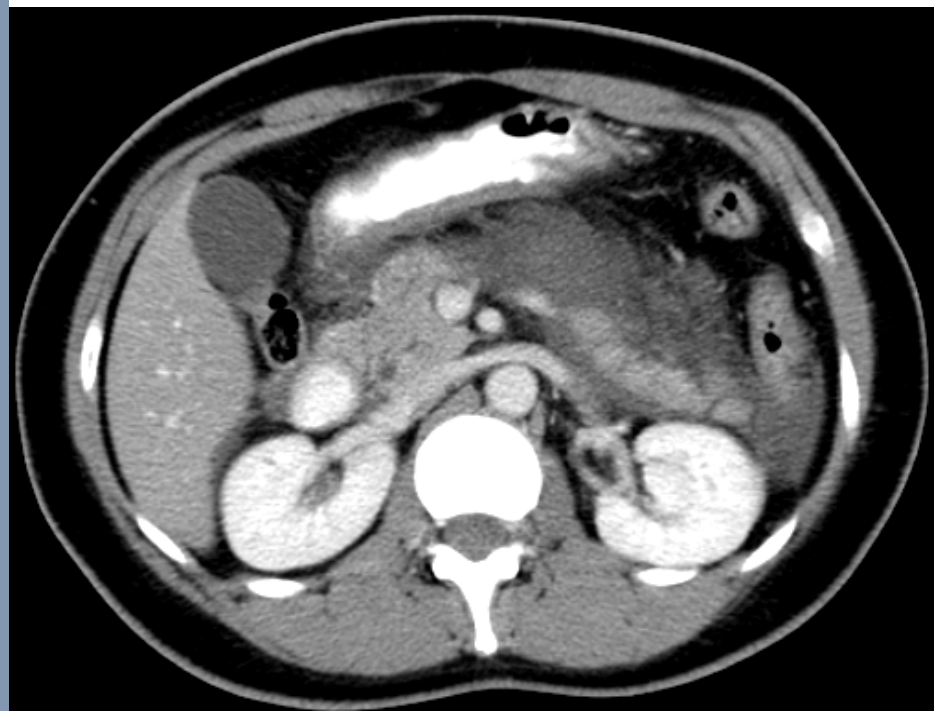

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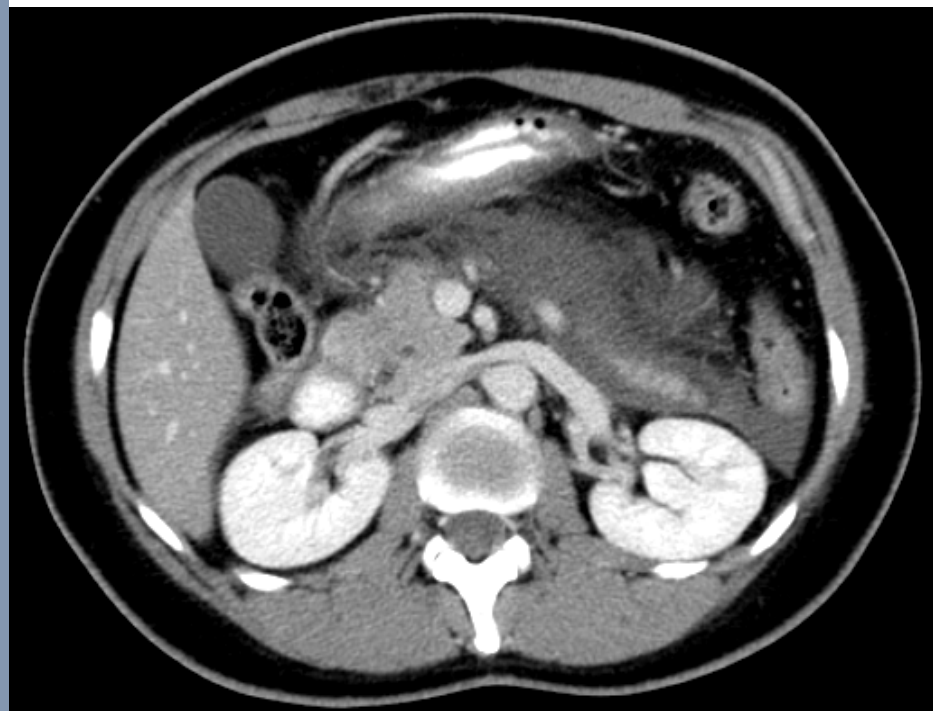
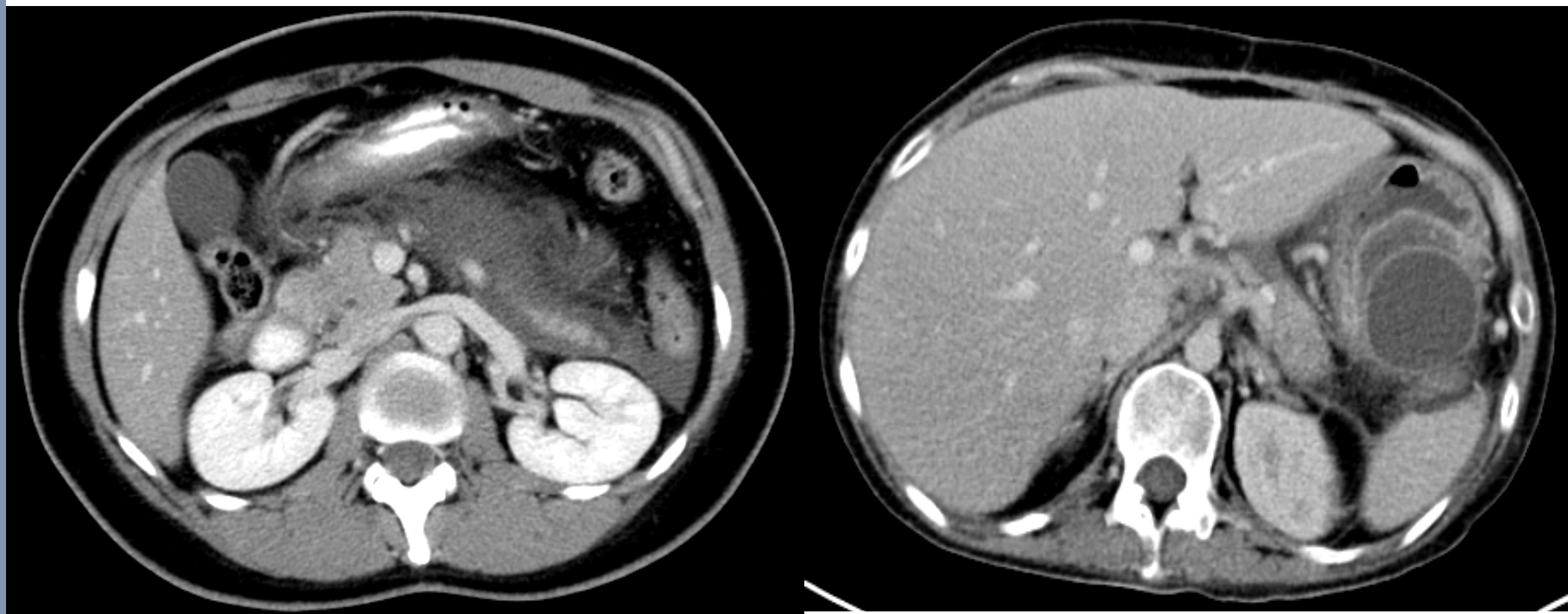


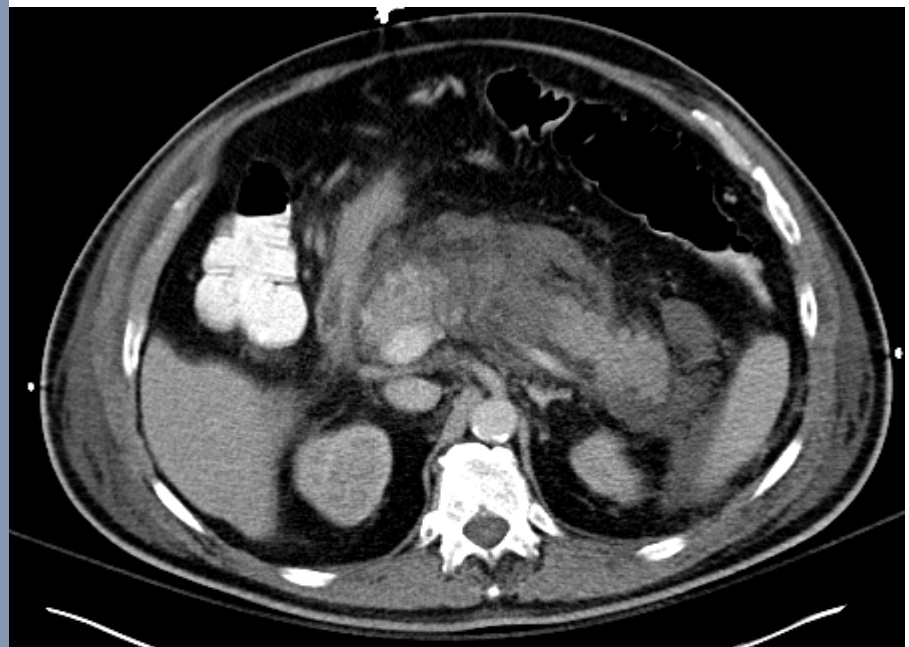
Terminology

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



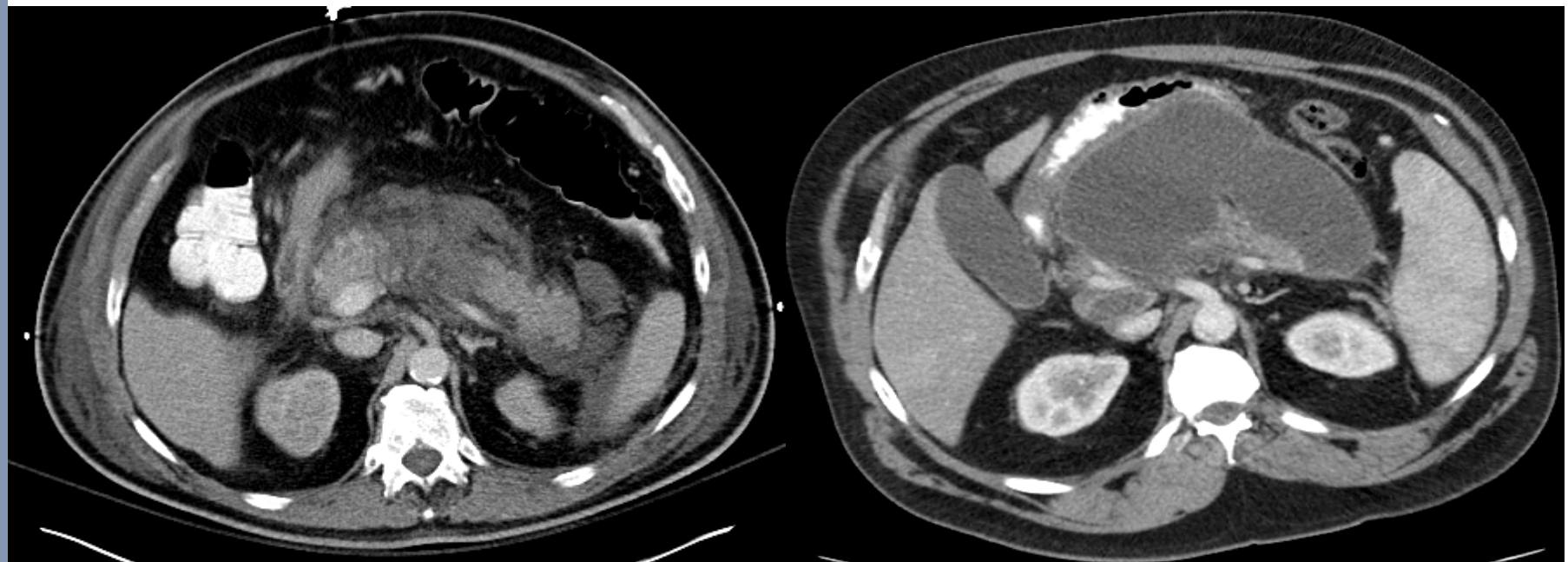
Terminology

- 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, IVF, IVF

- What type?

  LR: decreases SIRS

Wu et al. CGH 2011.
Tenner et al. Am J Gastro 2013.

Initial Management

IVF, IVF, IVF

- What type?

  LR: decreases SIRS

- How much?

  Goal directed IVF

  5-10cc/kg/h (250-500cc/h x 24h)

  Urine output >0.5-1cc/kg/h

  Bolus 1 liter or more if volume depleted (e.g., decr BP, tachy)

Wu et al. CGH 2011.
Tenner et al. Am J Gastro 2013.

Initial Management

IVF, IVF, IVF

- Goal: decrease BUN
- Early aggressive IVF first 12-24h most critical
- Reassess patient q6-12h
- Recheck key labs (BUN, Hct) in 6-12h and adjust IVF accordingly

Tenner et al. Am J Gastro 2013.

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

- Increase LR from 250cc/h to 350 cc/h, consider 1 liter bolus
- 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 Solids Early in Mild Pancreatitis

No nausea/vomiting or ileus
Abdominal pain decreasing → Start with solids

- No increased recurrence of pain
- Decreased length of stay mean 1 day

Sathiaraj E. Alim Pharm 2008.
Meng et al. World J Gastro 2011.
Tenner et al. Am J Gastro 2013.
Bakker OJ et al. NEJM 2014.

Early Feeding Is Better in Moderate to Severe Pancreatitis

Early oral or enteral feed 24-48h → *Infection and organ failure*

- If PO not tolerated after 3-5d, NJT/ NGT > TPN
- Fluid collections or elevated pancreatic enzymes not contraindication to nutrition

Sathiaraj E. Alim Pharm 2008.
Meng et al. World J Gastro 2011.
Tenner et al. Am J Gastro 2013.
Bakker OJ et al. NEJM 2014.
Ramanathan et al. Nutr Cl Prac 2019.

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 ~10%

Abdominal Compartment Syndrome

- Abdominal compartment syndrome (ACS) = intraabdominal pressure >20 mmHg + new onset organ dysfunction
- In acute pancreatitis, 20-40% mortality with ACS
- Measure in severe pancreatitis, persistent SIRS, or APACHE II ≥8; tense, distended abdomen

Trikudanathyan et al. Pancreatology 2014.; Husu HL et al. World J Emerg Surg 2021

Abdominal Compartment Syndrome

- Bladder pressure with bladder catheter
- NGT/rectal tube
- Optimize sedation and analgesia
- Consider muscle relaxants
- Diuretics
- Enemas, prokinetic agents
- Early enteral nutrition
- Percutaneous drainage of fluid
- Surgical decompression when IAH>25mmHg

Trikudanathyan et al. Pancreatology 2014.; Husu HL et al. World J Emerg Surg 2021

CCY Timing in Mild Gallstone Pancreatitis

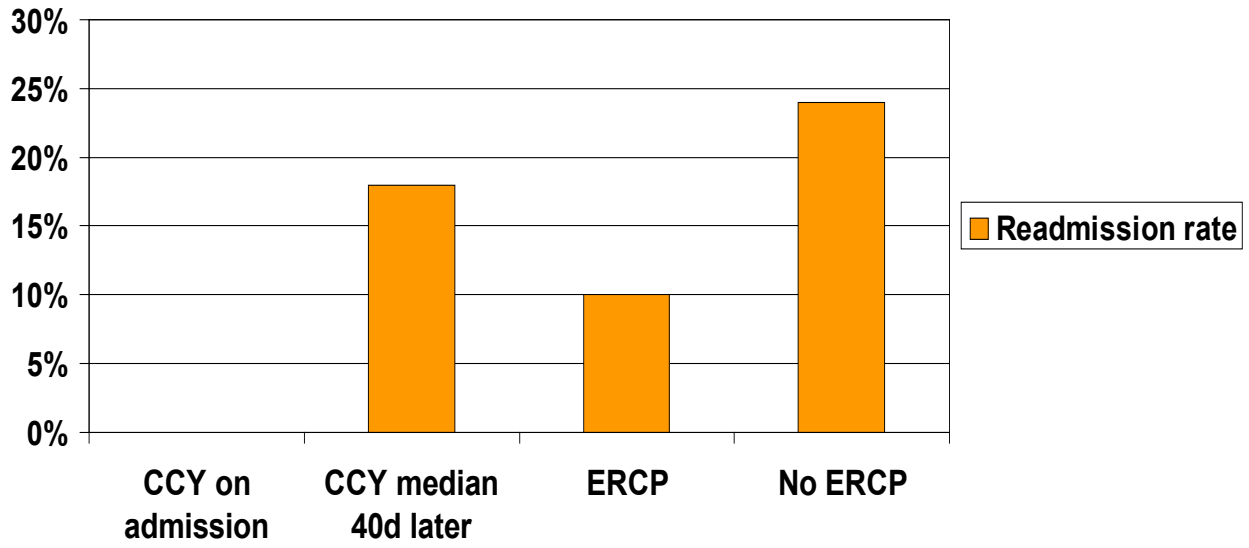
- When should patients undergo CCY after mild acute gallstone pancreatitis?

Baal et al. Ann Surg 2012; Williams et al. Gut 2017.

CCY Timing in Mild Gallstone Pancreatitis

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

BEFORE DISCHARGE



- In non-surgical pts, ERCP with sphincterotomy

Baal et al. Ann Surg 2012; Williams et al. Gut 2017.

Role of ERCP in Acute Gallstone Pancreatitis

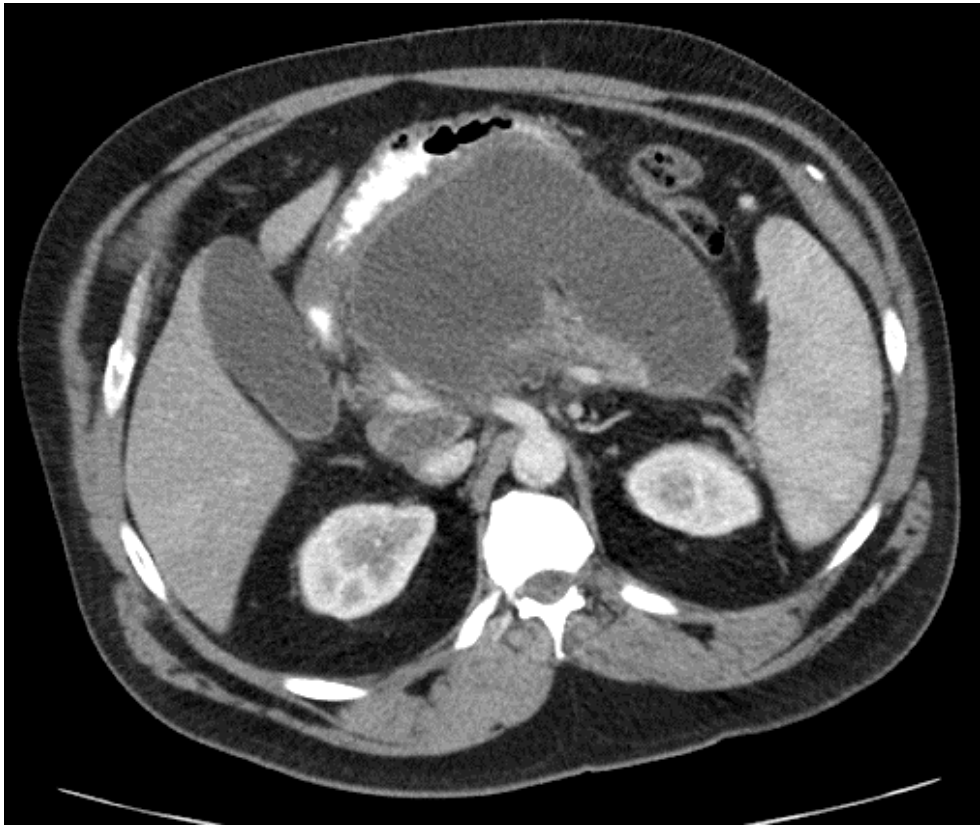
- ERCP within 72hrs
  - ✓Cholangitis
  - ✓CBD stone
  - ✓Post-operative CBD stone removal

- Not indicated for severe gallstone pancreatitis
  - ✓Urgent ERCP did not reduce complications or mortality compared with conservative management

Schepers NJ et al. Lancet 2020.

Case 4

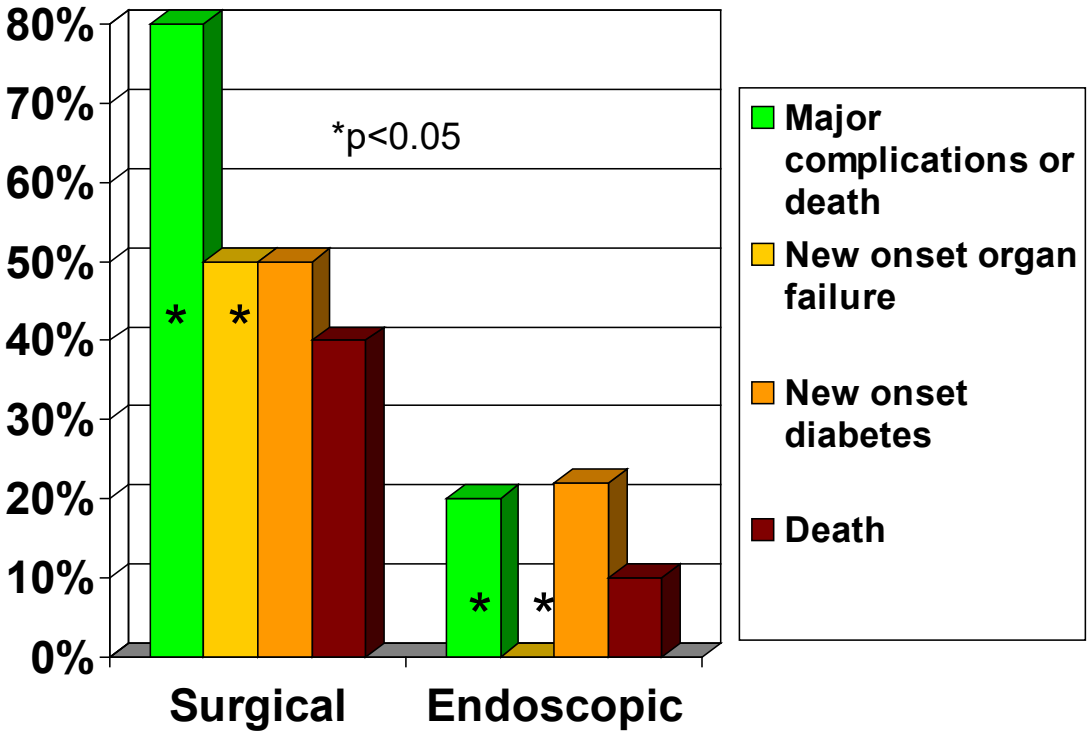
- 54yo male necrotizing gallstone pancreatitis 5 weeks ago, transiently intubated now on floor with abdominal pain and unable to eat. No organ failure.



Approach to WON

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

Endoscopic vs. Surgical Necrosectomy



Bakker et al. JAMA 2012; van Brunschot et al. Lancet 2018.

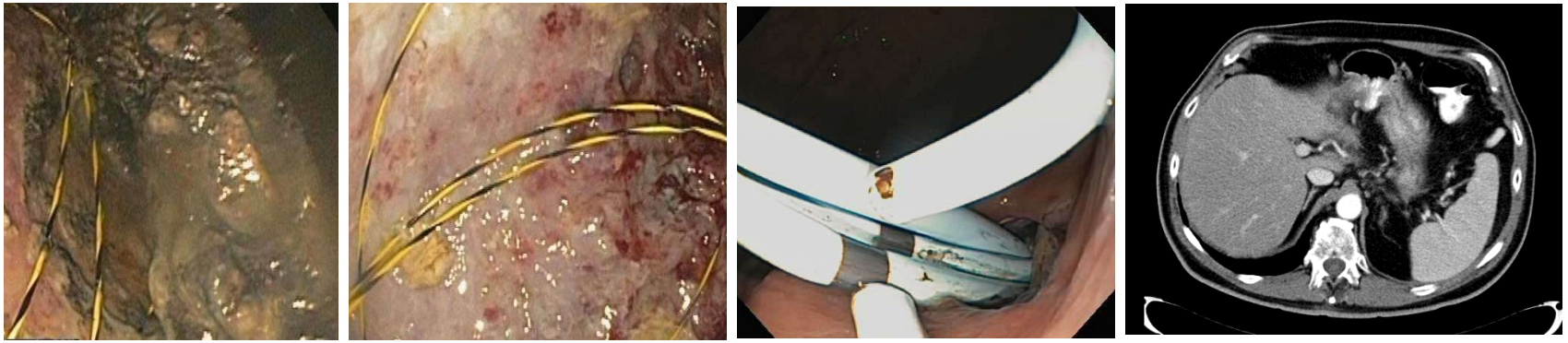
Endoscopic v. Percutaneous Approach

Primary Modality Results

Procedural Experience		
	DEN (n = 12)	**SUA (n = 12)**
Time from onset to initial procedure, wk	7.2 ± 1.8	5.2 ± 1.0
Procedures per patient *	1.4 ± 0.2 DEN	2.0 ± 0.2 PCD
Fluid culture positive	8	6
ICU LOS, days *	0.2	5.4 ± 2.5
Floor LOS, days	5.0 ± 1.4	11.6 ± 3.4
Clinical resolution‡	11/12	3/12

Kumar N et al. Pancreas 2014.

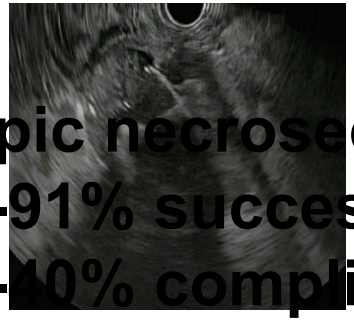
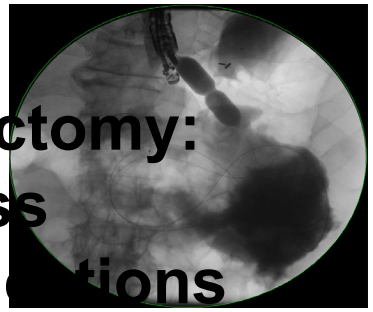
Endoscopic Necrosectomy



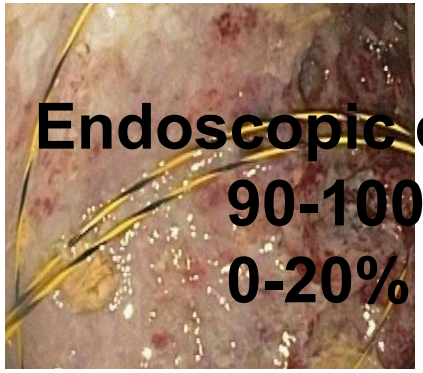
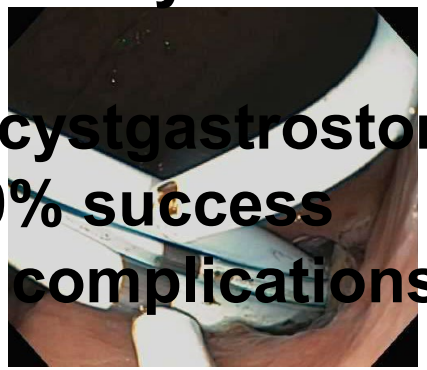
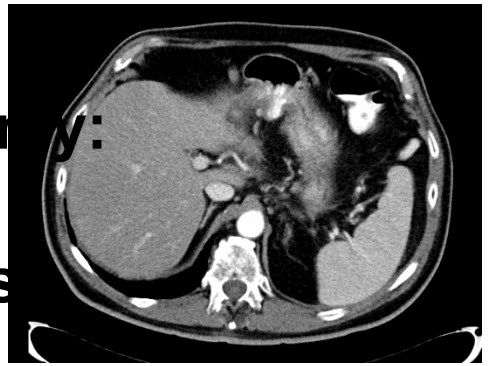
Thompson CC et al. Pancreatology 2016.

Endoscopic Necrosectomy



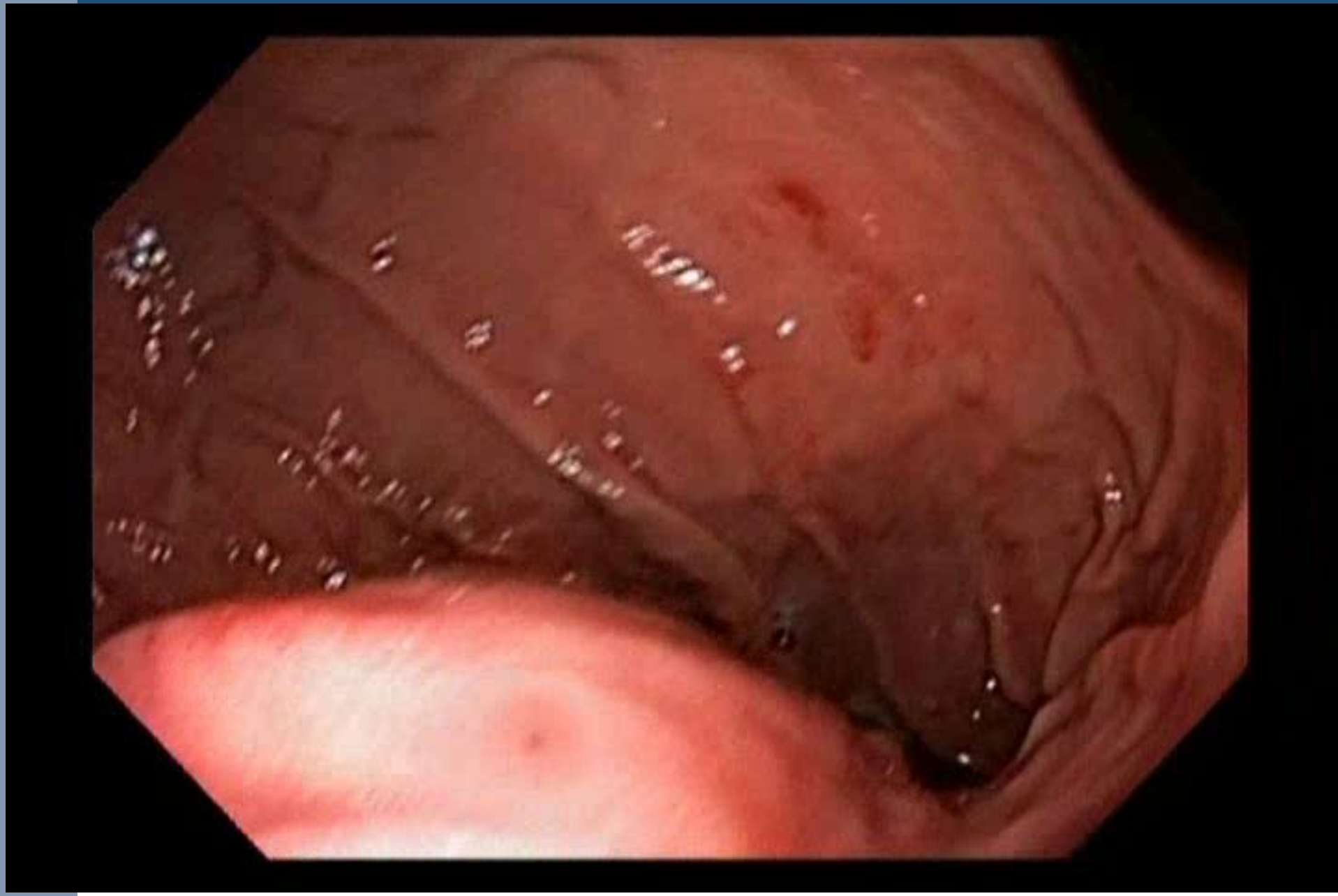




Endoscopic necrosectomy:
69-91% success
20-40% complications
6% mortality

Endoscopic cystgastrostomy:
90-100% success
0-20% complications

Thompson CC et al. Pancreatology 2016.



Courtesy of Dr. Christopher Thompson
Director of Endoscopy BWH

Pancreatic Necrosis/ Pseudocyst

- Decision points:
  - **Symptoms** present?
  - Necrosis/ fluid **collection mature**? (≥4 weeks)
- No symptoms: no intervention, but should be followed in pancreas center

Pancreatic Necrosis/ Pseudocyst

- Symptomatic sterile or infected necrosis:
  - **Endoscopic necrosectomy (>4 wks with wall)**
  - **Radiologic percutaneous drain (<4 wks)**
  - Surgical necrosectomy

Take Home Points

- CBD stones: intermediate probability, EUS, MRCP, IOC
- CCY after ERCP for CBD stone
- Emergent ERCP (<24h) only severe cholangitis (Tokyo)
- Early ERCP (<72h) in acute gallstone pancreatitis: cholangitis or retained CBD stone
- In acute pancreatitis, determine etiology (gallstone, Etoh, smoking)
- Tons (LR 250-500cc/h) of IVF especially 1st 24h
- Recheck BUN, Hct within 1st 24h and tailor fluids

Take Home Points

- Mild pancreatitis: PO solids when pt improving
- Moderate/ severe pancreatitis: PO/NGT/ NJT within 72 hours
- 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!