Pancreatitis

Rahm Makan

Acute Pancreatitis

- Incidence 20-40/100000 (Europe)
- Rising incidence due to
  - Increased alcoholism
  - Increased incidence of obesity related gallstones

Roberts SE, Morrison-Rees S, John A, et al. The incidence and aetiology of acute pancreatitis across Europe.Pancreatology 2017;17:155–65

Acute Pancreatitis

- Definition:
  - Symptoms consistent with pancreatitis
    - Epigastric or left upper quadrant pain radiating to the back
  - Serum amylase or lipase greater than three times the upper limit of normal.
  - Radiological imaging consistent with pancreatitis

Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis— 2012. Revision of classification and definitions by international consensus. Gut 2013;62:102–11.

Risk factors

- Obstruction
  - **Gallstones** (**40-60%**), parasites, tumours, annular pancreas
- **Alcohol**(**~30%**)/toxins/drugs
- Metabolic
  - Hypertriglyceridaemia, Diabetes, Hypercalcaemia
- Infection
- Vascular disorders
  - Vasculitis, emboli, Hypotension
- Trauma
- Post ERCP
- Genetic
- Sphincter of ODDI dysfunction
- Smoking

Genetics

- Mutant trypsins - R122H, N29I
- CFTR
- SPINK1

Choudari CP, Fogel EL, Sherman S, et al. Pancreas divisum, pancreatitis and CFTR mutations. Gastrointest Endosc 1999;49:AB187.

Drugs

- Acetaminophen
- 5-Aminosalicylic acid compounds (sulfasalazine, azodisalicylate,
- mesalamine)
- l-Asparaginase
- Azathioprine
- Benazepril
- Bezafibrate
- Cannabis
- Captopril
- Carbimazole
- Cimetidine
- Clozapine
- Codeine
- Cytosine arabinoside
- Dapsone
- Didanosine
- Dexamethasone
- Enalapril
- Erythromycin
- Estrogen
- Fluvastatin
- Furosemide
- Hydrochlorothiazide
- Hydrocortisone

- Isoniazid
- Lamivudine
- Lisinopril
- Losartan
- Meglumine
- Methimazole
- Methyldopa
- Metronidazole
- 6-Mercaptopurine
- Nelfinavir
- Norethindrone/mestrol
- Pentamidine
- Pravastatin
- Procainamide
- Pyritinol
- Simvastatin
- Sulfamethazine
- Sulfamethoxazole
- Stibogluconate
- Sulindac
- Tetracycline
- Trimethoprim/sulfamethoxazole
- Valproic acid
- Interferon-α

Pathogenesis

- Conversion of trypsinogen to trypsin within acinar cells by Trypsin Activation Protein (TAP)
- Trypsin catalyses the conversion of pro-enzymes to active enzymes
  - Elastase
  - Phospholipase A2
  - Carboxypeptidase
- These enzymes auto digest the pancreas resulting in the release of more enzymes.
- Complement and kinin systems get activated
- Mechanisms to inhibit trypsin fail
  - Pancreatic secretory trypsin inhibitor (SPINK1) becomes overwhelmed and unable to inhibit trypsin
  - Mesotrypsin
  - Enzyme Y
  - Trypsin itself splits and inactivates trypsin
  - Alpha 1- antitrypsin, alpha 2 macroglobulin
  - Sequestration of pancreatic enzymes in compartments within acinar cell
  - Low intra cellular calcium levels

Bettinger JR, Grendell JH. Intracellular events in the pathogenesis of acute pancreatitis. Pancreas 1991;6:S2–6.

Pathogenesis

- Cellular pathway of injury
  - Acinar cell injury
  - Local inflammatory cytokines(TNF, PAF, IL-1,6,8)
  - Microcirculatory changes leading to ischaemia and oedema
- Disruption of pancreatic ducts leading to fluid collections
- Release of pancreatic enzymes into portal circulation
- ARDS causes by phospholipase A2 (lecithinase) which digests lung surfactant

Steer ML. Pathogenesis of acute pancreatitis. Digestion 1997;58:46–9.

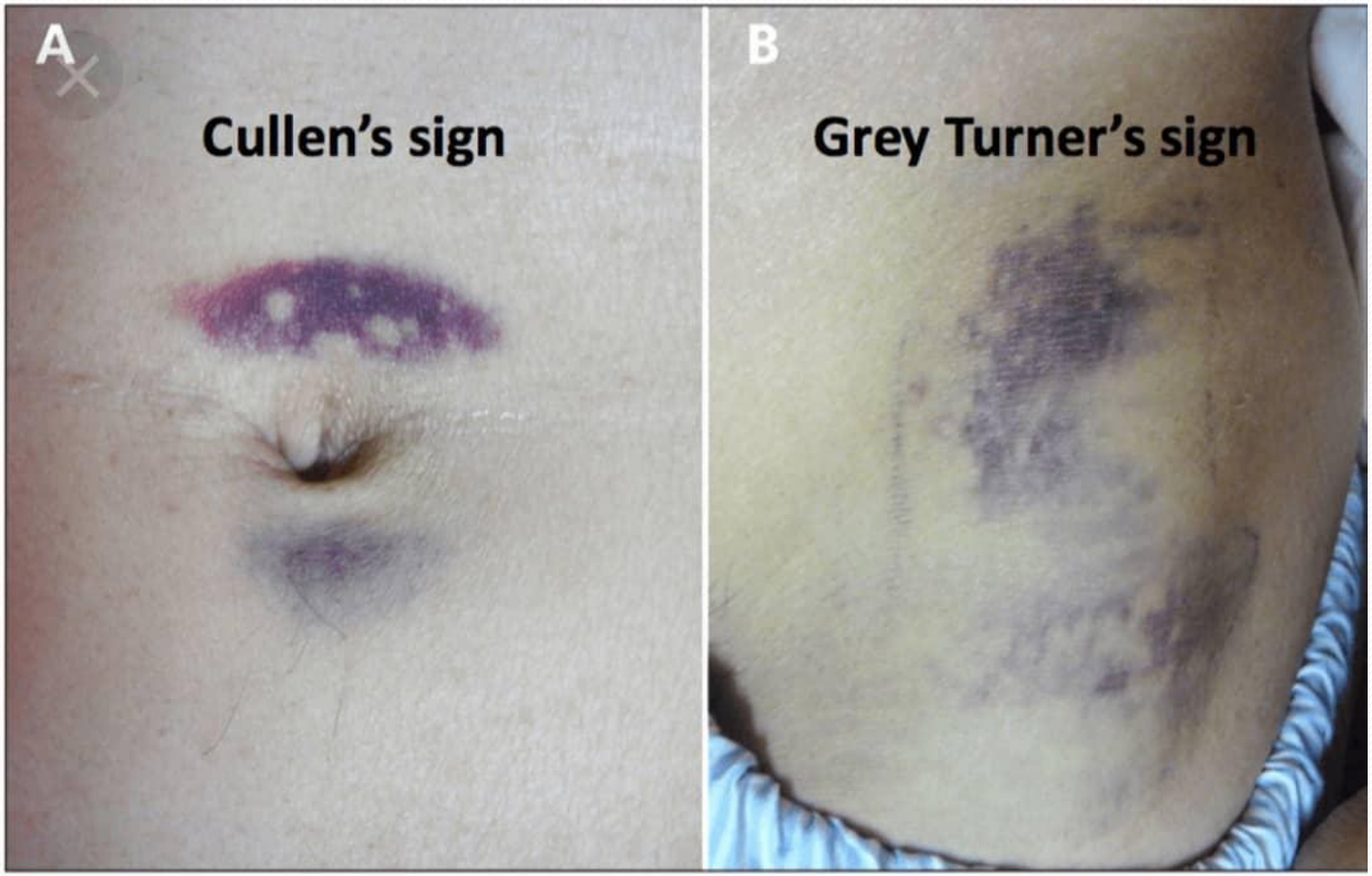
Alcohol

- Mechanisms
  - Necrosis-fibrosis sequence from recurrent and subclinical bouts of pancreatitis
  - Direct toxic effect of alcohol on acinar cells
  - Oxidative stress due to free radicals
  - Sentinel acute pancreatitis event – 2 hit model, inciting acute factor with underlying risk factors

Migliori M, Manca M, Santini D, et al. Does acute alcoholic pancreatitis precede the chronic form or is the opposite true? A histological study. J Clin Gastroenterol 2004;38:272–5.

Clinical presentation

- Epigastric pain, RUQ, rapid onset, no relieving factors, unbearable, steady.
- Guarding, distension from ileus
- Gray turner and Cullen signs
- Epigastric mass if pseudo cyst developed
- Haemodynamic instability depending no severity
- Delirium from alcohol withdrawal


A
Cullen's sign
B
Grey Turner's sign

Differential Diagnosis

BOX 58.6 Differential Diagnosis of Acute Pancreatitis

Biliary pain
Acute cholecystitis
Perforated hollow viscus (e.g., perforated peptic ulcer)
Mesenteric ischemia or infarction
Intestinal obstruction
Myocardial infarction
Dissecting aortic aneurysm
Ectopic pregnancy

Mortality Associated with Acute severe Pancreatitis

- 80-85% of patients will have mild disease
- 20% will have moderate to severe with a mortality rate of 13 to 35%.

- Therefore importance is placed on predicting which patients will have severe disease so that they can be monitored for complications.

Leppäniemi et al. World Journal of Emergency Surgery (2019) 14:27

Initial approach to patient

- Triage patients at risk of developing severe disease by presence/risk of organ failure and extensive necrosis
- Determine type of pancreatitis (obtain imaging)
  - Interstitial (mild)
  - Necrotising (more severe)
- Cautious fluid resuscitation
- Determine cause and treat if possible

Pierre-François Laterre, Christine Collienne, Improving the management of severe acute pancreatitis: The new guidelines from the French Society of Anaesthesia and Intensive Care Medicine, Anaesthesia Critical Care & Pain Medicine, Volume 41, Issue 3, 2022, 101103, ISSN 2352-5568,

BOX 58.2 Factors Associated With Severe Acute Pancreatitis

PATIENT CHARACTERISTICS

Age >55 yr[11,13,210,327]
Obesity (BMI >30 kg/m^2)[313]
Altered mental status[223,224]
Comorbid disease[11]
Systemic inflammatory response syndrome (SIRS)[11,20,217,223,224]
- Two or more of the following (SIRS criteria)
- Pulse >90/min
- Respirations >20/min or $PaCO_2$ <32 mm Hg
- Temperature >38°C or <36°C
- WBC count >12,000 or <4000/mm^3 or >10% band forms

LABORATORY FINDINGS

BUN >20 mg/dL or rising BUN level[225]
Elevated serum creatinine level[314]
Hematocrit >44% or rising hematocrit[231]

IMAGING FINDINGS

Pleural effusion(s)[195]
Pulmonary infiltrate(s)[11]
Multiple or extensive extrapancreatic fluid collections[203]

BUN, Blood urea nitrogen level.

Scoring systems

- Assess severity
  - Revised Atlanta Classification (most widely used)
  - APACHE II-O (predicts mortality)
  - BISAP
  - CT scoring system
  - CXR with bilateral pleural effusions confirms severe disease

- APACHE II demonstrated highest accuracy for prediction of SAP
- BISAP is simpler and has similar accuracy as APACHE II

Leppäniemi et al. World Journal of Emergency Surgery (2019) 14:27

The APACHE II Score

Physiologic Variable	High Abnormal Range						Low Abnormal Range		
	+4	+3	+2	+1	0	+1	+2	+3	+4
Rectal Temp (°C)	≥41	39-40.9		38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	≤29.9
Mean Arterial Pressure (mmHg)	≥160	130-159	110-129		70-109		50-69		≤49
Heart Rate	≥100	140-179	110-139		70-109		50-69	40-54	≤39
Respiratory Rate	≥50	35-49		25-34	12-24	10-11	6-9		≤5
Oxygenation a) FIO_2 ≥0.5 record A-aDO_2 b) FIO_2 <0.5 record PaO_2	≥500	350-499	200-349		<200 PO_2>70	PO_2 61-70		PO_2 55-60	PO_2 <55
Arterial pH	≥7.7	7.6-7.69		7.5-7.59	7.33-7.49		7.25-7.32	7.15-7.24	<7.15
HCO_3 (mEq/l)	≥52	41-51.9		32-40.9	22-31.9		18-21.9	15-17.9	<15
K (mEq/l)	≥7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		<2.5
Na (mEq/l)	≥100	160-179	155-159	150-154	130-149		120-129	111-119	≤110
S. Creat (mgm/dl)	≥3.5	2-3.4	1.5-1.9		0.6-1.4		<0.6		
Hematocrit (%)	≥60		50-59.9	46-49.9	30.45.9		20-29.9		<20
TLC (10^3/cc)	≥40		20-39.9	15-19.9	3-14.9		1-2.9		<1
GCS									

Age -score

<44 → 0
45-54 → 2
55-64 → 3
65-74 → 5
≥75 → 6

GCS:

15 → 0
14 → 1
13 → 2
12 → 3
11 → 4
10 → 5
9 → 6
8 → 7
7 → 8
6 → 9
5 → 10
4 → 11
3 → 12

JAMA 1993;270(24):2957-2963

APACHE II – O Score

- A modified APACHE II score including an obesity score to predict acute severe pancreatitis.
- BMI score is added onto the APACHE II score
  - 0 = normal (BMI <26)
  - 1 = mild obesity (BMI 26–30)
  - 2 = obese (BMI >30)
- At a cut-off of > 8, APACHE-O had sensitivity 82%, specificity 86%, positive predictive value 74%, negative predictive value 91% and overall accuracy 85%.

C.D. Johnson, S.K.C. Toh, M.J. Campbell Combination of APACHE-II score and an obesity score (APACHE-O) for the prediction of severe acute pancreatitis, Pancreatology, Volume 4, Issue 1, 2004, Pages 1-6, ISSN 1424-3903, https://doi.org/10.1159/000077021.

Modified Marshall Organ failure score

Organ system	Score 0*	Score 1	Score 2	Score 3	Score 4
Cardiovascular (systolic blood pressure)†	> 90 mm Hg	< 90 mm Hg (fluid responsive)	< 90 mm Hg (not fluid responsive)	< 90 mm Hg (pH < 7.3)	< 90 mm Hg (pH < 7.2)
Renal (serum creatinine)‡	< 1.4 mg/dL (≤ 134 micromol/L)	1.4–1.8 mg/dL (134–169 micromol/L)	1.9–3.6 mg/dL (170–310 micromol/L)	3.6–4.9 mg/dL (311–439 micromol/L)	> 4.9 mg/dL (> 439 micromol/L)
Respiratory (PaO2/FiO2)§	> 400 mm Hg	301–400 mm Hg	201–300 mm Hg	101–200 mm Hg	≤ 101 mm Hg

* A score of 2 or more in any organ system indicates organ failure.

† Off inotropic support.

‡ A score for patients with preexisting chronic kidney disease depends on the extent of further deterioration of baseline renal function. No formal correction exists for a baseline serum creatinine ≥ 1.5 mg/dL (≥ 134 micromol/L).

§ PaO2 in mm Hg; FiO2 is fractional inspired O2 in decimal fraction (eg, 0.5, rather than 50%).
For nonventilated patients, the FiO2 can be estimated from the following:
Supplemental oxygen: FiO2 (decimal fraction)

- Room air: 0.21
- 2 L/minute: 0.25
- 4 L/minute: 0.3
- 6–8 L/minute: 0.4
- 9–10 L/minute: 0.5

Santorini Consensus

Table 3
Outcome Statements for the Diagnosis of Acute Pancreatitis

In clinical practice, it is wise to consider all localized collections following necrotizing pancreatitis to be localized necrosis until proven otherwise (evidence category C)
Lipase estimation has slightly superior sensitivity and specificity and greater overall accuracy than amylase (evidence category A)
It is accepted that ultrasonography plays little part in the diagnosis or staging of acute pancreatitis (evidence category C)
Pancreatic imaging by CT provides good evidence of the presence or absence of pancreatitis (evidence category C)

Table 6
Suggested Cutoff Values for Proven Markers of Severity

Obesity	BMI > 30
Chest radiography	Left/bilateral effusion
APACHE II	≥6
APACHE O[a]	≥6
CRP	>150 mg/L

[a]APACHE II plus 1 point BMI 25–30, 2 points BMI > 30.

Dervenis C, Johnson CD, Bassi C, Bradley E, Imrie CW, McMahon MJ, Modlin I. Diagnosis, objective assessment of severity, and management of acute pancreatitis. Santorini consensus conference. Int J Pancreatol. 1999 Jun;25(3):195-210. doi: 10.1007/BF02925968. PMID: 10453421.

Acute Pancreatitis

- Atlanta Classification
  - Mild
    - No organ failure, no local or systemic complications
  - Moderately severe
    - Transient organ failure <48hrs
    - Local or systemic complications without persistant organ failure, includes pseudo cyst, fluid collections, necrosis
  - Severe
    - Persistent organ failure > 48h
      - APACHE-II>8.

Banks PA, Bollen TL, Dervenis C, et al: Classification of acute pancreatitis 2012: Revision of the Atlanta classification and definitions by international consensus. *Gut* 62:102–111, 2013. doi: 10.1136/gutjnl-2012-302779

Atlanta Classification

BOX 58.1 2012 Atlanta Classification Revision of Acute Pancreatitis[12]

MILD ACUTE PANCREATITIS

No organ failure
No local or systemic complications

MODERATELY SEVERE ACUTE PANCREATITIS

Transient organ failure (<48 hr) and/or
Local or systemic complications* without persistent organ failure

SEVERE ACUTE PANCREATITIS

Persistent organ failure (>48 hr)——single organ or multiorgan

*Local complications are peripancreatic fluid collections, pancreatic necrosis and peripancreatic necrosis (sterile or infected), pseudocyst, and walled-off necrosis (sterile or infected).

Bedside **I**ndex for **S**everity in **A**cute **P**ancreatitis (BISAP)

BISAP score

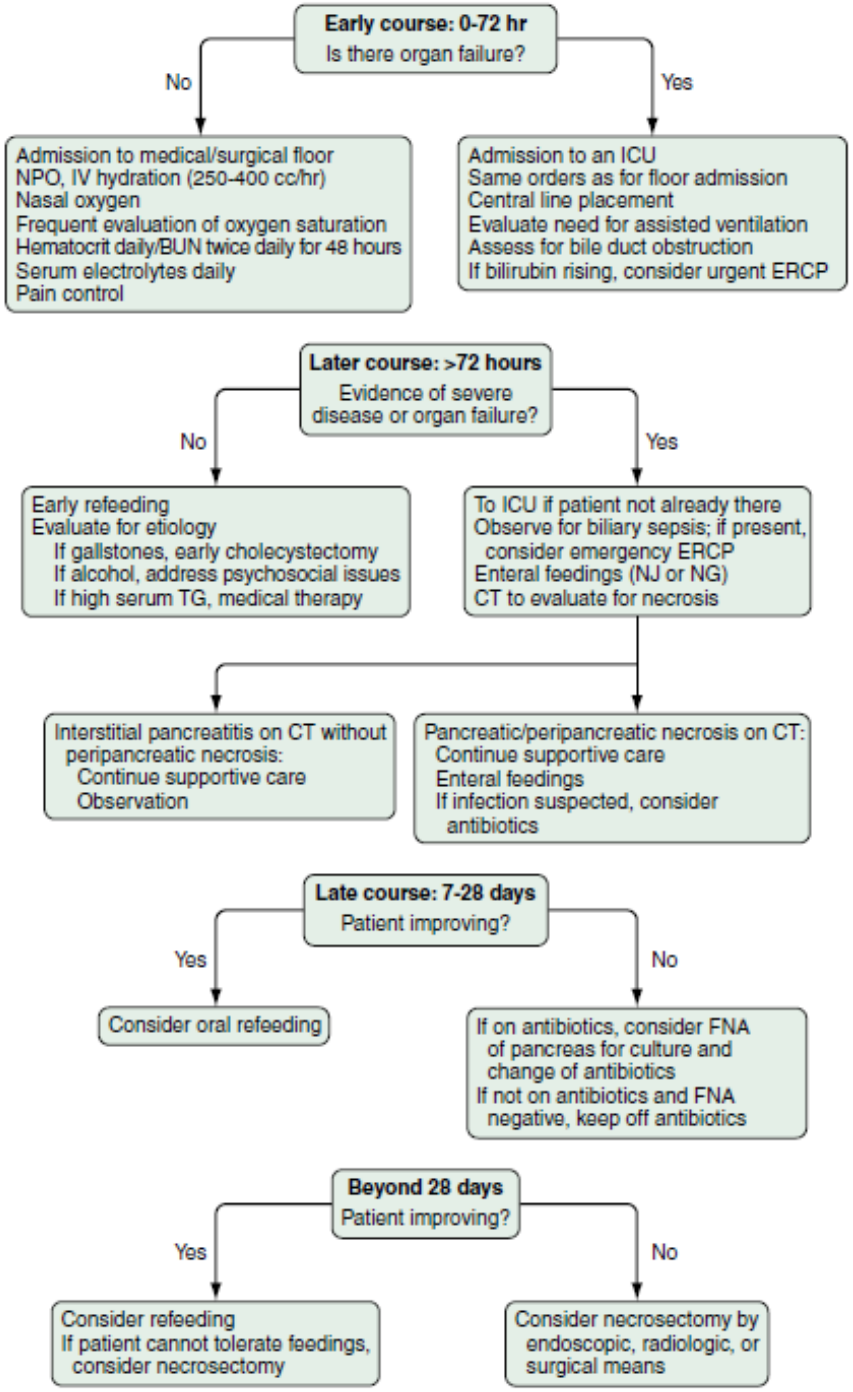
BUN	• BUN >25 mg/dL (8.9 mmol/L) (1 point)
Impaired mental status	• Abnormal mental status with a Glasgow coma score <15 (1 point)
SIRS	• Evidence of SIRS (systemic inflammatory response syndrome) (1 point)
Age	• age >60 years old (1 point)
Pleural effusion	• Imaging study reveals pleural effusion (1 point)

0-2 Points: Lower mortality (<2 percent)

3-5 Points: Higher mortality (>15 percent

Course of disease

- Acute phase (first 7 days)
  - organ failure, SIRS
  - 75-80% resolve without progressing
- Sub acute phase
  - persistence of organ failure from acute phase
  - onset of local complications (fluid collections) and infection,


Early course: 0-72 hr
Is there organ failure?
No
Yes
Admission to medical/surgical floor
NPO, IV hydration (250-400 cc/hr)
Nasal oxygen
Frequent evaluation of oxygen saturation
Hematocrit daily/BUN twice daily for 48 hours
Serum electrolytes daily
Pain control
Admission to an ICU
Same orders as for floor admission
Central line placement
Evaluate need for assisted ventilation
Assess for bile duct obstruction
If bilirubin rising, consider urgent ERCP
Later course: >72 hours
Evidence of severe disease or organ failure?
No
Yes
Early refeeding
Evaluate for etiology
If gallstones, early cholecystectomy
If alcohol, address psychosocial issues
If high serum TG, medical therapy
To ICU if patient not already there
Observe for biliary sepsis; if present, consider emergency ERCP
Enteral feedings (NJ or NG)
CT to evaluate for necrosis
Interstitial pancreatitis on CT without peripancreatic necrosis:
Continue supportive care
Observation
Pancreatic/peripancreatic necrosis on CT:
Continue supportive care
Enteral feedings
If infection suspected, consider antibiotics
Late course: 7-28 days
Patient improving?
Yes
No
Consider oral refeeding
If on antibiotics, consider FNA of pancreas for culture and change of antibiotics
If not on antibiotics and FNA negative, keep off antibiotics
Beyond 28 days
Patient improving?
Yes
No
Consider refeeding
If patient cannot tolerate feedings, consider necrosectomy
Consider necrosectomy by endoscopic, radiologic, or surgical means

Lab tests

- Serum amylase – rises within 6-12hrs of onset, half life ~10hrs
- Serum Lipase – more sensitive than amylase, greater than 3 times the upper limit of normal

Diagnostic Sensitivity and Specificity of Different Pancreatic Enzymes in the Diagnosis of Acute Pancreatitis[a]

	Sensitivity, %	Specificity, %
Total amylase	67–100	85–98
Pancreatic amylase	67–100	83–98
Lipase	82–100	82–100
Trypsin	89–100	79–83
Elastase	97–100	79–96

Dervenis C, Johnson CD, Bassi C, Bradley E, Imrie CW, McMahon MJ, Modlin I. Diagnosis, objective assessment of severity, and management of acute pancreatitis. Santorini consensus conference. Int J Pancreatol. 1999 Jun;25(3):195-210. doi: 10.1007/BF02925968. PMID: 10453421.

Imaging

- Chest and Abdominal X-ray helps to exclude other causes
- Ultrasound can be used to assess for gallstones and progression of pseudo cyst
- CT is useful
  - Excludes other pathology
  - Stage severity of AP
  - Assesses for complications (Pancreatic necrosis is >30% non-enhancing pancreatic tissue on imaging)
- MRI better than CT
  - Distinguishes necrotic debris better than CT and
  - Assess disruption of pancreatic duct

Arvanitakis M, Delhaye M, De Maertelaere V. Computed tomography and magnetic resonance imaging in the assessment of acute pancreatitis. Gastronenterology 2004;126:715–23.

CT

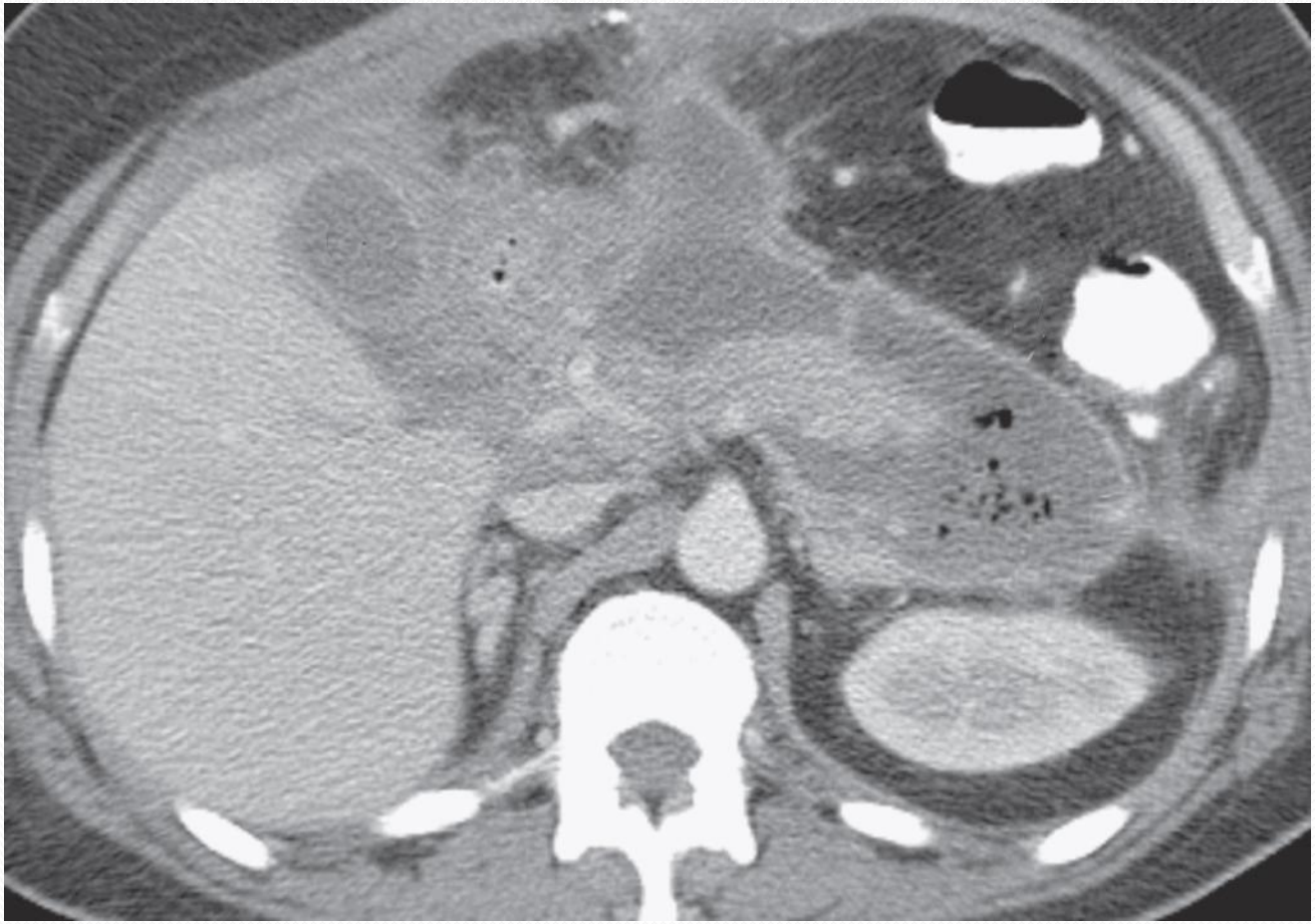


TABLE 58.1 CT Grading System of Balthazar and the CT Severity Index (CTSI)

Balthazar Grades	Definition	Points
A	Normal pancreas consistent with mild pancreatitis	0
B	Focal or diffuse enlargement of the gland, including contour irregularities and inhomogeneous attenuation but without peripancreatic inflammation	1
C	Grade B plus peripancreatic inflammation	2
D	Grade C plus associated single fluid collection	3
E	Grade C plus 2 or more peripancreatic fluid collections or gas in the pancreas or retroperitoneum	4

CTSI=Balthazar Grade Points Plus Necrosis Score*

	Necrosis Score	Points
	Absence of necrosis	0
	Necrosis of up to 33% of the pancreas	2
	Necrosis of 33%-50%	4
	Necrosis of >50%	6

*Highest attainable CTSI score: 4 (Balthazar grade E) + 6 (necrosis of >50%) = 10 points.

Treatment

- First week
  - Supportive care
  - Early oral intake – maintains mucosal barrier and prevents bacterial translocation
  - Analgesia – opiates
  - IVI fluids for volume loss – prevents AKI and pancreatic necrosis
    - Extravasation of protein rich fluid into peritoneal cavity
  - NGT drainage if ileus or intractable vomiting
  - Monitor intra abdominal pressure for intra-abdominal hypertension especially in ventilated patients
  - Antibiotics for proven infections – no prophylactic
  - ERCP if stone identified

Pierre-François Laterre, Christine Collienne, Improving the management of severe acute pancreatitis: The new guidelines from the French Society of Anaesthesia and Intensive Care Medicine, Anaesthesia Critical Care & Pain Medicine, Volume 41, Issue 3, 2022, 101103, ISSN 2352-5568,

Fluid Resuscitation – opposing views

- IAP/APA recommends goal-directed therapy with 5–10 mL/kg/h until noninvasive or invasive targets are reached, and that early resuscitation within 24 hours decreases rates of persistent systemic inflammatory response syndrome and organ failure.
- French Society of Anesthesia and Intensive Care Medicine - aggressive vascular loading during the first 24 hours as an initial fluid resuscitation strategy is not recommended, rather based on haemodynamic response to fluids.
- WATERFALL Study by de-Madaria et al was halted prematurely due to patients developing fluid overload in the aggressive fluid resus arm - supports moderate fluid resuscitation

de-Madaria E, Buxbaum JL, Maisonneuve P, et al. Aggressive or Moderate Fluid Resuscitation in Acute Pancreatitis. N Engl J Med 2022;387:989-1000.

Nutrition

- In mild to moderate pancreatitis
  - PADI trial - Immediate refeeding resulted in shorter length of stay, fewer costs, without causing complications
  - Tube feeding is only indicated in patients with persistent nausea, vomiting, abdominal pain who cannot tolerate oral feeds.

Ramírez-Maldonado et al Immediate Oral Refeeding in Patients With Mild and Moderate Acute Pancreatitis: A Multicenter, Randomized Controlled Trial (PADI trial). Annals of Surgery 274(2):p 255-263, August 2021.

Nutrition

- In severe acute pancreatitis
  - Concept of "bowel rest" has fallen away. Injured acinar cells do not respond to physiological stimulation.
  - Enteral nutrition (preferred over tube) maintains gut integrity, reduces bacterial endotoxins and pancreatic enzyme translocation.
  - When compared to TPN, enteral nutrition was associated with a significant reduction in death with risk ratio (RR) of 0.36 (95%CI: 0.20-0.65) and multiple organ failure with RR of 0.39 (95%CI: 0.21-0.73)
  - Start after adequate resuscitation and stable haemodynamics
  - In patients that require tube feeding, continuous feeds over bolus is recommended. Nasogastric is not inferior to nasojejunal feeds in terms of pain, aspiration and mortality.
- TPN is indicated for intestinal failure, obstruction or severe ileus.
- Parenteral L-glutamine reduces morbidity and mortality
- Omega 3 fatty acids beneficial for reducing mortality, infectious complications, and length of hospital stay

Lang AL. Nutrition and Acute Pancreatitis. J Clin Med. 2021 Feb 18;10(4):836. doi: 10.3390/jcm10040836. PMID: 33670647; PMCID: PMC7922255.

Antibiotics

- Prophylactic antibiotics are not recommended, no decrease in mortality and morbidity.
- Infected necrosis – diagnosis is challenging, Pro-calcitonin is most sensitive to detect infection, CT guided FNA is best option to get a specimen for MCS.
- Gas seen in the retro peritoneum is an indication of infection
- Choice of antibiotic for gram -/+ and anaerobes: piperacilin/tazobactam, carbapenems, metronidazole all offer good penetration into pancreas.
- Aminoglycosides have poor pancreatic penetration

Mourad MM, Evans R, Kalidindi V, Navaratnam R, Dvorkin L, Bramhall SR. Prophylactic antibiotics in acute pancreatitis: endless debate. Ann R Coll Surg Engl. 2017 Feb;99(2):107-112. doi: 10.1308/rcsann.2016.0355. Epub 2016 Dec 5.

Leppäniemi et al. World Journal of Emergency Surgery (2019) 14:27

Post ERCP Pancreatitis (PEP)

- Occurs in 7% of therapeutic ERCP and 25% of patients with sphincter of oddi dysfunction.
- More likely to occur in normal duct anatomy
- Patient profile with the highest risk: Woman with suspected choledocholithiasis with normal bilirubin, underwent sphincterotomy and no stone was found = 27% developed PEP
- Serum amylase>276 and lipase>1000 2 hours after procedure offers 100% PPV
- If values are normal 3hours after procedure, only 1% develop PEP
- Prevention: Prophylactic pancreatic stents, IVI fluids pre procedure and rectal NSAIDS

Aliperti G. Complications related to diagnostic and therapeutic endoscopic retrograde cholangiopancreatography. Gastrointest Endosc Clin North Am 1996;6:379–407.

Hypertriglyceridaemia induced Severe Acute Pancreatitis

- Elevated FFAs and chylomicrons increase plasma viscosity which may induce ischaemia and trigger inflammation in pancreas.
- Diagnosis is definitive if triglyceride level > 11,3mmol/l.
- Triglycerides rise in acute pancreatitis causing a false elevation. Levels drop after 48hours, therefore earlier or prior blood tests are most accurate.
- Amylase and lipase levels also falsely reduced due to assay interference.

] Samarasinghe S, Avari P, Meeran K, Cegla J. Management of hypertriglyceridaemic pancreatitis in the acute setting and review of literature. BMJ Case Rep 2018

Cruciat, G., Nemeti, G., Goidescu, I. *et al.* Hypertriglyceridemia triggered acute pancreatitis in pregnancy – diagnostic approach, management and follow-up care. *Lipids Health Dis* **19**, 2 (2020). https://doi.org/10.1186/s12944-019-1180-7

Hypertriglyceridaemia induced Severe Acute Pancreatitis

- Treatment
  - Plasmapheresis – rapidly reduces levels however costly, poor availability and limited evidence showing it reduces mortality and morbidity.
  - Insulin activates lipoprotein lipase and reduces chylomicron levels.
  - Unfractionated heparin also activates lipoprotein lipase
  - Fibrates
  - Novel gene therapies

Cruciat, G., Nemeti, G., Goidescu, I. *et al.* Hypertriglyceridemia triggered acute pancreatitis in pregnancy – diagnostic approach, management and follow-up care. *Lipids Health Dis* **19**, 2 (2020). https://doi.org/10.1186/s12944-019-1180-7

Acute Pancreatitis in Pregnancy

- Incidence of 1/1000 to 1/5000 pregnancies, death rate up to 37% and foetal death rate up to 60%.
- Most common in third trimester, 1/3 develop SAP
- Cholelithiasis, alcohol and hypertriglyceridaemia are most common causes.

M ¸adro, A. Pancreatitis in Pregnancy—Comprehensive Review. Int. J. Environ. Res. Public Health 2022, 19, 16179. https://doi.org/10.3390/ ijerph192316179

Acute pancreatitis in pregnancy

- Pregnancy increases risk of cholelithiasis
- First trimester
  - Change in bile composition (increased cholesterol)
  - Effect of progesterone on gallbladder and bile duct contractility leads to duct malfunction
  - Vomiting leading to dehydration and concentration of bile
  - Stone formation which increases risk of pancreatitis in 2nd and 3rd trimester.

M ¸adro, A. Pancreatitis in Pregnancy—Comprehensive Review. Int. J. Environ. Res. Public Health 2022, 19, 16179. https://doi.org/10.3390/ ijerph192316179

Acute pancreatitis in pregnancy

- Management is conservative as far as possible, however surgery may need to be considered for gallstone pancreatitis
- Open vs. laparoscopic cholecystectomy
  - Compared to open surgery, laparoscopic intervention in pregnancy is associated with a significant reduction in the time of surgery, the length of stay in a hospital, wounds and other complications, postoperative pain, the incidence of thromboembolic complications, postoperative intestinal obstruction, and a faster return to normal functioning
- Second trimester is the best time to perform laparoscopic cholecystectomy if indicated.
- ERCP is indicated only for symptomatic cholelithiasis, risk of teratogenicity and malignancy.

M ˛adro, A. Pancreatitis in Pregnancy—Comprehensive Review. Int. J. Environ. Res. Public Health 2022, 19, 16179. https://doi.org/10.3390/ ijerph192316179

Counselling

- Alcohol cessation
- Smoking cessation

Interventional Treatments

- Cholecystectomy for cholelithiasis
  - Risk of recurrence is 18% in 6 weeks
  - Done at same admission
- ERCP with sphincterotomy

Nikkola J, Laukkarinen J, Huhtala H, et al. The intensity of brief interventions in patients with acute alcoholic pancreatitis should be increased, especially in young patients with heavy alcohol consumption. Alcohol 2017;52:453–9.

Urgent ERCP

- Indicated in first 72hrs of acute billiary pancreatitis with
  - cholangitis or persistent cholestasis
  - Stone in CBD
- No change in mortality or complication rates in patients without cholangitis vs. conservative treatment.

Nicolien J Schepers et al
Urgent endoscopic retrograde cholangiopancreatography with sphincterotomy versus conservative treatment in predicted severe acute gallstone pancreatitis (APEC): a multicentre randomised controlled trial, The Lancet, Volume 396, Issue 10245, 2020,

Fluid collections

- Acute Necrotic Collection(ANC): form <4 weeks after onset and involve pancreatic parenchyma and surrounding tissues, contain necrotic fluid and enzymes. Resolve spontaneously.
- Walled off necrosis (WON): Mature encapsulated collection of pancreatic tissue or necrosis >4weeks of onset.

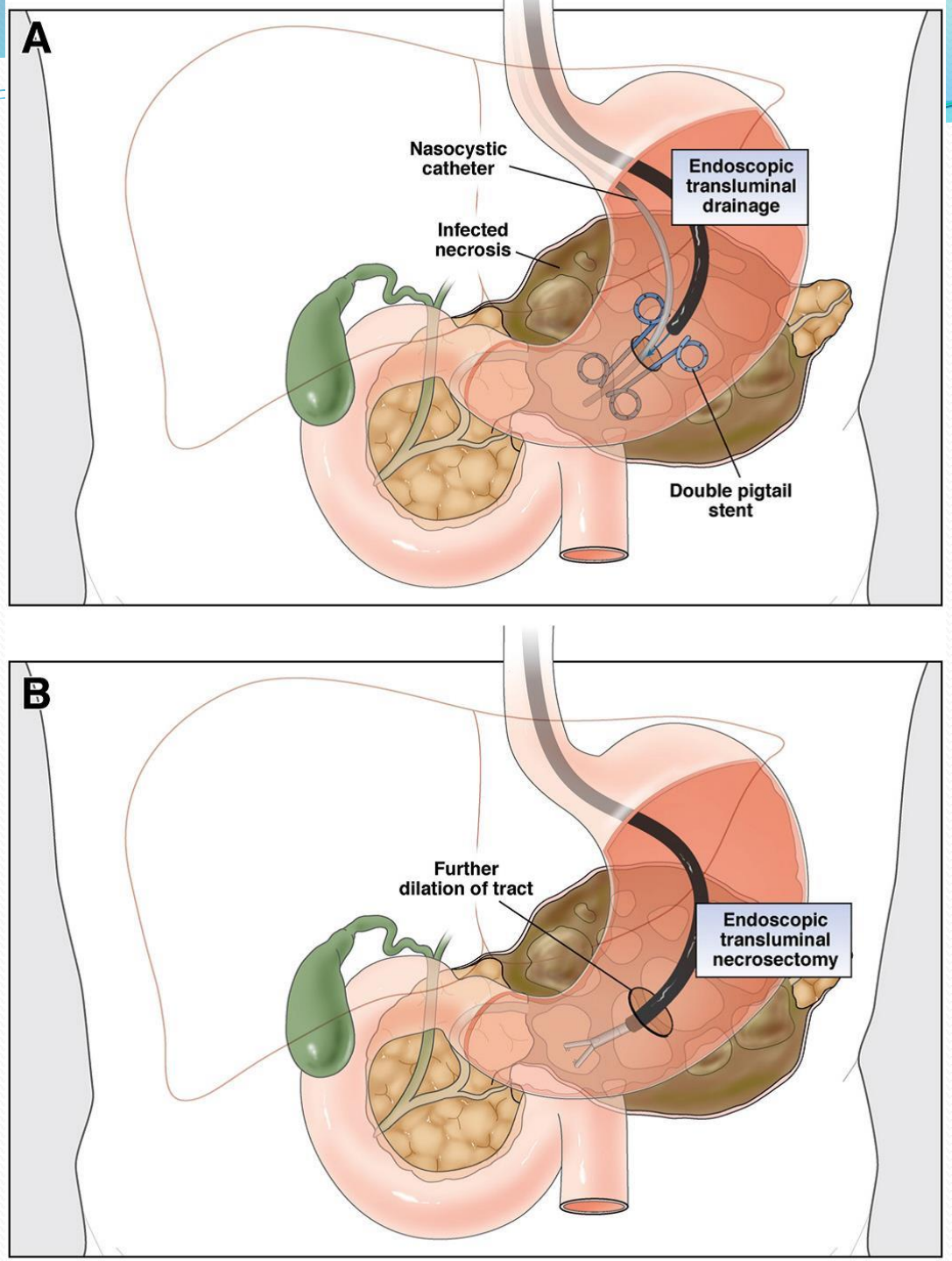
- Drainage is indicated only if collections are:
  - Infected necrosis
  - Causing obstruction
  - Causing Systemic inflammatory effects with loss of weight and debility
  - due to Pancreatic duct disruption
  - Causing Fistula formation

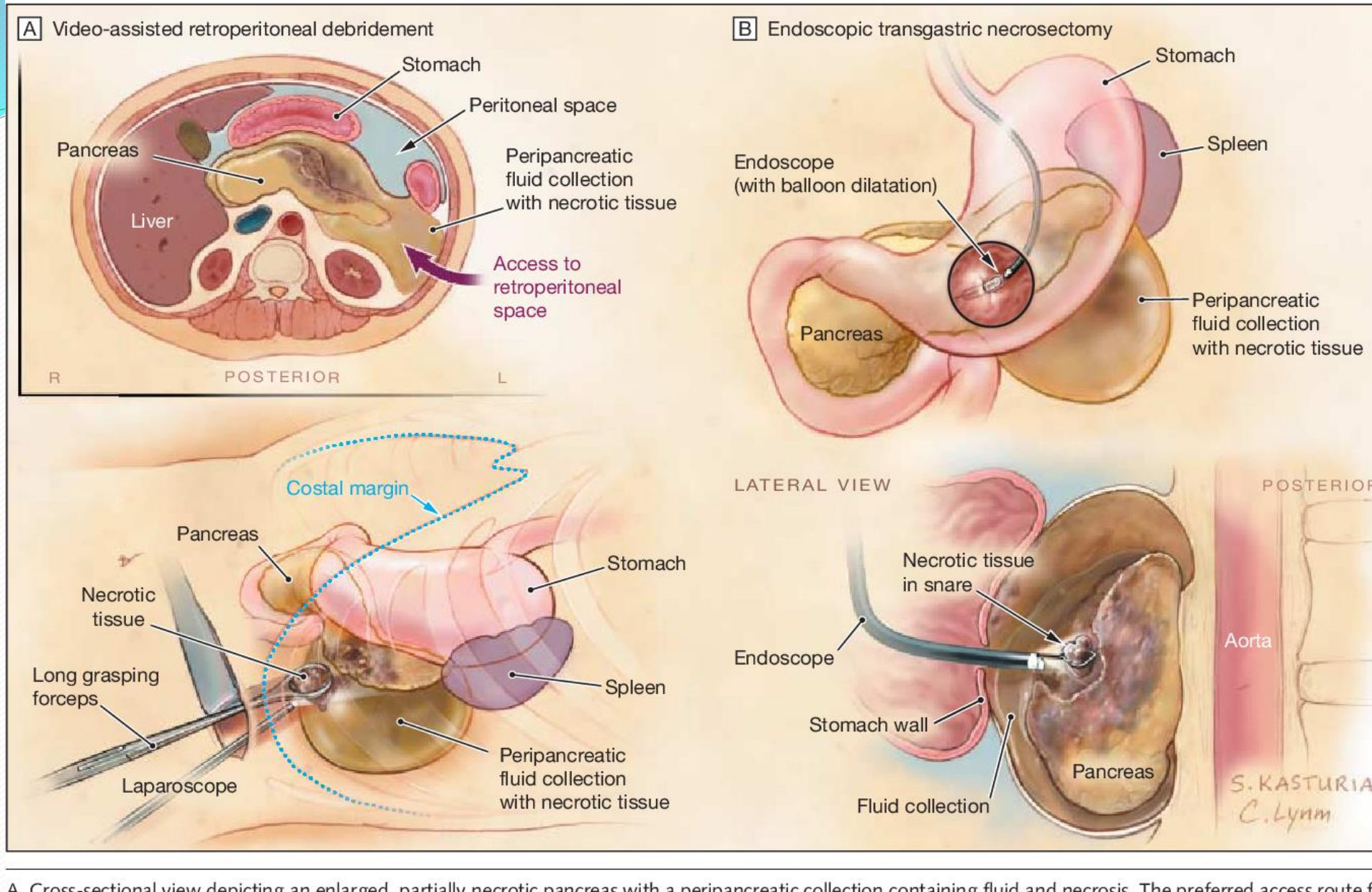
Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification nd definitions by international consensus. Gut. 2013;62:102– 11.

Surgical options for drainage of collections

- Percutaneous pigtail drainage (radiological)
- Endoscopic gastrostomy with pancreatic necrosectomy via expanding metal stent
  - Endoscopic drainage should be preferred over radiology whenever possible due to better drainage and decreased risk of percutaneous fistula, and over surgery because of high morbidity and mortality
- Laparoscopic pancreatic necrosectomy
- Open pancreatic necrosectomy

Necrotizing Pancreatitis: Current Management and Therapies
Christine Boumitri, Elizabeth Brown, Michel Kahaleh
Clin Endosc 2017;50(4):357-365.


A
Nasocystic catheter
Endoscopic transluminal drainage
Infected necrosis
Double pigtail stent
B
Further dilation of tract
Endoscopic transluminal necrosectomy



A, Cross-sectional view depicting an enlarged, partially necrotic pancreas with a peripancreatic collection containing fluid and necrosis. The preferred access route f video-assisted debridement is within the left retroperitoneal space to reach the necrotic collection between the left kidney and descending colon. A laparoscope inserted, and long grasping forceps are used to debride the necrosis. B, The access route for natural orifice transluminal endoscopic surgery is through the posterior w of the stomach. The necrotic collection most often bulges into the stomach facilitating endoscopic transgastric necrosectomy. After balloon dilatation of the punctu site in the stomach wall, the endoscope is introduced into the retroperitoneal space and loose necrotic material is removed.

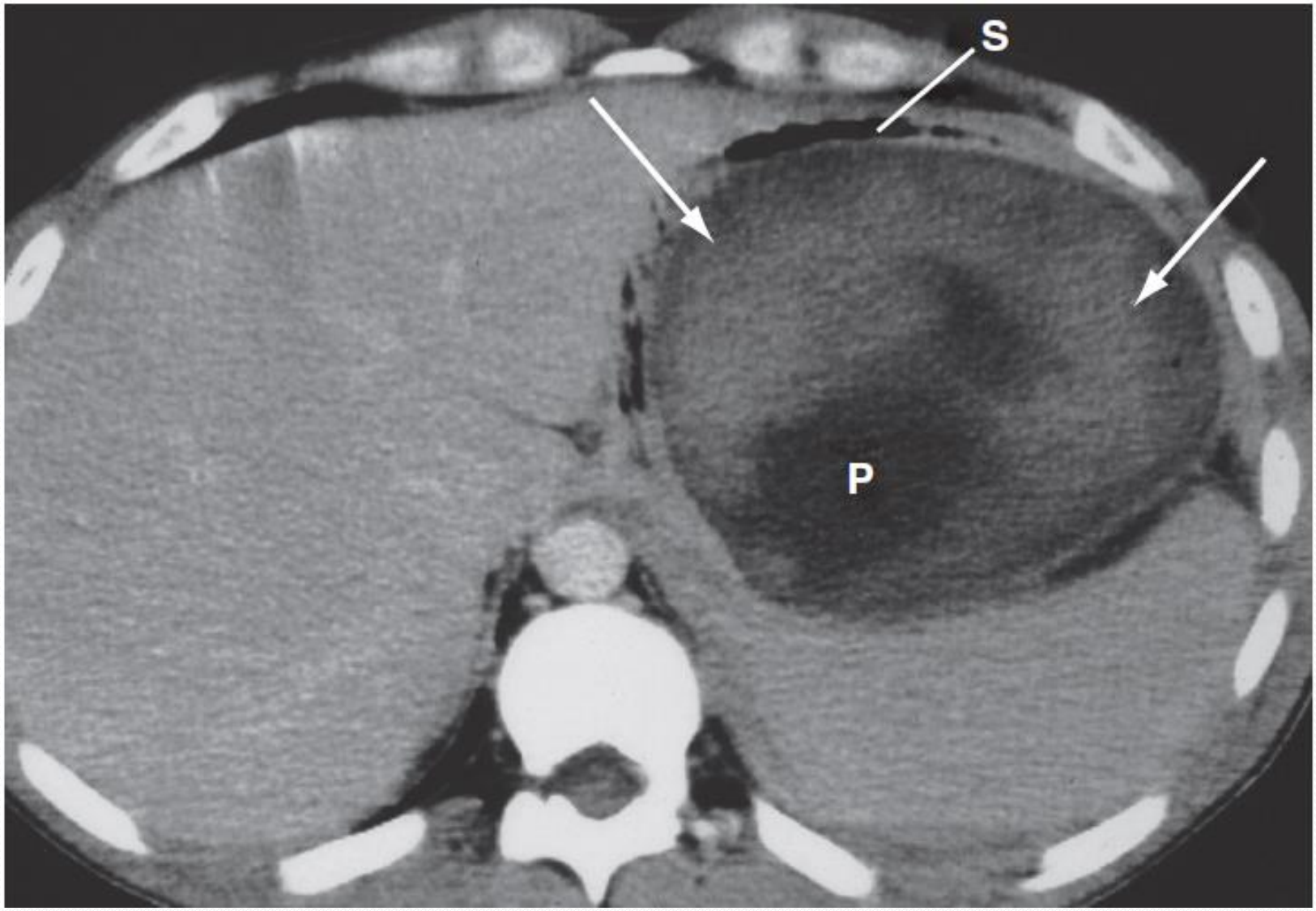
Indications for open surgical intervention

- Abdominal compartment syndrome
- Acute on-going bleeding when endovascular approach is unsuccessful
- Bowel ischaemia or acute necrotizing cholecystitis during acute pancreatitis
- Bowel fistula extending into a peripancreatic collection
- Unsatisfactory result from percutaneous or endoscopic procedure.

Leppäniemi et al. World Journal of Emergency Surgery (2019) 14:27

Complications

- Upper GIT bleeding
  - Mallory Weiss tear from vomiting, PUD
  - Portal or splenic vein thrombus due to nearby inflammation can lead to oesophageal varices.
  - Pseudo aneurysm
  - Haemosuccus pancreaticus
- Abdominal compartment syndrome
- Long-term
  - Endocrine insufficiency – 15% diabetic at 12months
  - Exocrine insufficiency in 40% of newly diagnosed diabetics from AP


S
P

BOX 58.7 Complications of Acute Pancreatitis

LOCAL

- Pseudocyst
- Sterile necrosis (peripancreatic, pancreatic, or both)
- Infected necrosis (peripancreatic, pancreatic, or both)
- Abscess
- GI bleeding
  - Pancreatitis-related
    - Splenic artery rupture or splenic artery pseudoaneurysm rupture
    - Splenic vein rupture
    - Portal vein rupture
    - Splenic vein thrombosis leading to gastroesophageal variceal bleeding
    - Pseudocyst or abscess hemorrhage
    - Post-necrosectomy bleeding
  - Nonpancreatitis-related
    - Mallory-Weiss tear
    - Alcoholic gastropathy
    - Stress-related mucosal gastropathy
- Splenic complications
  - Infarction
  - Rupture
  - Hematoma
  - Splenic vein thrombosis
- Fistulization to or obstruction of the small intestine or colon
- Hydronephrosis

SYSTEMIC

- Respiratory failure
- Renal failure
- Shock
- Hyperglycemia
- Hypocalcemia
- DIC
- Fat necrosis (subcutaneous nodules)
- Retinopathy
- Psychosis

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