Evidence based management of acute pancreatitis

Arjun Chatterjee, MD

Gastroenterology & Hepatology Fellow, Cleveland Clinic

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Faculty disclosures

- Arjun Chatterjee, MD

No relevant financial relationships with ineligible companies to disclose.

Learning objectives

1. Choose initial fluids and nutrition using current evidence
2. Recognize deterioration and select appropriate imaging, antibiotics, and intervention
3. Prevent recurrent pancreatitis before discharge

AUDIENCE QUESTION

Case 1: initial fluid orders

A 52-year-old woman, 70 kg, has epigastric pain and vomiting for 10 hours. Lipase is 1,800 U/L (ULN 60).

BP 112/70, HR 104. Dry mucosa, BUN 28 mg/dL, Cr 1.1 mg/dL. No heart failure or CKD.

Which initial fluid plan is most appropriate?

A. LR 20 mL/kg bolus, then 3 mL/kg/h

B. LR 10 mL/kg bolus, then 1.5 mL/kg/h with reassessment

C. No IV fluid until CT confirms pancreatitis

D. Normal saline at 500 mL/h for 24 hours

Answer B: moderate LR with reassessment

- Clinical hypovolemia: LR bolus 10 mL/kg
- Then approximately 1.5 mL/kg/h initially
- For 70 kg: 700 mL bolus, then 105 mL/h
- Reassess early and adjust to perfusion, congestion, and oral intake

Diagnosis, etiology, and imaging: first 24 hours

- Diagnose AP with 2 of 3: typical pain, enzymes ≥3× ULN, or characteristic imaging
- Find the cause now: alcohol/medications/prior AP + LFTs, triglycerides, calcium, and RUQ ultrasound
- CT/MRI is not routine when pain + enzymes establish the diagnosis; use it for uncertainty or deterioration
- For necrosis/severity staging, CT is most informative after ~72 h; do not trend lipase as a treatment target

Recurrent or unexplained pancreatitis

- Re-check history/medications and obtain LFTs, triglycerides, calcium, and a high-quality abdominal ultrasound

- If still unexplained: repeat ultrasound when appropriate → EUS → MRCP for occult biliary/structural disease

- Consider occult pancreatic tumor when no cause is found, particularly in adults >40 years or with red flags

- Recurrent disease, young onset, or family history may justify genetic evaluation/counseling

Severity depends on organ failure

Category	Definition
Mild	No organ failure or local/systemic complications
Moderately severe	Transient organ failure (<48 h) and/or local or systemic complications
Severe	Persistent organ failure (>48 h), single or multiple organs

- **Early red flags: persistent SIRS, rising BUN/creatinine, new oxygen need, or evolving organ dysfunction — escalate before the 48-hour label is known**

Early risk flags and organ failure

• SIRS at admission — especially if persistent at 48 hours — identifies a higher-risk trajectory

• Persistent organ failure >48 hours is the defining feature of severe AP and the most important severity outcome

• Modified Marshall score ≥2 in respiratory, cardiovascular, or renal systems defines organ failure

• Serial physiology and treatment response matter more than a single admission prediction score

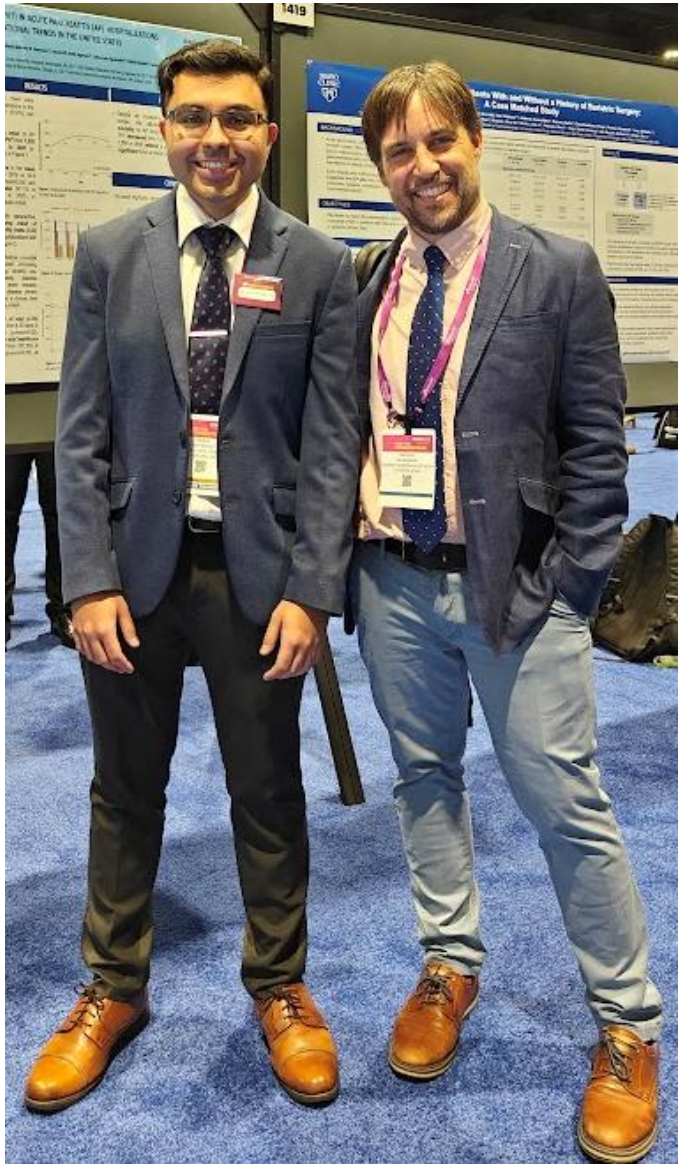
Reassessment determines the level of care

- Reassess BP/MAP, heart rate, oxygen requirement, mental status, urine output, and volume status

- Trend BUN, creatinine, hematocrit, electrolytes, and trajectory of SIRS rather than a single score

- Persistent SIRS or worsening perfusion/oxygenation warrants monitored care and earlier escalation

- Scoring systems (BISAP, Ranson's, APACHE-II) and imaging alone are not accurate in determining which patients will develop moderately severe or severe AP. They are best at predicting mild AP.



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Aggressive or Moderate Fluid Resuscitation in Acute Pancreatitis

E. de-Madaria, J.L. Buxbaum, P. Maisonneuve, A. García García de Paredes, P. Zapater, L. Guilabert, A. Vaillo-Rocamora, M.Á. Rodríguez-Gandía, J. Donate-Ortega, E.E. Lozada-Hernández, A.J.R. Collazo Moreno, A. Lira-Aguilar, L.P. Llovet, R. Mehta, R. Tandel, P. Navarro, A.M. Sánchez-Pardo, C. Sánchez-Marin, M. Cobreros, I. Fernández-Cabrera, F. Casals-Seoane, D. Casas Deza, E. Lauret-Braña, E. Martí-Marqués, L.M. Camacho-Montaño, V. Ubieto, M. Ganuza, and F. Bolado, for the ERICA Consortium*

CLEVELAND CLINIC JOURNAL OF MEDICINE

What fluids should I order for my patient with acute pancreatitis?

Anusha Agarwal, MD, Arjun Chatterjee, MD and Prabhleen Chahal, MD

Cleveland Clinic Journal of Medicine August 2024, 91 (8) 466-468; DOI: https://doi.org/10.3949/ccjm.91a.24027

1-Minute Consult

A fluid prescription includes a stopping plan

Bedside finding	Action
Hypovolemia without congestion	Measured LR bolus, then reassess response
Adequate perfusion + oral intake	Reduce or stop IV fluids
New hypoxemia or congestion	Pause/reduce fluids; evaluate the cause
Persistent hypotension or organ failure	Critical care; individualized hemodynamic support

- **Reassess within 3–6 h. Reasonable adequacy targets: MAP 65–85, urine output ≥0.5 mL/kg/h, Hct <44%; follow BUN/Cr and congestion**

Vomiting
Decreased oral intake
Fluid sequestration
Vasodilation
Increased vascular permeability

IV volume depletion

Bacterial translocation

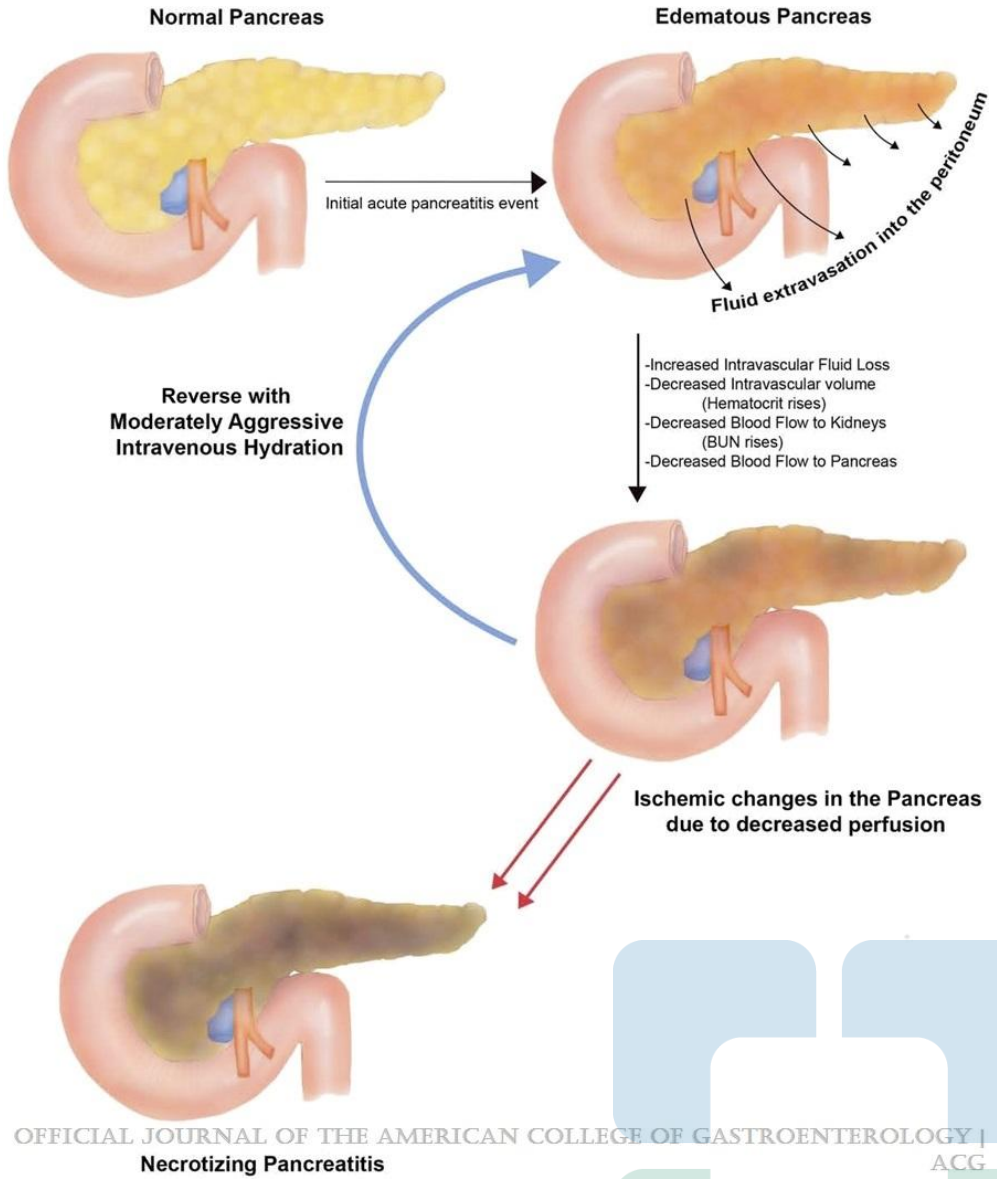
Intestinal ischemia

Hypotension
Shock
Prerenal azotemia
Cardiac ischemia

Pancreatic ischemia

Pancreatic necrosis

INDUCED



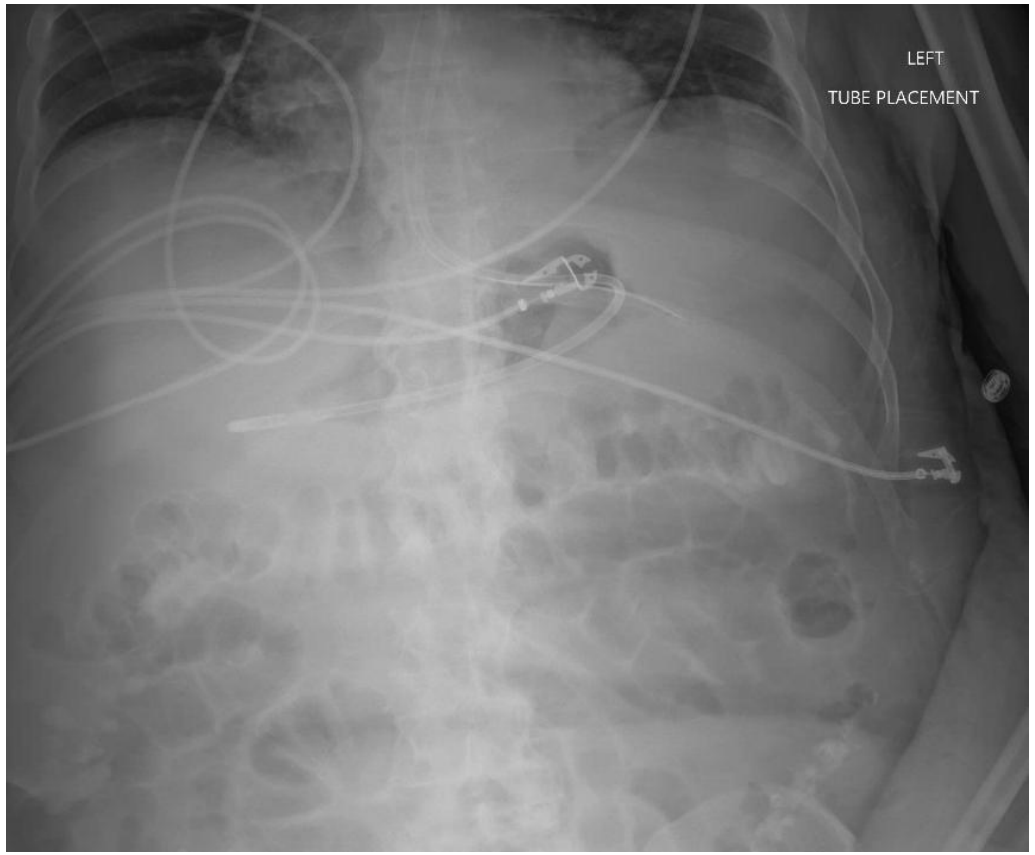
Case 1 variation: new oxygen need

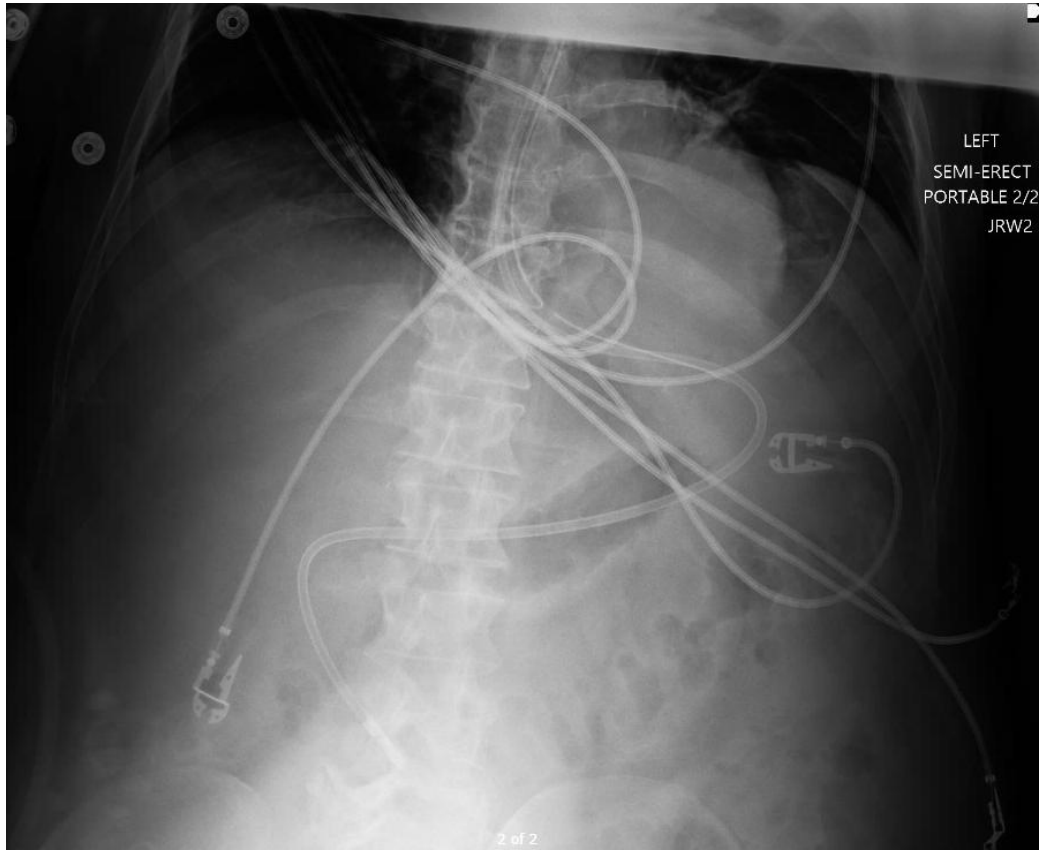
- New dyspnea and a 3 L oxygen requirement after repeated IV fluid: stop and reassess before the next liter

- Examine perfusion and lungs; review cumulative balance, urine output, BUN/Cr, and bedside imaging when useful

- Consider overload alongside ARDS, atelectasis, aspiration, pneumonia, and other causes of hypoxemia

- Do not reflexively bolus or diurese. Treat the dominant physiology; escalate if organ failure evolves





20. Using a nasogastric rather than nasojejunal route for delivery of enteral feeding is preferred because of comparable safety and efficacy.

Pancreas. 2026 Mar 1;55(3):e316-e322. doi: 10.1097/MPA.0000000000002583.

Outcomes of Early Enteral Feeding (<48 Hours) in Patients With Predicted Severe Acute Pancreatitis

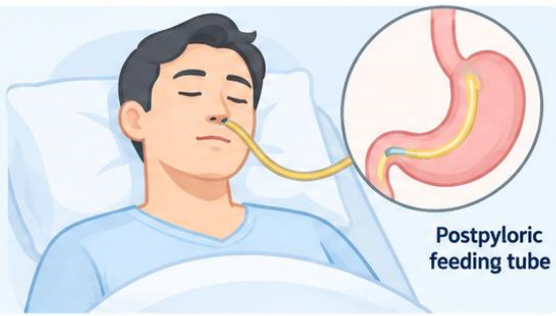
Study Design

Retrospective cohort

83 adults with predicted severe acute pancreatitis

Early EEN: 27 patients (<48 h)
Late feeding: 56 patients (>48 h)

Predicted SAP = BISAP score ≥ 2



Key Findings

Shorter ICU stay
14.7 vs 25.4 days
P = 0.011

Fewer pancreatic fluid collections
22.2% vs 48.2%
P = 0.043

Fewer GI complications
48.1% vs 75%
P = 0.03

Take-Home Message

Starting enteral nutrition within 48 hours was associated with better outcomes, including fewer complications, lower ICU needs, and lower costs.

Early enteral nutrition should be considered standard care in predicted severe acute pancreatitis, with future prospective studies needed.

Arjun Chatterjee [1], Zehra Naseem [2], Ridhima Kaul [2], Renan Prado [2], Raj Jessica Thomas [3], Hisham Wehbe [1], Rupayan Kundu [2], Renee Wu [4], Qijun Yang [4], John McMichael [1], Syed Mohiuddin [1], Tyler Stevens [1], Prabhleen Chahal [5]

Analgesia and supportive ward care

- Titrate analgesia to pain severity, breathing, mobility, sleep, and ability to eat

- Use multimodal/nonopioid therapy when appropriate; opioids remain appropriate for substantial pain

- Avoid NSAIDs with AKI or significant bleeding risk; reassess IV opioid need as physiology improves

- Treat nausea, monitor glucose/electrolytes, mobilize, and provide standard VTE prophylaxis when safe





Drug-induced pancreatitis: diagnose cautiously

Rare diagnosis • false attribution is common

WHEN TO SUSPECT

- A new medication or dose change has a plausible temporal relationship to the attack
- Common causes have been actively assessed: gallstones, alcohol, triglycerides, calcium, and structural disease when appropriate
- Improvement after withdrawal (dechallenge) supports causality, but is nonspecific
- **Positive rechallenge** = recurrence after re-exposure; strongly supports causality. **Do not intentionally rechallenge.**

EVIDENCE MATTERS

Best-supported drugs

- **Azathioprine**
- **6-mercaptopurine**
- **Didanosine**

Most other reported drug associations rely on case reports or lower-quality evidence.

Clinical move: stop the most plausible culprit, continue standard AP care, document the reasoning, and avoid a permanent drug label without convincing evidence.

Saini et al. Clin Transl Gastroenterol 2023;14:e00621 / Tenner et al. Am J Gastroenterol 2024;119:419–437

AUDIENCE QUESTION

Case 1: does she need urgent ERCP?



Ultrasound shows gallstones. CBD is 5 mm. Bilirubin falls from 2.2 to 1.0 mg/dL.

She is afebrile, improving, and tolerating a diet.

What is the best next step?

A. Urgent ERCP for every episode of gallstone pancreatitis

B. Antibiotics and interval cholecystectomy in 6 weeks

C. Surgical evaluation for cholecystectomy this admission

D. Daily lipase until normal before any intervention

Answer C: cholecystectomy this admission

- Improving mild biliary AP: arrange cholecystectomy before discharge
- Urgent ERCP is unnecessary without cholangitis or ongoing obstruction
- A falling bilirubin supports spontaneous passage of the stone
- Severe or necrotizing disease needs individualized surgical timing

ERCP depends on the biliary complication

Clinical situation	Approach
Acute cholangitis	Antibiotics + urgent ERCP, usually within 24 h
Persistent biliary obstruction	Prompt GI review and therapeutic ERCP as indicated
Uncertain retained stone, stable patient	EUS or MRCP before diagnostic ERCP
No cholangitis or ongoing obstruction	Supportive care + recurrence prevention

- **APEC: predicted severity alone did not justify routine urgent ERCP**

PONCHO: same-admission cholecystectomy

- PONCHO: recovering patients with mild gallstone pancreatitis
- Gallstone-related readmission or death within 6 months
- 17% with interval surgery versus 5% with same-admission surgery
- Arrange the surgical plan before discharge

THE LANCET

Same-admission versus interval cholecystectomy for mild gallstone pancreatitis (PONCHO): a multicentre randomised controlled trial

David W da Costa, MD [a,†] · Stefan A Bouwense, MD [d,†] · Nicolien J Schepers, MD [b,f] · Marc G Besselink, PhD [h] · Hjalmar C van Santvoort, PhD [h] · Sandra van Brunschot, MD [i] · et al. Show more

Case 2: deterioration on day 4

A 61-year-old man with alcohol-associated AP initially stabilizes after measured resuscitation

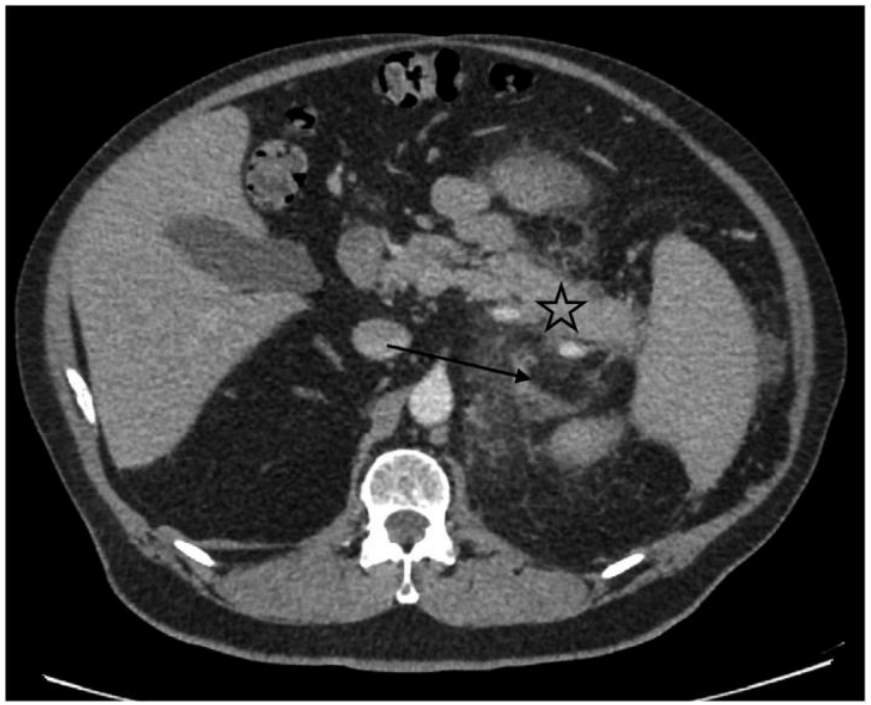
By day 4: persistent pain/vomiting, failed oral intake, rising oxygen need, and worsening physiology

Contrast CT now shows pancreatic necrosis with an acute necrotic collection

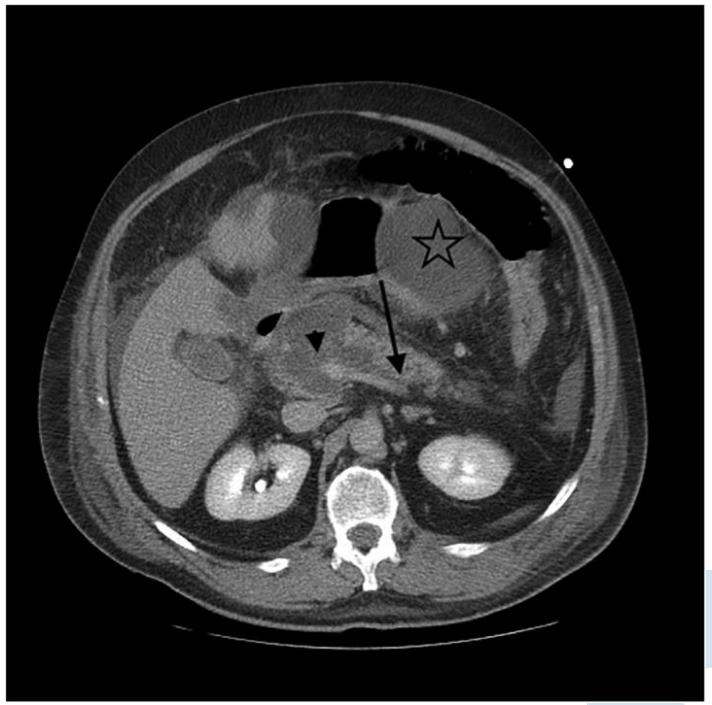
Escalate monitoring, maintain enteral nutrition, and involve a multidisciplinary/high-volume pancreas team early

CT appearance of pancreatic necrosis

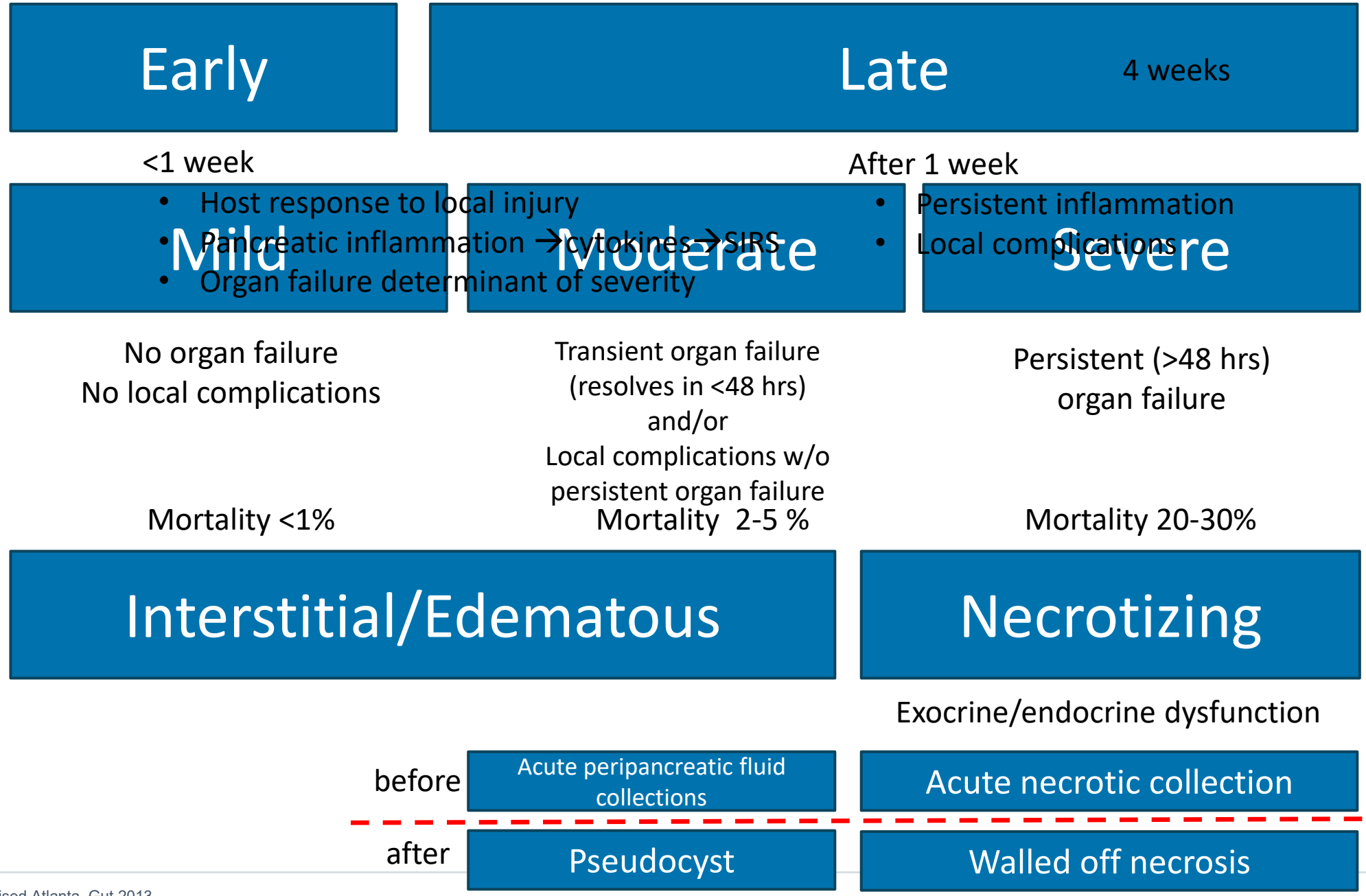
- Interstitial pancreatitis



- Necrotizing pancreatitis



- **Necrosis alone does not establish infection or require drainage**


Early
Late
4 weeks
<1 week
Host response to local injury
Pancreatic inflammation →cytokines→SIRS
Organ failure determinant of severity
After 1 week
Persistent inflammation
Local complications
Mild
Moderate
Severe
No organ failure
No local complications
Transient organ failure
(resolves in <48 hrs)
and/or
Local complications w/o
persistent organ failure
Persistent (>48 hrs)
organ failure
Mortality <1%
Mortality 2-5 %
Mortality 20-30%
Interstitial/Edematous
Necrotizing
Exocrine/endocrine dysfunction
before
Acute peripancreatic fluid collections
Acute necrotic collection
after
Pseudocyst
Walled off necrosis

Antibiotics for suspected or proven infection

- Sterile necrosis: no prophylactic antibiotics

- Suspect infected necrosis with gas, positive cultures/bacteremia, sepsis, or unexplained clinical deterioration

- Fever, leukocytosis, CRP, or procalcitonin alone should not trigger antibiotics; search for extrapancreatic infection and obtain cultures

- If infection is likely: IV enteric coverage → cultures/local resistance → source-control plan

AUDIENCE QUESTION

Case 2: infected necrosis on day 12



He develops fever and bacteremia. CT shows gas within necrosis.

After antibiotics, BP is stable and oxygen need is improving.

What is the best next step?

A. Immediate open necrosectomy

B. Drain every infected collection within 24 hours

C. Antibiotics and close monitoring, deferring drainage if improvement continues

D. Stop antibiotics because the collection is not yet walled off

Answer C: antibiotics and reassessment

- Continue antibiotics, enteral nutrition, and close reassessment
- When feasible, allow the collection to organize, often about 4 weeks
- Deterioration or inadequate source control can require earlier drainage
- Persistent shock, ischemia, or perforation cannot wait for maturation

Antibiotic selection in infected necrosis

- Choose IV therapy with pancreatic penetration and enteric coverage
- Examples include piperacillin–tazobactam or a carbapenem when indicated
- Adjust for allergy, kidney function, cultures, and local resistance
- Reassess duration with clinical response and source control. Routine antifungal prophylaxis is unnecessary

POINTER: timing of drainage

Outcome	Immediate	Postponed
Complication index, mean	57	58
Interventions, mean	4.4	2.6
Mortality	13%	10%

Conditional recommendation (low certainty): favor delayed drainage over immediate drainage for suspected infected pancreatic/peripancreatic collections in the early phase.

POINTER: 39% in the postponed arm avoided drainage.

The NEW ENGLAND JOURNAL of MEDICINE

Immediate versus Postponed Intervention for Infected Necrotizing Pancreatitis

Authors: Lotte Boxhoorn, M.D., Sven M. van Dijk, M.D., Ph.D., Janneke van Grinsven, M.D., Ph.D., Robert C. Verdonk, M.D., Ph.D., Marja A. Boermeester, M.D., Ph.D., Thomas L. Bollen, M.D., Ph.D., Stefan A.W. Bouwense, M.D., Ph.D., +36, for the Dutch Pancreatitis Study Group* Author Info & Affiliations

Published October 6, 2021 | N Engl J Med 2021;385:1372-1381 | DOI: 10.1056/NEJMoa2100826 | VOL. 385 NO. 15

A step-up approach to necrosis

1. Stabilize organs, provide enteral nutrition, and treat proven/suspected infection
2. If stable, delay intervention ~3–4 weeks when feasible; drain earlier if medical treatment fails or the patient deteriorates
3. If intervention is required and the collection is endoscopically amenable, favor an endoscopic transluminal approach over a minimally invasive surgical step-up approach
4. Use a minimally invasive step-up strategy rather than open necrosectomy; escalate only as needed

Complications that require urgent escalation

New finding	Concern and response
Bleeding or falling hemoglobin	Pseudoaneurysm/hemorrhage: urgent imaging and IR/surgery
Tense abdomen + worsening organ function	Compartment syndrome: ICU and surgical assessment
Peritonitis or suspected bowel ischemia	Urgent surgical evaluation
Uncontrolled sepsis or worsening organ failure	Reassess antibiotics, drainage, and source control

VTE prophylaxis and splanchnic thrombosis

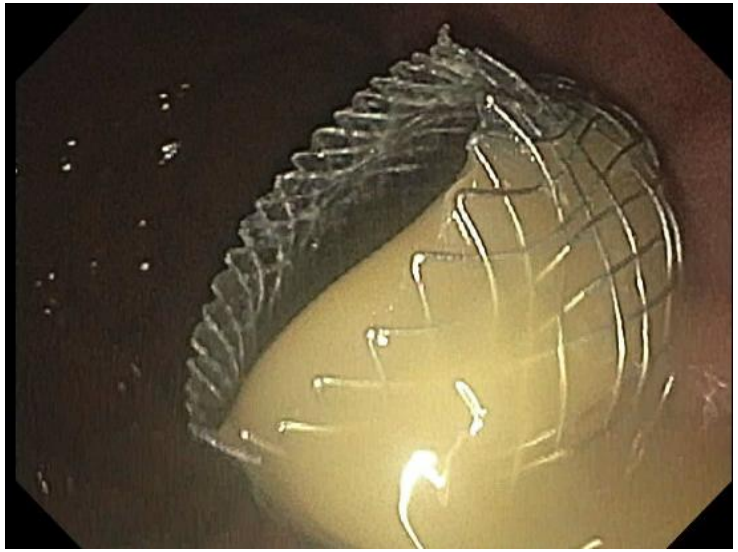
- Continue standard inpatient VTE prophylaxis when bleeding risk permits

- Acute pancreatitis–associated splanchnic vein thrombosis is a separate therapeutic-anticoagulation decision

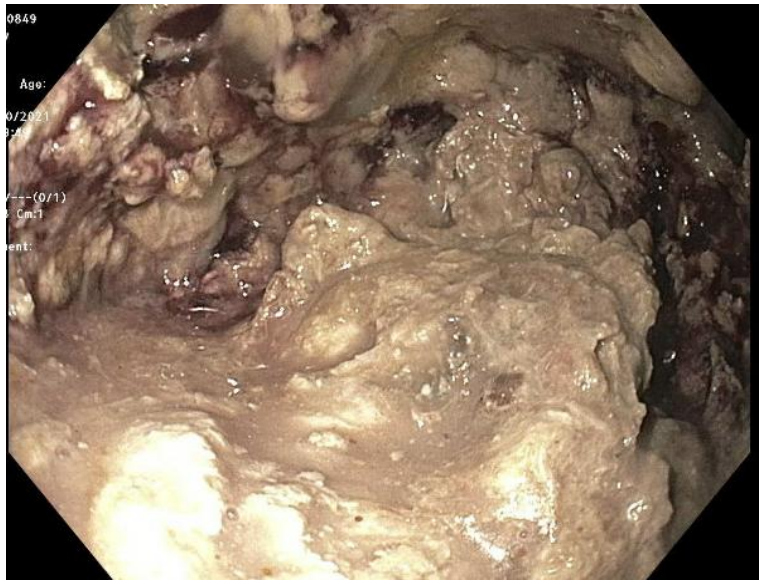
- Conditional recommendation (very low certainty): favor anticoagulation over no anticoagulation for acute splanchnic vein thrombosis

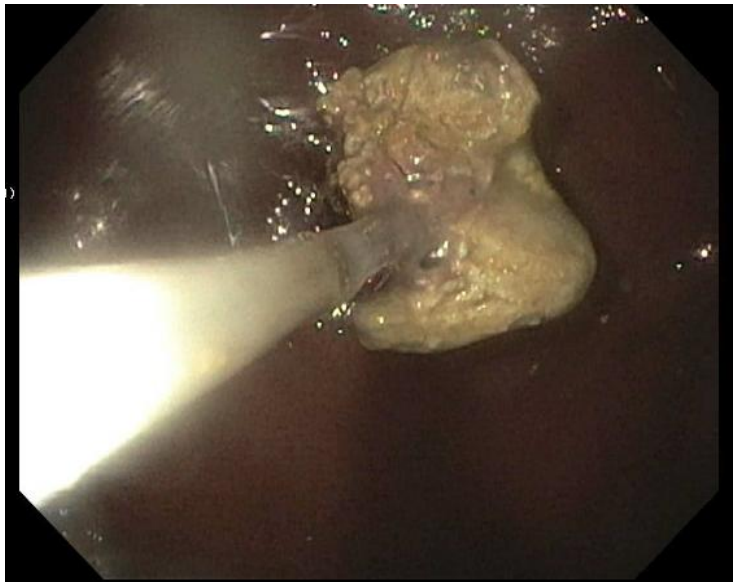
- Implementation: generally anticoagulate portal or superior mesenteric thrombosis; do not routinely anticoagulate isolated splenic-vein thrombosis


14:45.01
MI =0.43 TIS< 0.4 100% 20Hz
R7.0 C69 D80 A1






Age:





Discharge and recurrence prevention

• Discharge when oral intake is adequate, physiology is stable, pain is manageable, and there is no persistent fever

• Biliary AP: same-admission cholecystectomy for mild disease; delay when severe disease/collections make surgery unsafe

• Address alcohol, smoking, triglycerides, and culprit medications before discharge — recurrence prevention starts now

• Unexplained AP: repeat US → EUS → MRCP as needed; consider occult pancreatic tumor, especially after age 40

• After complicated AP: assess steatorrhea/weight; screen glucose/A1c at 3–6 months and annually

Future Directions in Pancreatitis Management

Targeted Therapy for Systemic Inflammation:

- Promising drugs include LMW Heparin (decreased mortality, multiple organ failure), extracorporeal removal of cytokines (CytoSorb®), and IL-6 antagonists (Tocilizumab).
- Ongoing trials for TNF-α antagonists, steroids, and Ca2+ channel (ORAI1) inhibitors

Ongoing Randomized Controlled Trials (RCTs):

- **HTGP:** Bi-TPAI trial (intensive insulin vs plasmapheresis) and ELEPHANT trial (plasmapheresis, insulin & heparin, aggressive IV resuscitation).
- **Biliary AP (inoperable):** Spanish multicenter double-blinded RCT on UDCA vs. placebo. RCTs are needed to prove the benefit of biliary sphincterotomy in high-risk patients. Prospective studies are needed for EUS-GBD as secondary prevention.
- **Pain Management:** Future studies need improved intervention design, sample sizes, and outcome assessment (e.g., co-primary endpoints for rescue analgesic dose and pain control)

Key takeaways: 5 decisions to carry into practice

1. Moderate LR + measured bolus only when indicated; reassess early and de-escalate
2. Feed early: oral low-fat solid diet first; enteral tube feeding if oral intake fails
3. Antibiotics for infection; ERCP for cholangitis/retained CBD stone — not simply because AP is biliary
4. Necrosis: multidisciplinary, step-up care; delay intervention when the patient is stable
5. Prevent recurrence before discharge; plan diabetes and exocrine-insufficiency follow-up

Selected references: guidelines and trials

IAP/APA/EPC/IPC/JPS Working Group. International Association of Pancreatology Revised Guidelines on Acute Pancreatitis 2025. Pancreatology. 2025;25:770–814. doi:10.1016/j.pan.2025.04.020

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