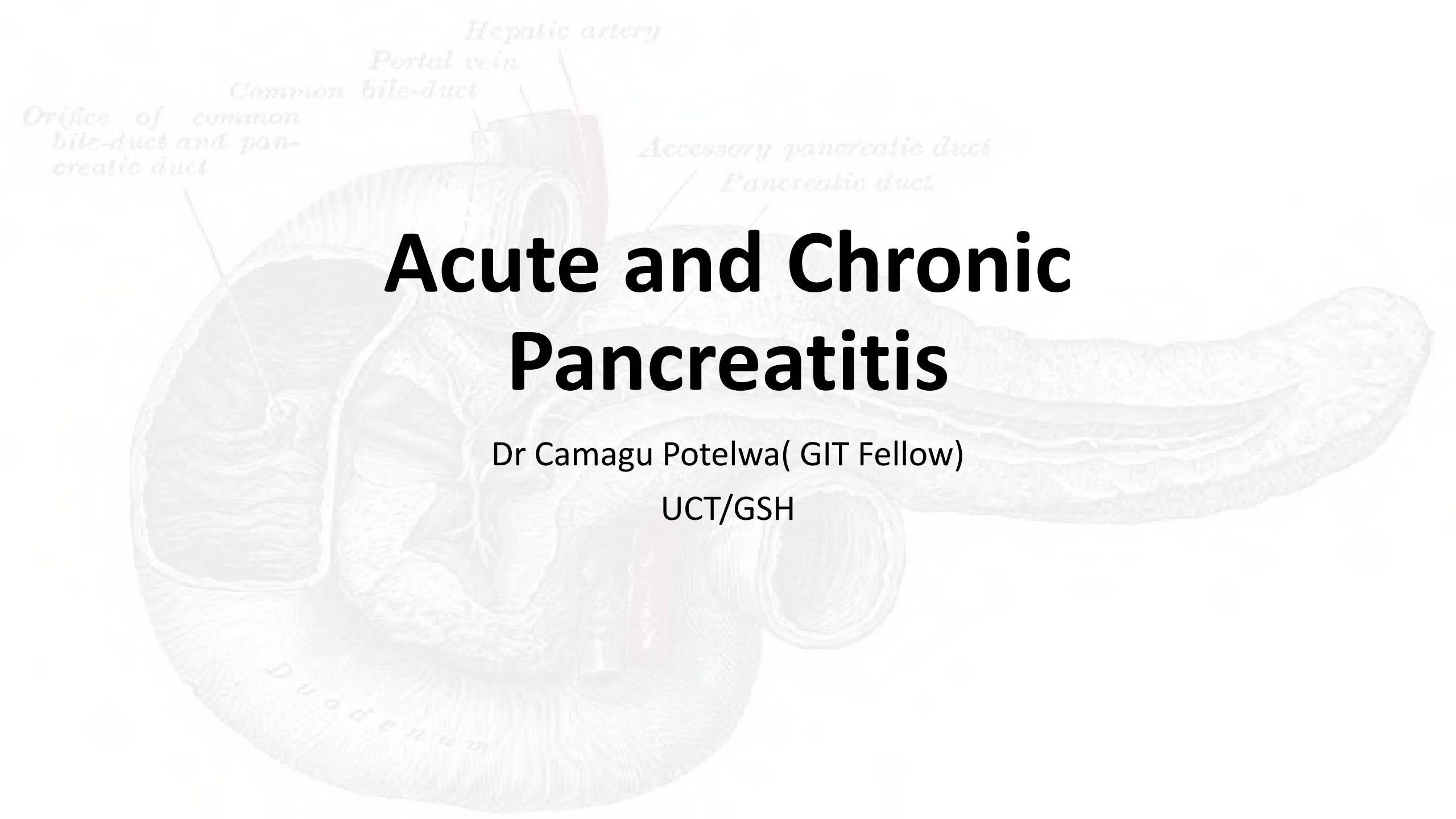



# Acute and Chronic Pancreatitis

Dr Camagu Potelwa( GIT Fellow)

UCT/GSH

# Introduction

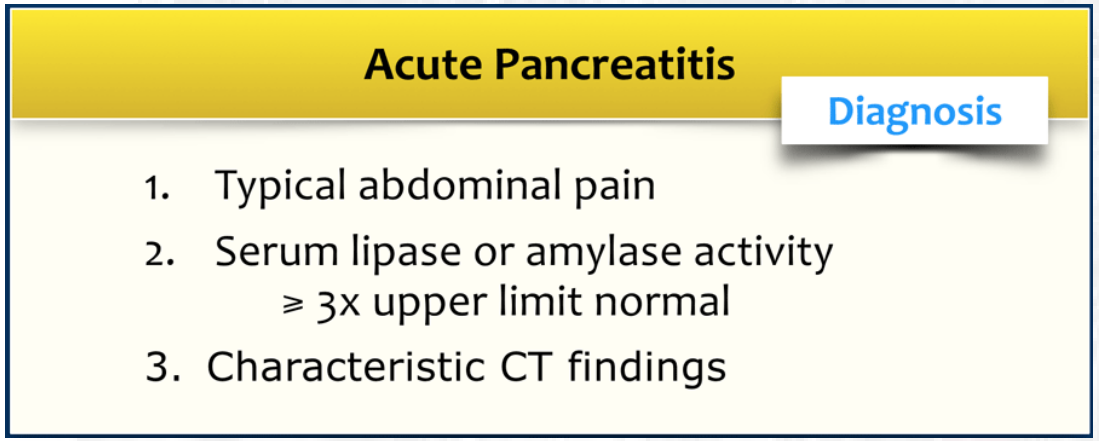
Acute pancreatitis (AP)

- Sudden onset of severe abdominal pain
- Elevated pancreatic enzymes
- Ranging in severity from mild, self-limiting cases to severe
- Life-threatening instances associated with multi-organ failure

- Chronic pancreatitis (CP)
  - Progressive fibroinflammatory syndrome
  - Leading to irreversible structural damage, fibrosis
  - Eventual loss of both exocrine and endocrine pancreatic function

*Diagnosis and Management of Acute Pancreatitis Trikudanathan, Guru et al. Gastroenterology, Volume 167, Issue 4, 673 - 688*

# Diagnosis of Acute Pancreatitis




Diagnostic Criteria

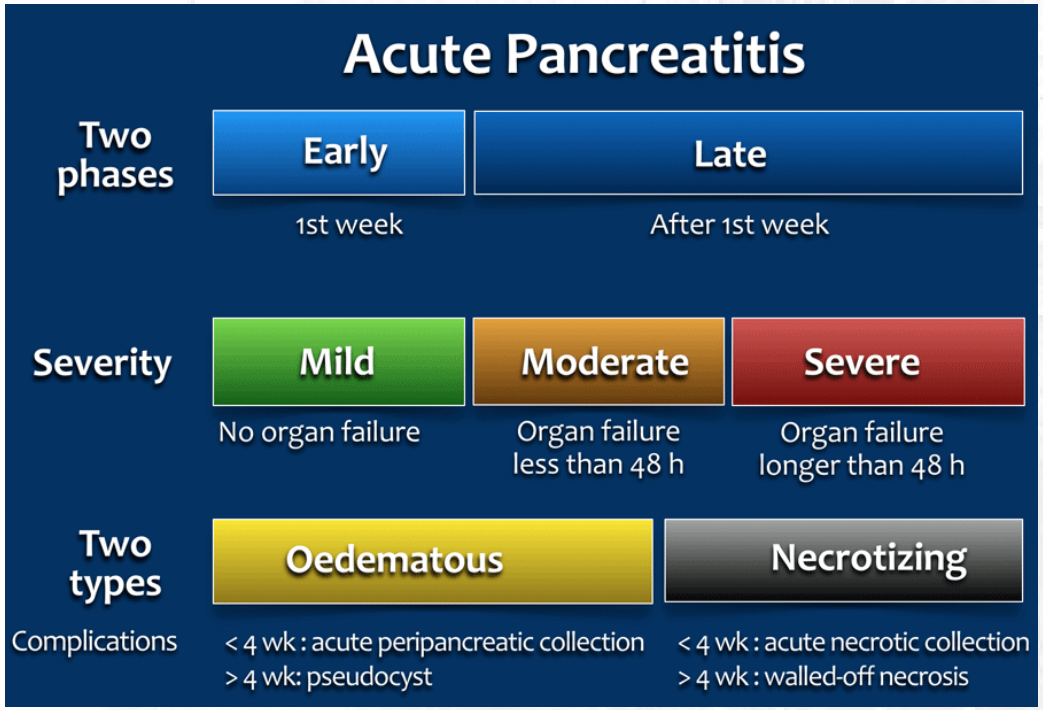
1. Abdominal pain consistent with acute pancreatitis: Acute onset of persistent, severe, epigastric pain often radiating to the back
2. Serum lipase or amylase activity at least three times greater than the upper limit of normal.
3. Characteristic findings of acute pancreatitis on contrast-enhanced CT (CECT) and less commonly MRI or US

The diagnosis is usually established when there is a combination of abdominal pain and elevated pancreatic enzymes

CECT is not required, unless there is uncertainty about the diagnosis

*Classification of Acute Pancreatitis—2012: revision of the Atlanta Classification and definitions by international consensus* ***by*** *Peter A Banks, Thomas L Bollen, Christos Dervenis, Hein G Gooszen, Colin D Johnson, Michael G Sarr, Gregory G Tsiotos, Santhi Swaroop Vege, Acute Pancreatitis Classification Working Group.Gut 2013;62:102-11*

# The Revised Atlanta Classification




***Temporally*, two phases of acute pancreatitis are identified in the Revised Atlanta Classification:**

1. *Early* - first week
   Only clinical parameters are important for treatment planning and are determined by the systemic inflammatory response syndrome - SIRS, which can lead to organ failure.
2. *Late* - after the first week
   Morphologic criteria based on CT findings combined with clinical parameters determine the care of the patient

The ***severity*** is classified into three categories based on clinical and morphologic findings:

1. *Mild* - No organ failure and no local or systemic complications.
2. *Moderate* **-** Presence of transient organ failure less than 48h and/or presence of local complications
3. *Severe* - Persistent organ failure > 48 hour
   15-20% of cases

***Morphologically,*** there are two types of acute pancreatitis:

1. Acute oedematous or interstitial pancreatitis
2. Acute necrotizing pancreatitis

- Usually the necrosis involves both the pancreas and the peripancreatic tissues.
- Less commonly only the peripancreatic tissues.
- Rarely only the pancreatic parenchyma

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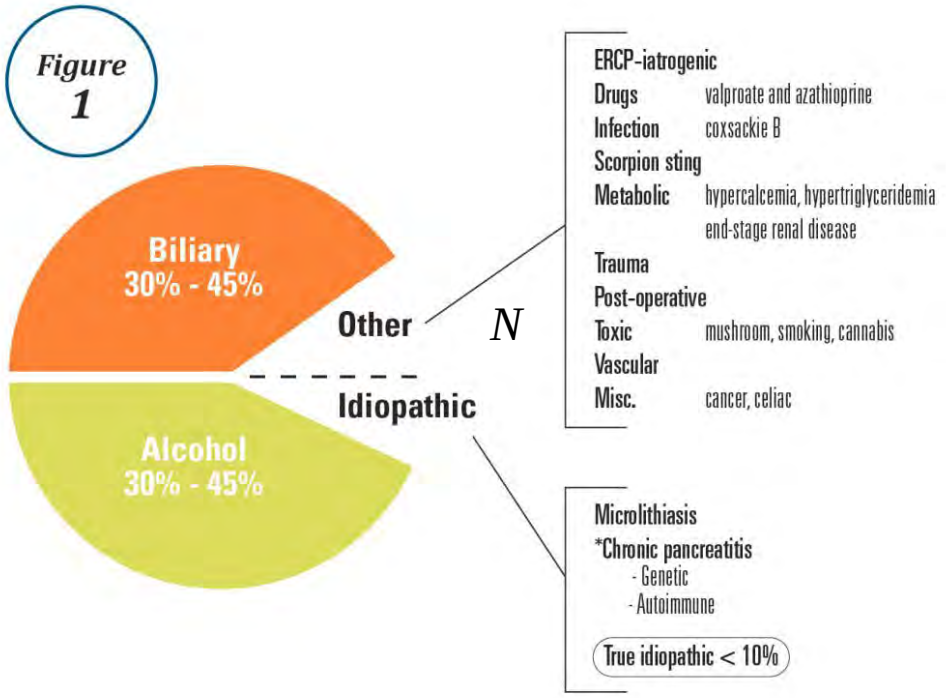
# Aetiology




New concepts in the management of acute pancreatitis | MDedge. (n.d.). https://blogs.the *hospitalist.org/content/new-concepts-management-acute pancreatitis*



REVIEWS AND PERSPECTIVES

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| Etiology | Clues to identify | Comments |
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| Alcohol 30% | Long-term use of alcohol (usually at least 5 y)<br>CAGE questions<br>PEth testing | Acute flares may be superimposed on underlying CP |
| Hypertriglyceridemia 2%–7% | Fasting TG ≥1000 mg/dL | If patient has not been eating due to pain, fasting TG may be low; testing after recovery or testing postprandial TG level may be needed<br>Subsequent attacks can occur with much lower elevations of TG |
| Drugs <5% | Multiple drugs reported but evidence usually only circumstantial | Strongest evidence for didanosine, asparaginase, azathioprine, valproic acid, 6-mercaptopurine, and mesalamine<br>Usually idiosyncratic |
| Genetic | Multiple modifier genes now identified | Genetic testing not usually performed, but may be considered in very young patients or in those with unexplained relapsing pancreatitis |
| Post-ERCP | <5% of those undergoing ERCP | Usually mild<br>Risk can be reduced with careful patient selection, technical approaches, and prophylaxis with indomethacin and preprocedure hydration |
| Infections rare | Overall quite rare | Viruses: CMV, EBV, mumps<br>Parasites and nematodes: Ascaris, Clonorchis, opisthorcus |
| Obstruction of major or minor ampulla or pancreatic duct leading to pancreatitis | Overall quite rare | Celiac disease<br>Small bowel Crohn's disease<br>Periampullary diverticulum<br>Ampullary or duodenal polyp or cancer<br>Pancreatic cancer<br>Pancreas divisum<br>Annular pancreas<br>Santorinicele<br>Controversial causes such as sphincter of Oddi dysfunction |
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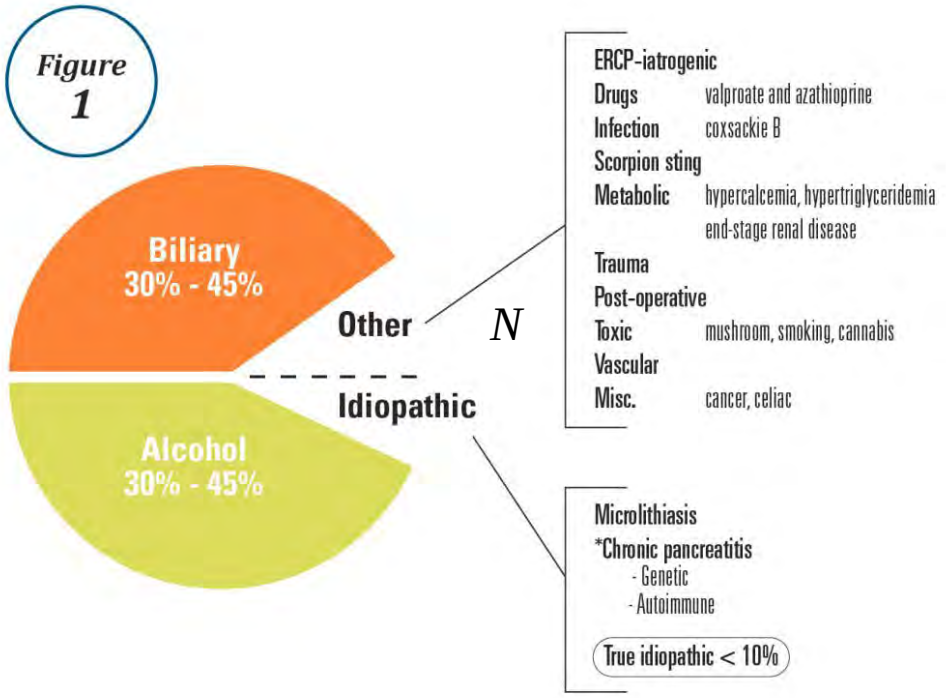


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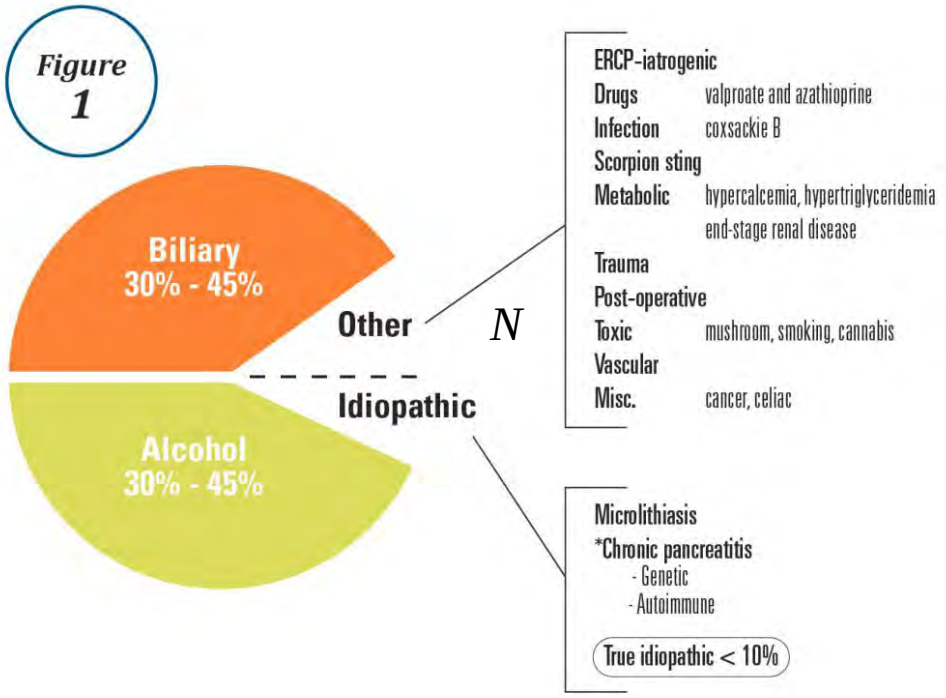


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F Anderson [1], S R Thomson, D L Clarke, E Loots

Affiliations + expand

PMID: 18807304

### Abstract

**Introduction:** The spectrum of aetiologies and outcomes of acute pancreatitis in South African settings is under-reported. We report our experience at a regional hospital and compare it with international norms.

**Patients and methods:** Data were prospectively collected on all admissions of patients with acute pancreatitis to a regional hospital during the period June 2001-April 2006. The causes of the pancreatitis were noted and complications and mortality rate were determined.

**Results:** From June 2001 to April 2006 there were 322 admissions of 282 patients with acute pancreatitis. The median age was 37 years (range 13-73 years). There were 94 females and 188 males. Episodes of pancreatitis were associated with alcohol consumption in 62% of cases and with gallstones in 14%; 4% of cases were associated with both gallstones and alcohol consumption, 8% with dyslipidaemia and 5% with retroviral disease. In 15% of admissions local complications developed, and 9% of admissions ended in death of the patient. Of the 28 deaths, 71% occurred in the first 2 weeks.

**Conclusions:** As in other South African reports, alcohol was the main cause of pancreatitis. Outcomes in this series are similar to those in Western studies except that the majority of deaths occurred early, implying that improved supportive care may improve overall survival.



- Alcohol 62%
- Gallstones 14%
- Both gallstones and Alcohol 4%
- Dsylipidaemia  8%
- HIV 5%
- 15% Developed local complications
- Mortality was 9%

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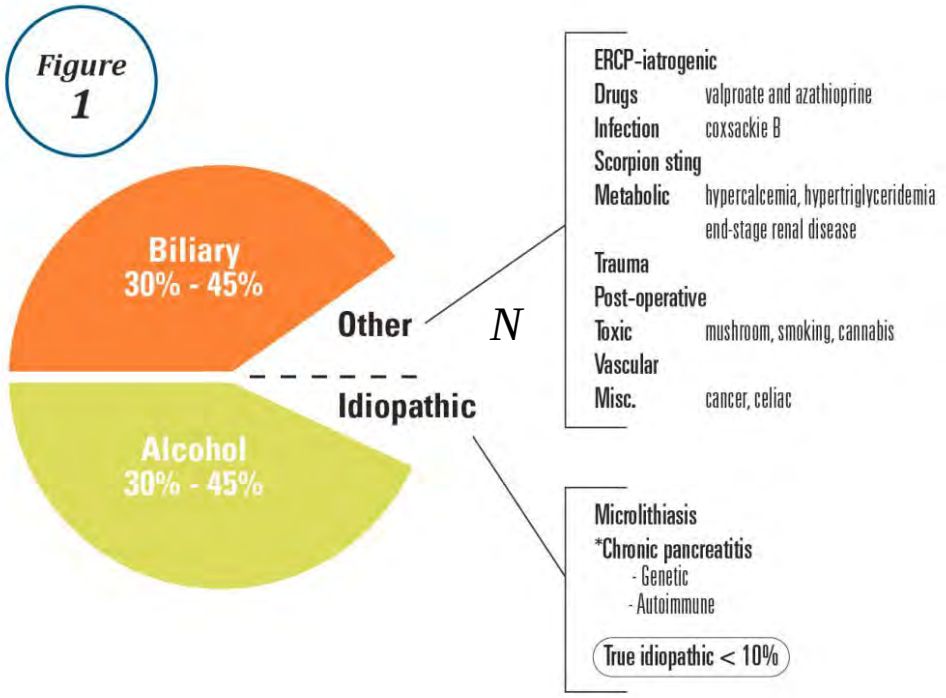


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# HIV and Pancreatitis

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*S Afr Med J* 2017;107(8):706-709. DOI:10.7196/SAMJ.2017.v107i8.10296

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- Drug-related pancreatitis was more frequent and alcohol as a cause less frequent in HIV related pancreatitis.

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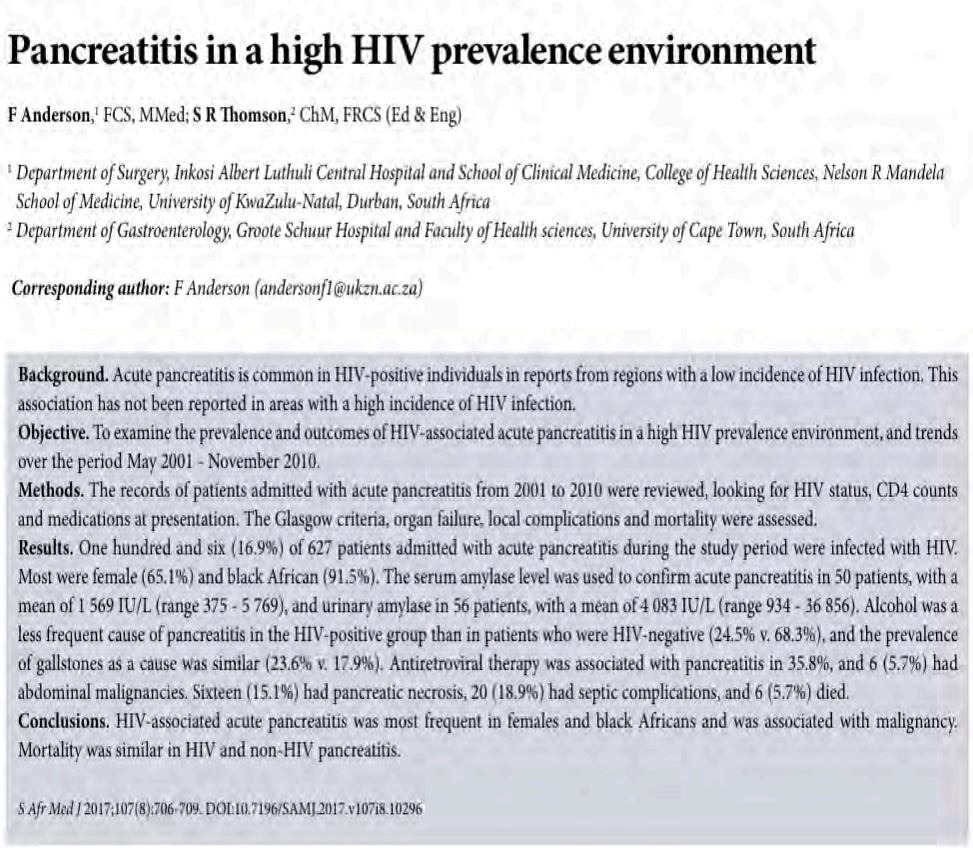
**Table 1. Characteristics of HIV-positive and HIV-negative patients (*N*=627)**

| | HIV-positive | HIV-negative | *p*-value |
|---|---|---|---|
| Total patients, *N* (%) | 106 (16.9) | 521 (83.1) | |
| Males/females, *n* (%) | 37 (34.9):69 (65.1) | 383 (73.6):138 (26.5) | 0.000 |
| Age (yr), mean (range) | 36 (12 - 60) | 40 (12 - 89) | 0.005 |
| Duration of symptoms (d), mean (range) | 9.2 (1 - 30) | 2 (1 - 14) | 0.000 |
| Body mass index (kg/m²), mean (range) | 26 (16 - 64) | 25.4 (16 - 59) | 0.76 |
| Aetiology, *n* (%) | | | |
| Alcohol | 26 (24.5) | 356 (68.3) | 0.0001 |
| Gallstones | 25 (23.6) | 93 (17.9) | 0.1741 |
| Malignancy | 6 (5.7) | 0 | 0.0001 |
| Ethnic group, *n* (%) | | | |
| Black African | 97 (91.5) | 226 (43.4) | 0.000 |
| Mixed race | 3 (2.5) | 41 (7.9) | 0.091 |
| Indian | 6 (5.7) | 232 (44.6) | 0.0001 |
| White | 0 | 22 (4.2) | 0.036 |
| Outcomes | | | |
| Glasgow ≥3, *n* (%) | 19 (17.9) | 98 (18.8) | 1.00 |
| Organ failure, *n* (%) | 10 (9.4) | 51 (9.8) | 0.961 |
| Hospital stay (d), mean (range) | 11.5 (1 - 44) | 10.2 (1 - 123) | 0.002 |
| Necrosis pancreas, *n* (%) | 16 (15.1) | 47 (9.0) | 0.074 |
| Sepsis, *n* (%) | 20 (18.9) | 50 (9.6) | 0.009 |
| Complications, *n* (%) | 19 (17.9) | 108 (20.7) | 0.54 |
| Mortality, *n* (%) | 6 (5.7) | 37 (7.1) | 0.611 |

# HIV and Pancreatitis



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- Drug-related pancreatitis was more frequent and alcohol as a cause less frequent in HIV related pancreatitis.
- The mortality rate of 5.7% in this study was similar to previous studies

*Acute pancreatitis Boxhoorn, Lotte et al. The Lancet, Volume 396, Issue 10252, 726 - 734*

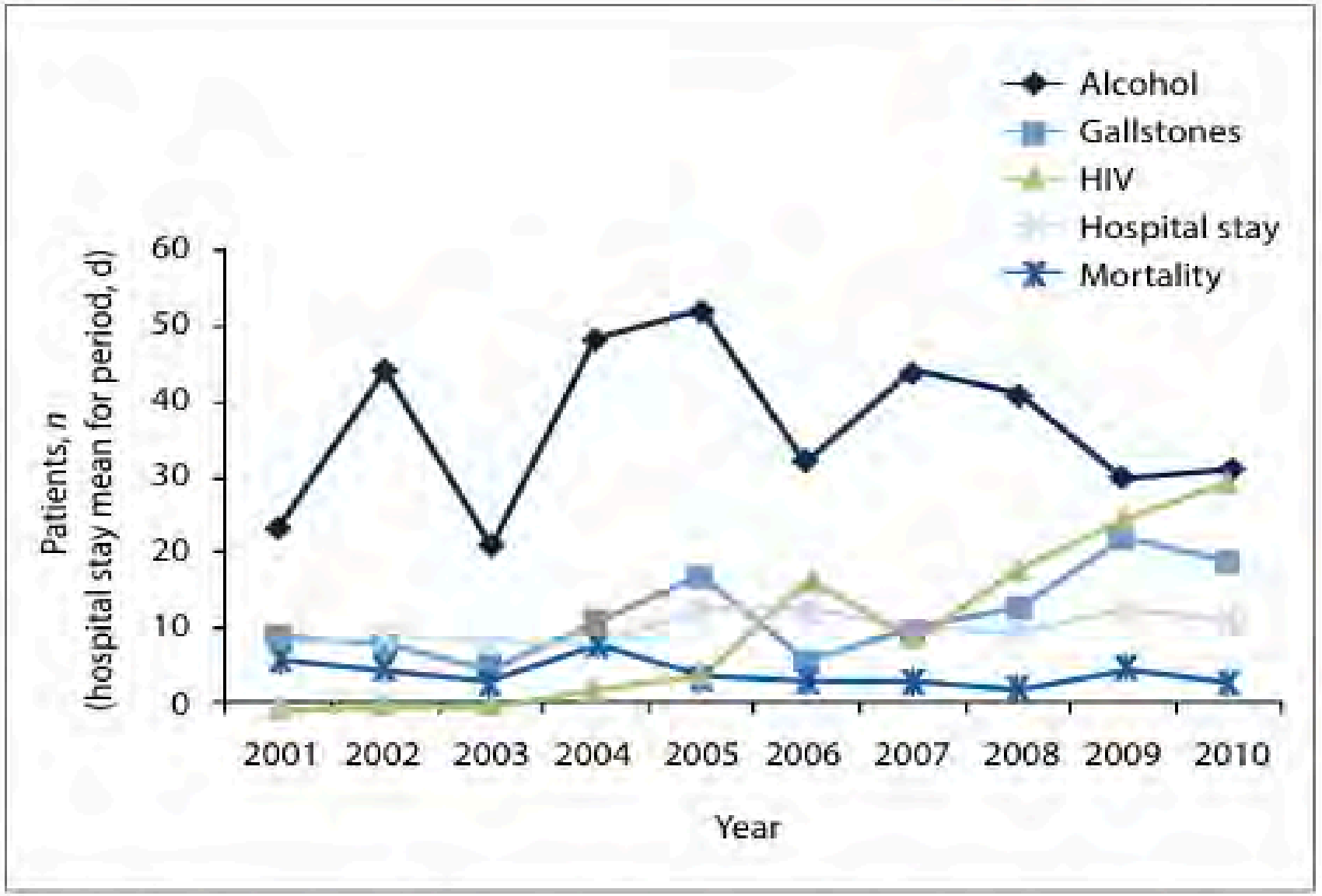


*Fig. 1. Trends in aetiology, hospital stay and mortality in all patients with pancreatitis (N=627).*

# Epidemiology

- The annual incidence of AP is estimated at 13–49 per 100,000 persons
- The risk of AP is similar among men and women and increases with age.
- Most patients have mild acute pancreatitis which resolves  with 1 weeks
- Approximately 20% of patients develop moderate or severe acute pancreatitis, with necrosis of the pancreatic or peripancreatic tissue or organ failure, or both, and a substantial mortality rate of 20–40%

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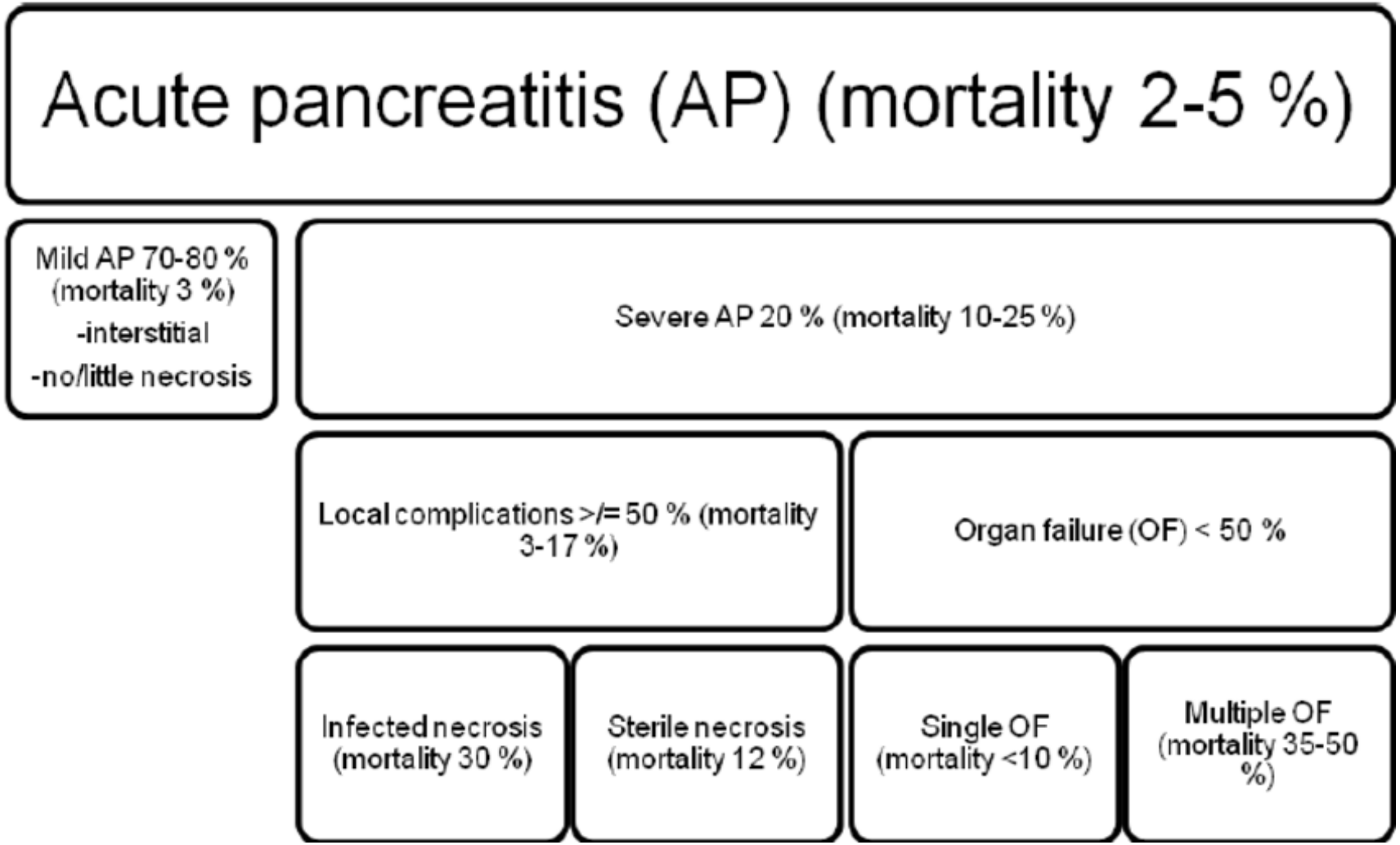
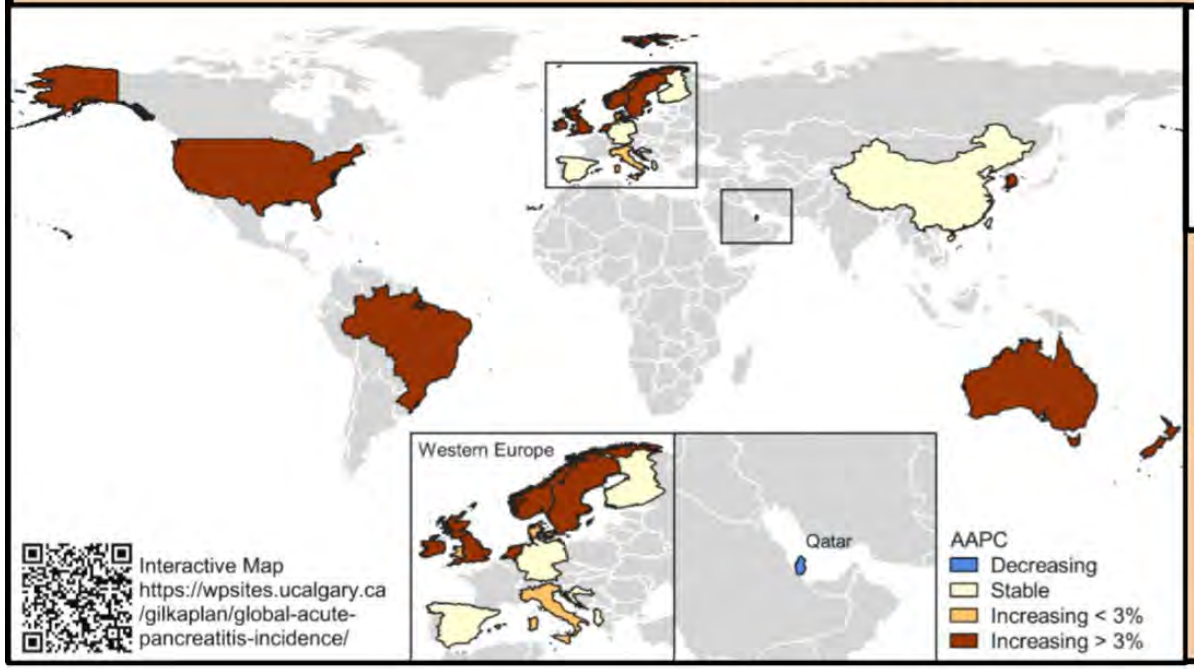
***Acute pancreatitis** Boxhoorn, Lotte et al. The Lancet, Volume 396, Issue 10252, 726 - 734*

# Epidemiology



# Epidemiology

## The global incidence of acute pancreatitis is increasing over time: A systematic review and meta-analysis




- 34 studies were analyzed for temporal trends in incidence of acute pancreatitis over time.
- Incidence of acute pancreatitis has increased over time with an average annual percent change (AAPC) of 3.07%.

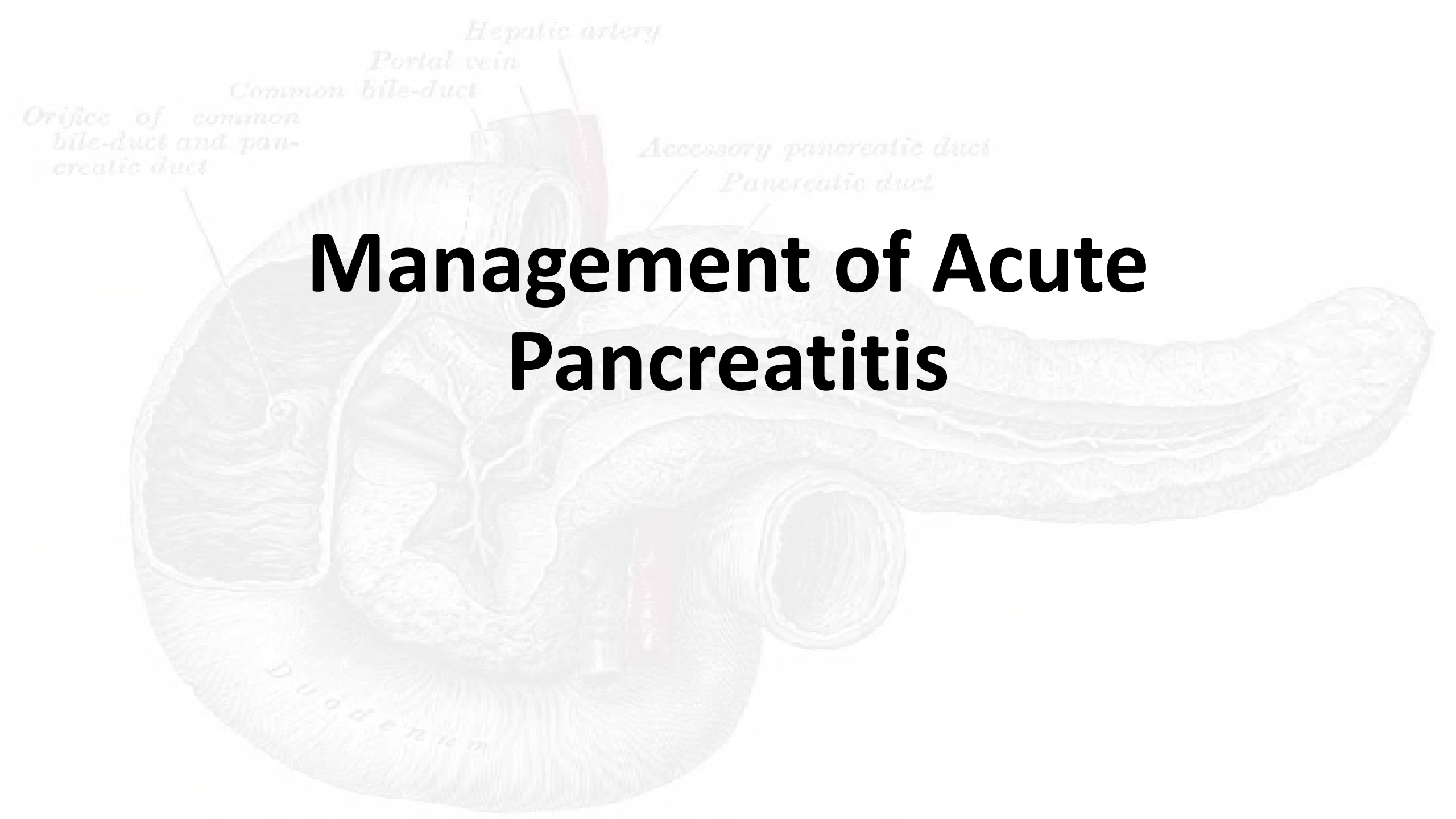
♀ = ♂

The increasing incidence of acute pancreatitis was similar between women and men.

AAPC of biliary and alcohol induced pancreatitis have increased significantly over time.

Gastroenterology

**Global Incidence of Acute Pancreatitis Is Increasing Over Time: A Systematic Review and Meta-Analysis** J. P. Iannuzzi, J. A. King, J. H. Leong, J. Quan, J. W. Windsor, D. Tanyingoh, et al. Gastroenterology 2022 Vol. 162 Issue 1 Pages 122-134




# Management of Acute Pancreatitis

# Management of Acute Pancreatitis

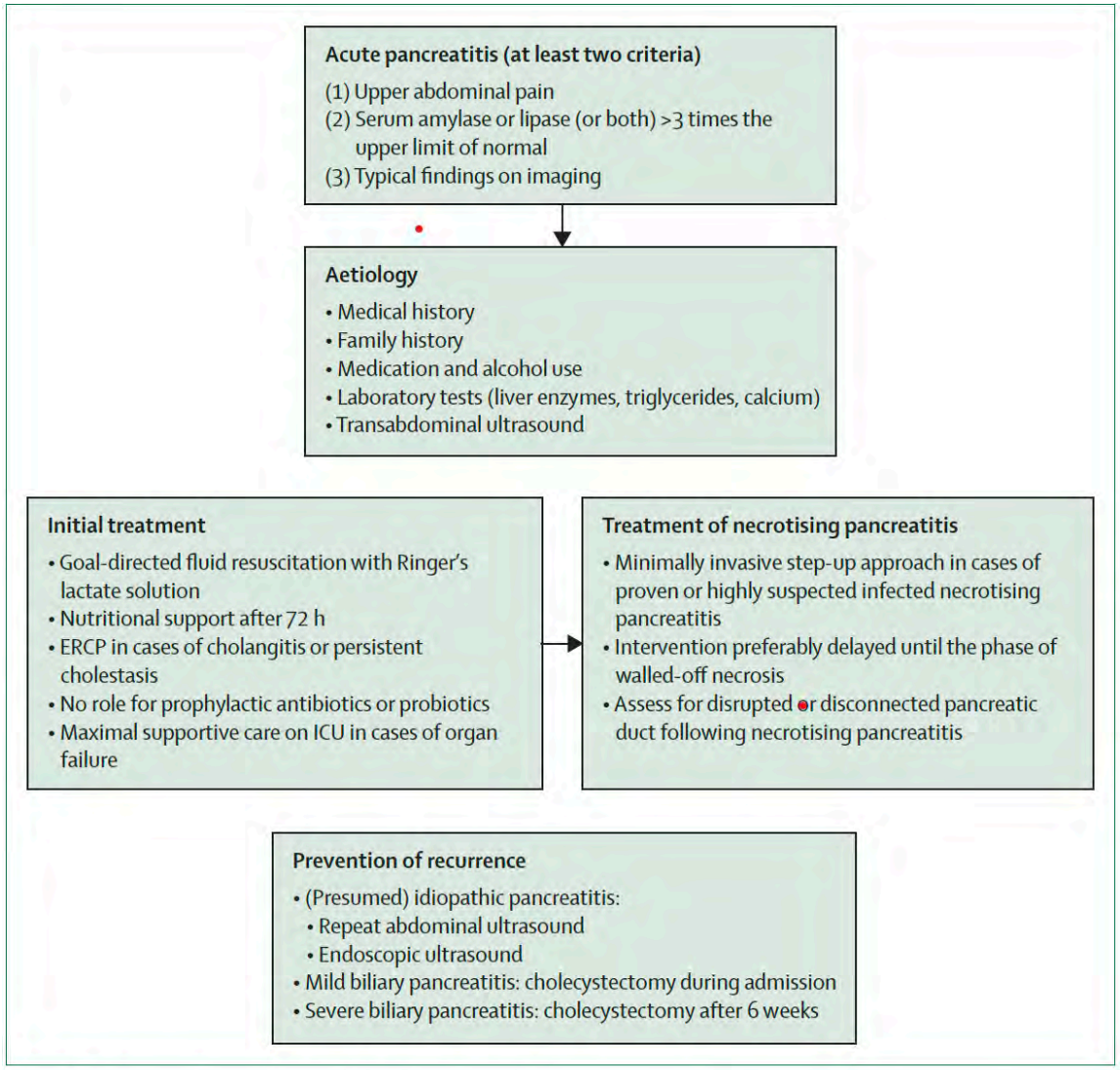
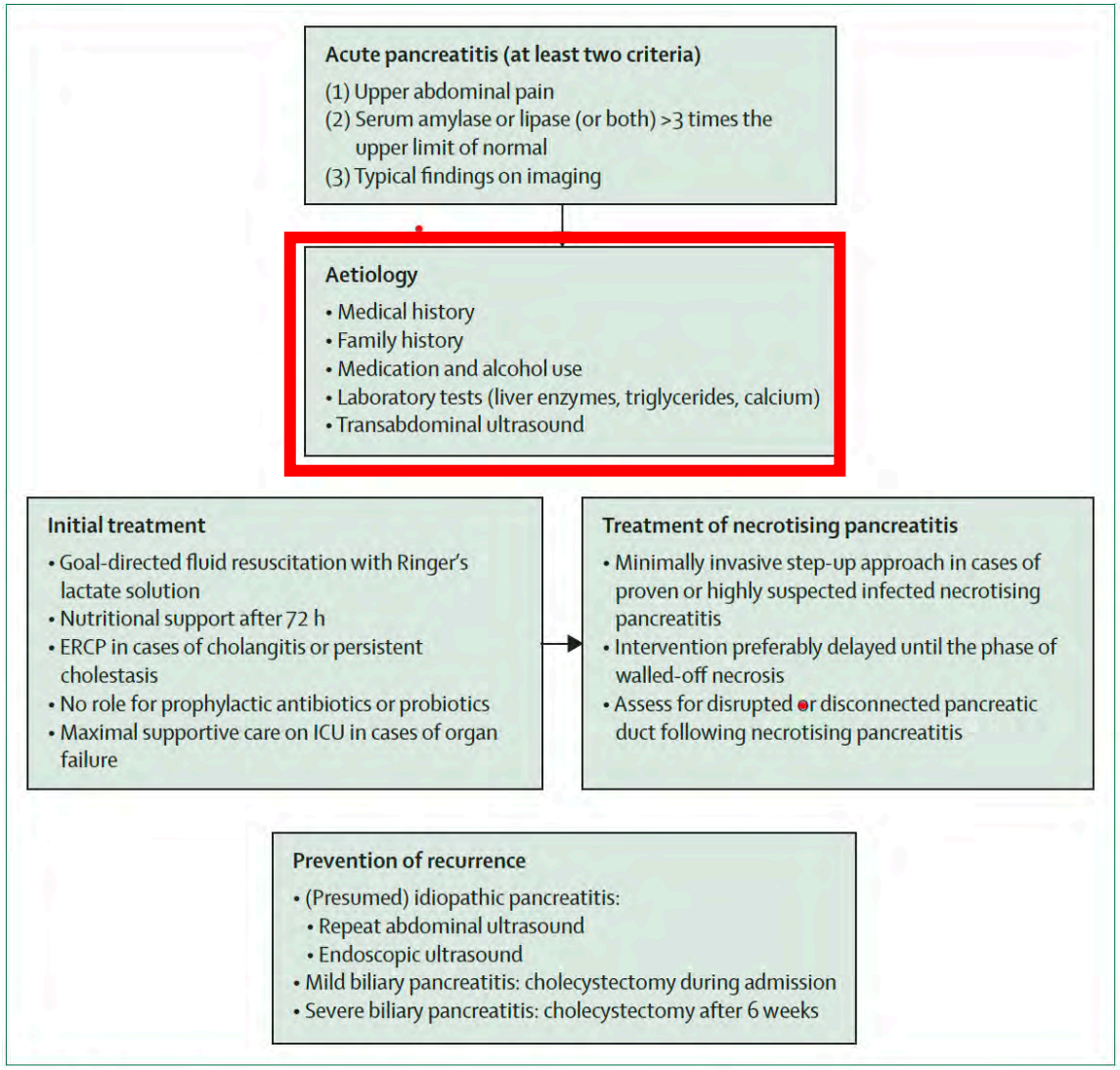



***Figure 1:*** **Treatment algorithm for acute pancreatitis**
ERCP=endoscopic retrograde cholangiopancreatography. ICU=intensive care unit.

*Acute pancreatitis* Boxhoorn, Lotte et al. The Lancet, Volume 396, Issue 10252, 726 - 734

# Management of Acute Pancreatitis

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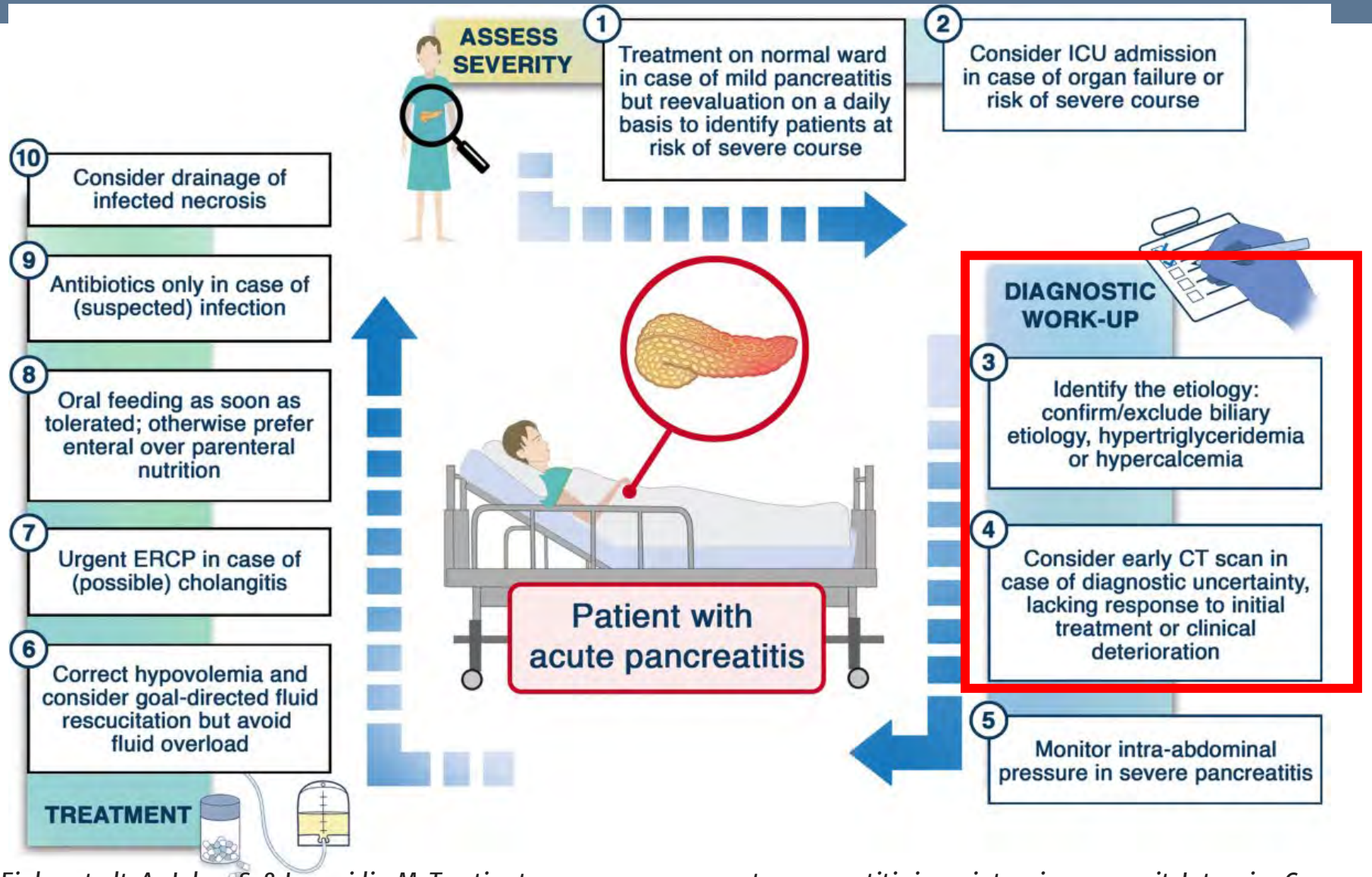
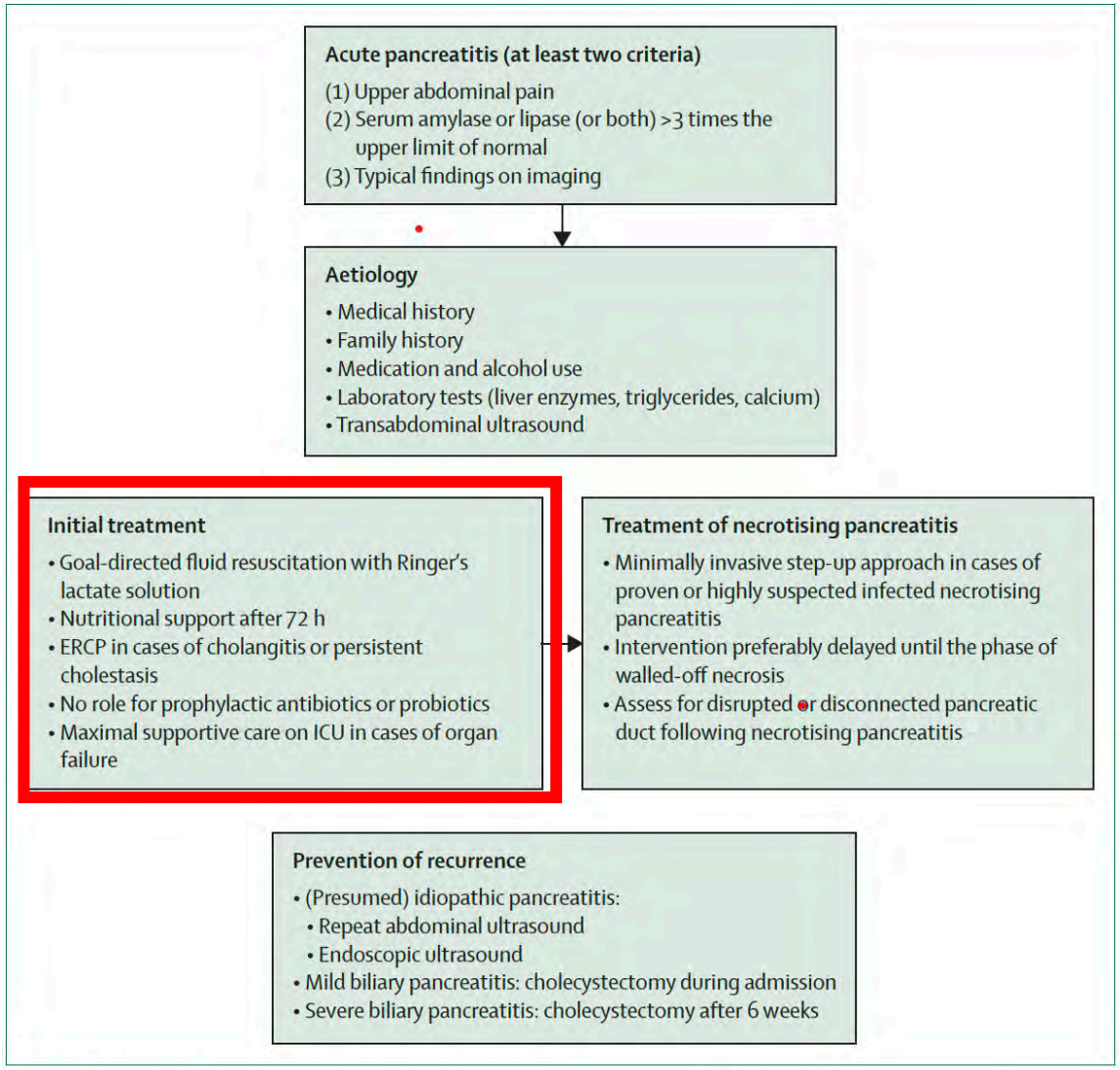



*Finkenstedt, A., Jaber, S. & Joannidis, M. Ten tips to manage severe acute pancreatitis in an intensive care unit. Intensive Care Med* **49**, *1127–1130 (2023).*

# Management of Acute Pancreatitis

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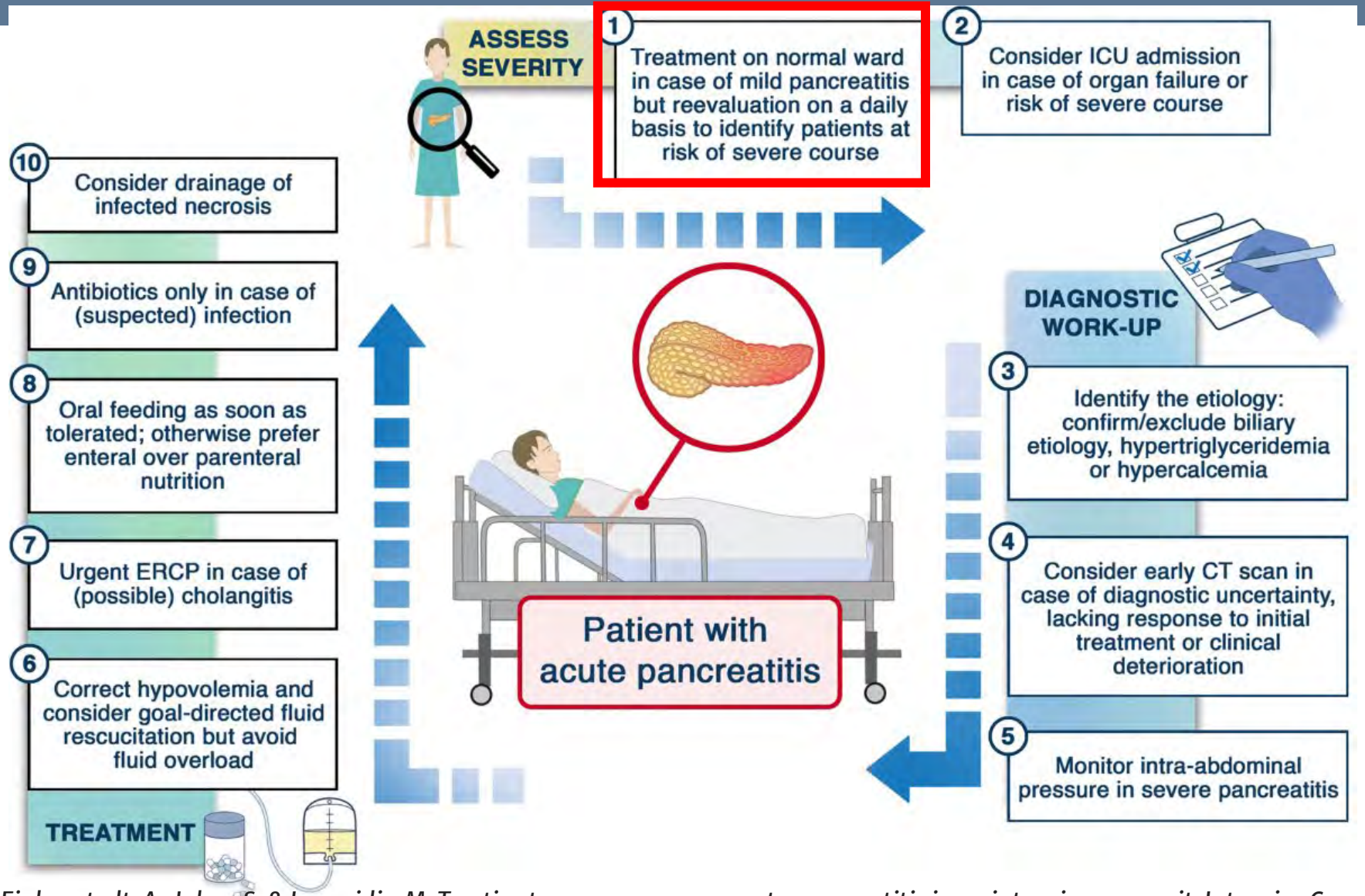


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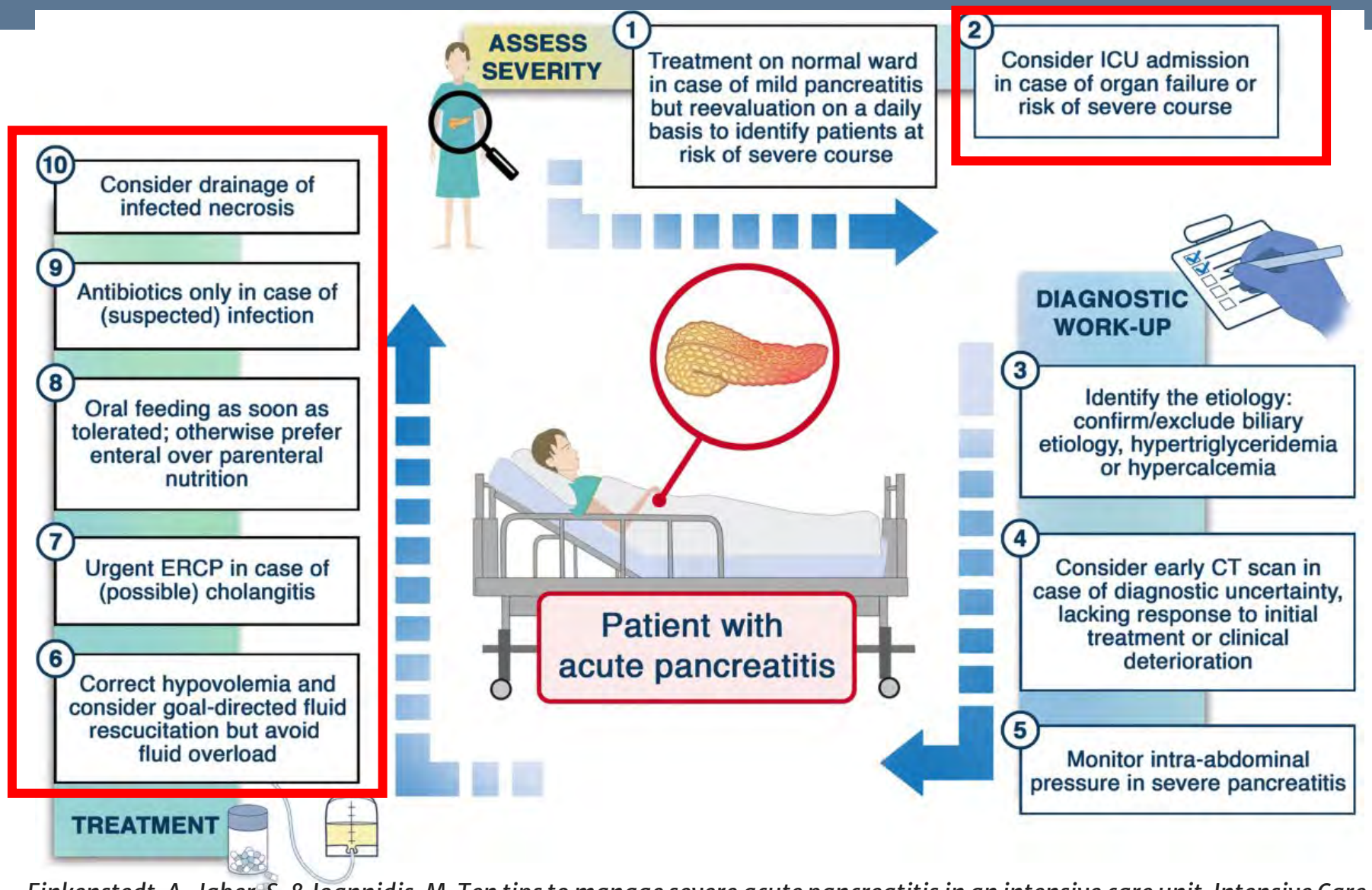


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# Fluid Resuscitation

## Rationale

Fluid resuscitation to prevent hypovolemia and organ hypoperfusion

- Intravascular volume depletion
- Third-space fluid sequestration in AP contribute
  - Renal and circulatory failure and
  - Lead to or  perturbations in pancreatic microcirculation, contributing to pancreatic necrosis and progression from mild to severe AP

*Diagnosis and Management of Acute Pancreatitis Trikudanathan, Guru et al. Gastroenterology, Volume 167, Issue 4, 673 - 688*

# Fluid Type ?

Current American Gastroenterological Association(AGA) guidelines recommend crystalloids initial resuscitation fluid and caution against colloids.

Crystalloids Ringers lactate(R/L) is preferred

- Reported to have anti-inflammatory properties and less acidic
- Associated with reduced surrogate markers of severity (C-reactive protein levels and SIRS) in comparison to Normal Saline

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# Fluid Rate

Guidelines endorse judicious goal-directed fluid resuscitation at a rate of 5-10 mL/kg/h during the first 12-24 hours, with further infusion rate titrated based on clinical and biochemical targets of perfusion.

These include :

- Clinical (heart rate <120/min, mean arterial pressure between 65 and 85 mm Hg, and urinary output >0.5 mL/kg/h) and
- Biochemical targets such as hematocrit (35%–45%) and blood urea nitrogen concentration.

These recommendations were conditionally based on low to moderate quality of evidence.

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# WATERFALL Study

WATERFALL study challenged current guidelines on the optimal rate of fluid administration.

- Patients were randomly assigned to **aggressive fluid resuscitation (20 mL/kg of bolus followed by 3 mL/kg/h) or moderate fluid resuscitation (10 mL/kg followed by 1.5 mL/kg/h).**
- Study halted early due to significant safety concerns, with a significant difference in fluid overload in the aggressive arm (20.5% vs 6.3%), without a significant difference in the incidence of moderately severe or severe AP (22.1% vs 17.3%) between the 2 groups.

*Diagnosis and Management of Acute Pancreatitis Trikudanathan, Guru et al. Gastroenterology, Volume 167, Issue 4, 673 - 688*

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-Marín, 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*

ABSTRACT

**BACKGROUND**

Early aggressive hydration is widely recommended for the management of acute pancreatitis, but evidence for this practice is limited.

**METHODS**

At 18 centers, we randomly assigned patients who presented with acute pancreatitis to receive goal-directed aggressive or moderate resuscitation with lactated Ringer's solution. Aggressive fluid resuscitation consisted of a bolus of 20 ml per kilogram of body weight, followed by 3 ml per kilogram per hour. Moderate fluid resuscitation consisted of a bolus of 10 ml per kilogram in patients with hypovolemia or no bolus in patients with normovolemia, followed by 1.5 ml per kilogram per hour in all patients in this group. Patients were assessed at 12, 24, 48, and 72 hours, and fluid resuscitation was adjusted according to the patient's clinical status. The primary outcome was the development of moderately severe or severe pancreatitis during the hospitalization. The main safety outcome was fluid overload. The planned sample size was 744, with a first planned interim analysis after the enrollment of 248 patients.

**RESULTS**

A total of 249 patients were included in the interim analysis. The trial was halted owing to between-group differences in the safety outcomes without a significant difference in the incidence of moderately severe or severe pancreatitis (22.1% in the aggressive-resuscitation group and 17.3% in the moderate-resuscitation group; adjusted relative risk, 1.30; 95% confidence interval [CI], 0.78 to 2.18; P=0.32). Fluid overload developed in 20.5% of the patients who received aggressive resuscitation and in 6.3% of those who received moderate resuscitation (adjusted relative risk, 2.85; 95% CI, 1.36 to 5.94, P=0.004). The median duration of hospitalization was 6 days (interquartile range, 4 to 8) in the aggressive-resuscitation group and 5 days (interquartile range, 3 to 7) in the moderate-resuscitation group.

**CONCLUSIONS**

In this randomized trial involving patients with acute pancreatitis, early aggressive fluid resuscitation resulted in a higher incidence of fluid overload without improvement in clinical outcomes. (Funded by Instituto de Salud Carlos III and others; WATERFALL ClinicalTrials.gov number, NCT04381169.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. de-Madaria can be contacted at emadaria@umh.es or at Servicio de Aparato Digestivo, Hospital General Universitario Dr. Balmis, Calle Pintor Baeza 12, Alicante 03010, Spain.

*A list of the trial collaborators in the ERICA Consortium is provided in the Supplementary Appendix, available at NEJM.org.

N Engl J Med 2022;387:989-1000.
DOI: 10.1056/NEJMoa2202884



CME at NEJM.org





2022

# WATERFALL TRIAL

## Aggressive or moderate fluid resuscitation in acute pancreatitis

multicenter, open-label, parallel-group, superiority, randomized controlled trial

**Objective: To evaluate the safety & efficacy of aggressive fluid resuscitation as compared with moderate fluid resuscitation for the management of acute pancreatitis**

**249 patients**

**Patients ≥18 yrs with acute pancreatitis (Revised Atlanta Classification-meeting 2 of the following 3 criteria: typical abdominal pain, serum amylase or lipase level >3 times the upper limit, or signs of acute pancreatitis on imaging) who presented ≤ 24 hrs after pain onset & diagnosed ≤ 8 hrs before enrollment**

| Aggressive fluid resuscitation (n=122) | | Moderate fluid resuscitation (n=127) |
|---|---|---|
| **PRIMARY OUTCOME** | | |
| 22.1 | Moderately severe or severe pancreatitis %<br>RR 1.30; 95% CI, 0.78 to 2.18; P=0.32 | 17.3 |
| **SECONDARY OUTCOMES** | | |
| 20.5 | Fluid Overload %<br>RR, 2.85; 95% CI, 1.36 to 5.94, P=0.004 | 6.3 |
| 6.6 | Severe pancreatitis %<br>RR 2.69; 95% CI, 0.56 to 12.88 | 1.6 |
| 20.5 | Any local complication %<br>RR 1.28; 95% CI, 0.74 to 2.22 | 16.5 |

**Conclusion: Among patients with acute pancreatitis, early aggressive fluid resuscitation resulted in a higher incidence of fluid overload without improvement in clinical outcomes.**

E de-Madaria et al. NEJM 2022; 387:989-1000 | Summary by Dr.Shreyash Bhoyar, MBBS

Visualmed

# Recommendation

Initial resuscitation of 1.5 mL/kg/h with a bolus of 10 mL/kg only if there are signs of :

- Initial hypovolemia,
- Close clinical and hemodynamic monitoring for euvolemic status during the first 72 hours,
- Appropriate diuresis if there is fluid overload.

*Diagnosis and Management of Acute Pancreatitis Trikudanathan, Guru et al. Gastroenterology, Volume 167, Issue 4, 673 - 688*

# Nutrition in Acute Pancreatitis

Patients with AP are considered moderate to high nutritional risk due to :

- Proinflammatory state
- Increased resting energy expenditure
- Catabolic nature of the disease
- Ongoing abdominal pain limiting oral intake
- Complications such as gastric outlet obstruction
- Concomitant paralytic ileus
- Micronutrient deficiency inherent with chronic alcohol consumption (if present).

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# Nutrition in Acute Pancreatitis

- Current guidelines recommend :
  Initiating early (as soon as tolerated) oral feeding with solid (low-fat) diet in patients with predicted mild AP and this approach reduces length of hospitalization.
- Traditionally the concept of “pancreatic rest” (initiation of oral nutrition only after complete resolution of abdominal pain and normalization of pancreatic enzymes) guided nutritional management in severe AP.
- Total parenteral nutrition (TPN) and a stepwise initiation of oral diet beginning with clear liquid were previously favoured.
- Studies noted that the pancreas is largely insensitive to meal stimulation during AP.
- Early enteral nutrition (EN) –preserves gut mucosal integrity and reduces gut bacterial translocation.
- EN was compared with TPN in AP in several RCTs results showed superiority of EN in mortality, multiorgan failure, and rate of infection.
- Current guidelines recommend :
  Initiating early (as soon as tolerated) oral feeding with solid (low-fat) diet in patients with predicted mild AP and this approach reduces length of hospitalization.

*Diagnosis and Management of Acute Pancreatitis Trikudanathan, Guru et al. Gastroenterology, Volume 167, Issue 4, 673 - 688*

# Nutrition in Acute Pancreatitis

Parenteral Nutrition:

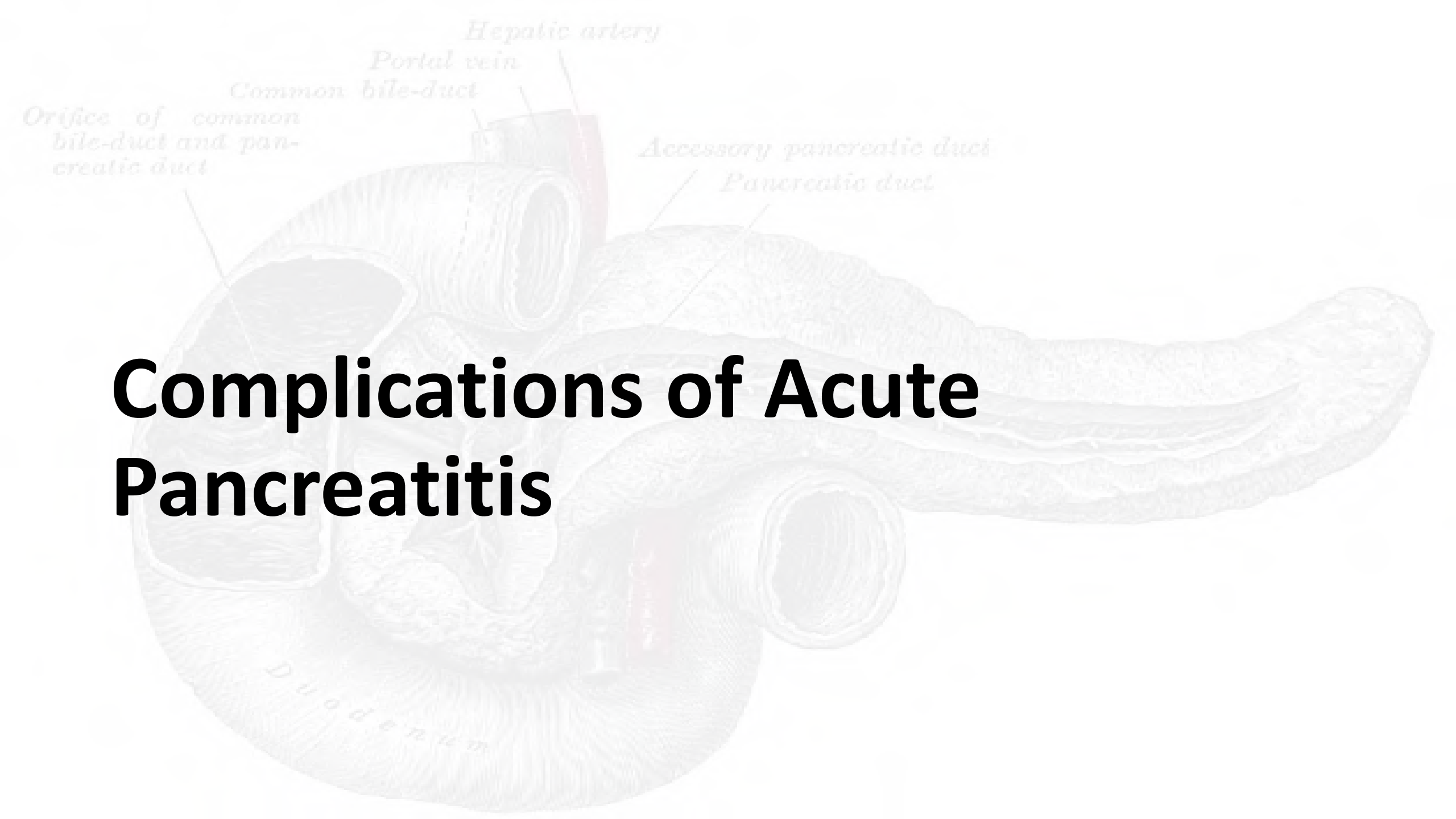
- Increase  cost burden,
- Increased risk of catheter-related sepsis
- Electrolyte and metabolic derangement
- Gut barrier failure, currently use of TPN is reserved for patients for whom EN is not possible or is not able to meet the minimum calorie requirements.

*Diagnosis and Management of Acute Pancreatitis Trikudanathan, Guru et al. Gastroenterology, Volume 167, Issue 4, 673 - 688*

# Nutrition in Acute Pancreatitis

- In patients with predicted severe AP, early EN was not shown to improve outcomes in comparison with attempts at oral feeding at 72 hours.
- The PYTHON trial in 208 patients with predicted severe AP :
  - Early EN (within 24 hours) did not reduce the rate of infection (25% vs 26%) or mortality (11% vs 7%) when compared with on-demand oral diet initiated 72 hours after admission.
- Therefore in  predicted severe AP, :
  - Initiate oral diet at 72 hours (or earlier if tolerated) and initiate tube-based EN if not tolerated.
  - The route of EN can either be nasogastric, nasoduodenal, or nasojejunal because all are safe and well tolerated.
- Naso-jejunal tube feeding is preferred if there is digestive intolerance from delayed gastric emptying and gastric outlet obstruction.
- Pancreatic enzyme supplementation can be also be considered in patients with proven or suspected exocrine pancreatic insufficiency.

*Diagnosis and Management of Acute Pancreatitis Trikudanathan, Guru et al. Gastroenterology, Volume 167, Issue 4, 673 - 688*




# Complications of Acute Pancreatitis

**BOX 58.7** Complications of Acute Pancreatitis

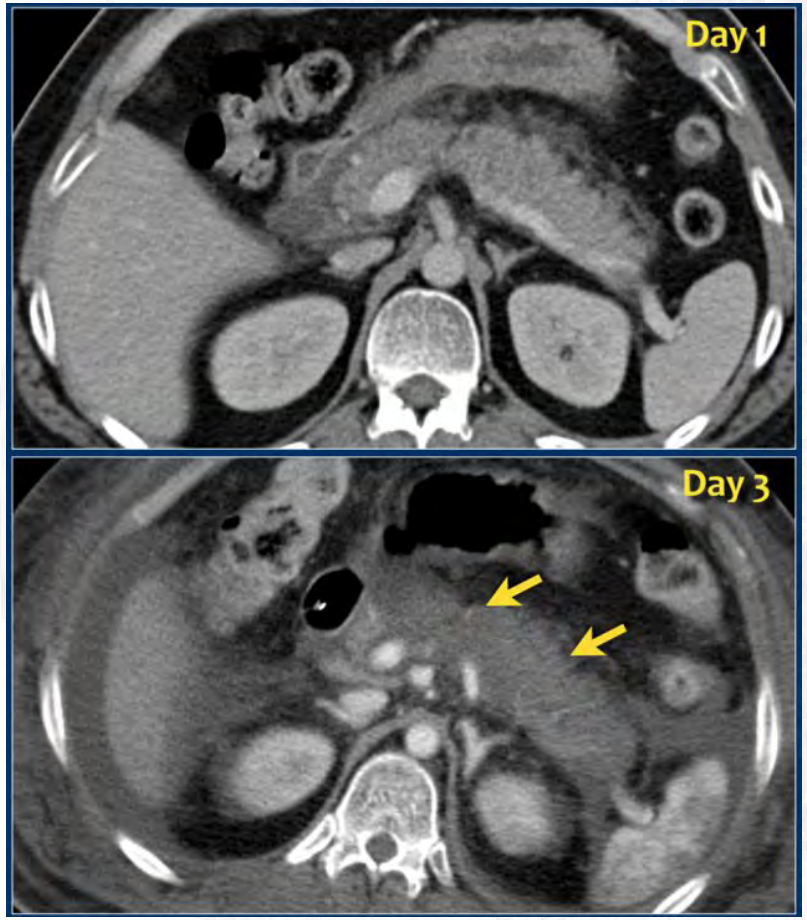
**LOCAL**

- 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

# CT




*The Radiology Assistant : Acute Pancreatitis*. (2015, May https://radiologyassistant.nl/abdomen/pancreas/acute-pancreatitis

- CT is the imaging modality of choice for the diagnosis and staging of acute pancreatitis and its complications.
- Ultrasound and ERCP with sphincterotomy and stone extraction play an important role in biliary pancreatitis.
- Since the diagnosis of acute pancreatitis is usually made on clinical and laboratory findings, an early CT is only recommended when the diagnosis is uncertain, or in case of suspected early complications such as bowel perforation or ischemia.
- An early CT may be misleading regarding the morphologic severity of the pancreatitis, because it may underestimate the presence and amount of necrosis.

# CT Severity Index

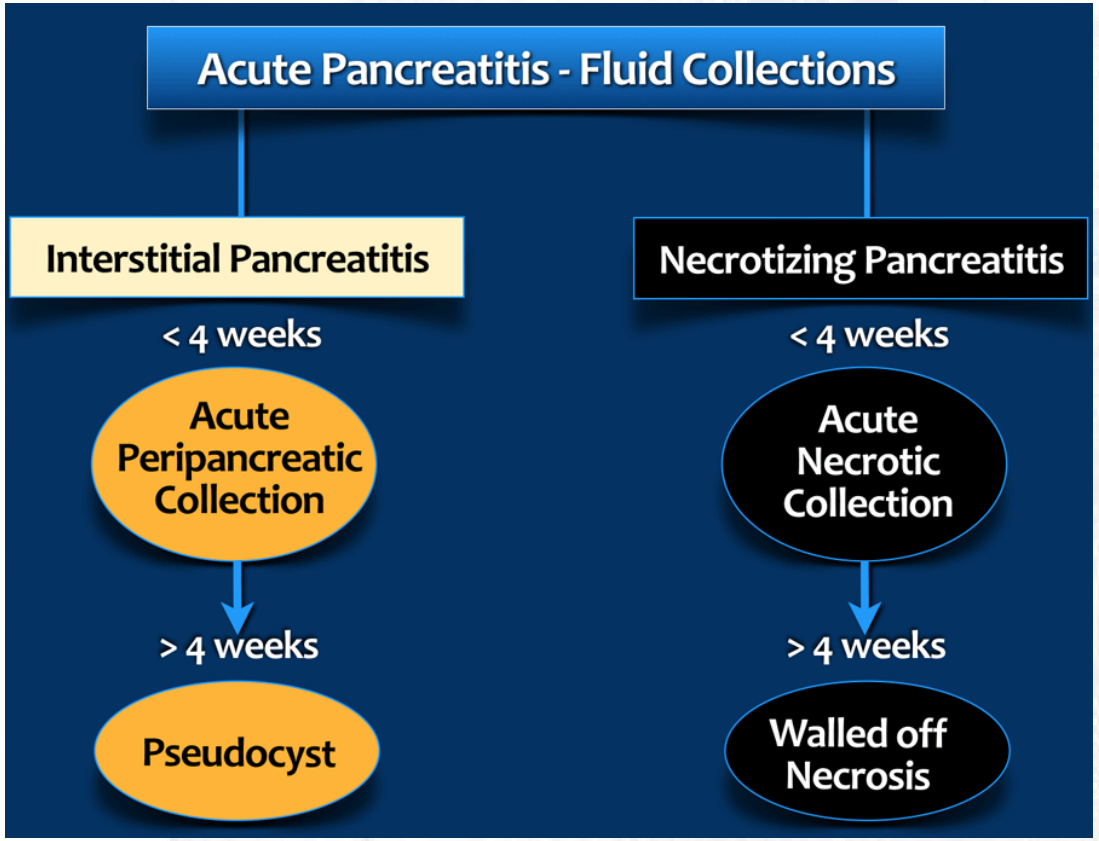
**CT Severity Index**

| | | points | |
|---|---|---|---|
| **Pancreatic inflammation** | | | |
| Normal pancreas | | 0 | choose one |
| Enlargement of the pancreas | | 1 | |
| Peripancreatic inflammation | | 2 | |
| 1 acute peripancreatic fluid collection | | 3 | |
| ≥ 2 acute peripancreatic fluid collections | | 4 | |
| **Pancreatic necrosis** | None | 0 | choose one |
| | < 30% | 2 | |
| | 30% - 50% | 4 | |
| | > 50% | 6 | |
| | | **Maximum 10 points** | |

- The CT severity index (CTSI) combines the Balthazar grade (0-4 points) with the extent of pancreatic necrosis (0-6 points) on a 10-point severity scale.
- On the day of admission, CT scoring systems not better than clinical scoring in predicting clinical outcome.

*The Radiology Assistant : Acute Pancreatitis.* (2015, May https://radiologyassistant.nl/abdomen/pancreas/acute-pancreatitis

# Acute Pancreatitis –Fluid Collections




**Atlanta Classification of Fluid Collections**

- The 2012 Revised Atlanta Classification discerns 4 types of peripancreatic fluid collections in acute pancreatitis depending on the content, degree of encapsulation and time.
    1. **Content**
        1. Fluid only in acute peripancreatic fluid collection (APFC) and Pseudocyst.
        2. Mixture of fluid and necrotic material in acute necrotic collection (ANC**) and** walled-off-necrosis (WON).
    2. **Degree of encapsulation**
        1. None or partial wall in APFC and ANC.
        2. Complete encapsulation in pseudocyst and WON.
    3. **Time**
        1. Within 4 weeks: APFC and ANC
        2. After 4 weeks: pseudocysts and WON. It takes about 4 weeks for a capsule to form.
- On CT, the discrimination between an APFC and ANC may be difficult, especially in the first weeks and the term "indeterminate peripancreatic collections" can be used.
- All these collections may remain sterile or become infected. Infection is rare during the first week.

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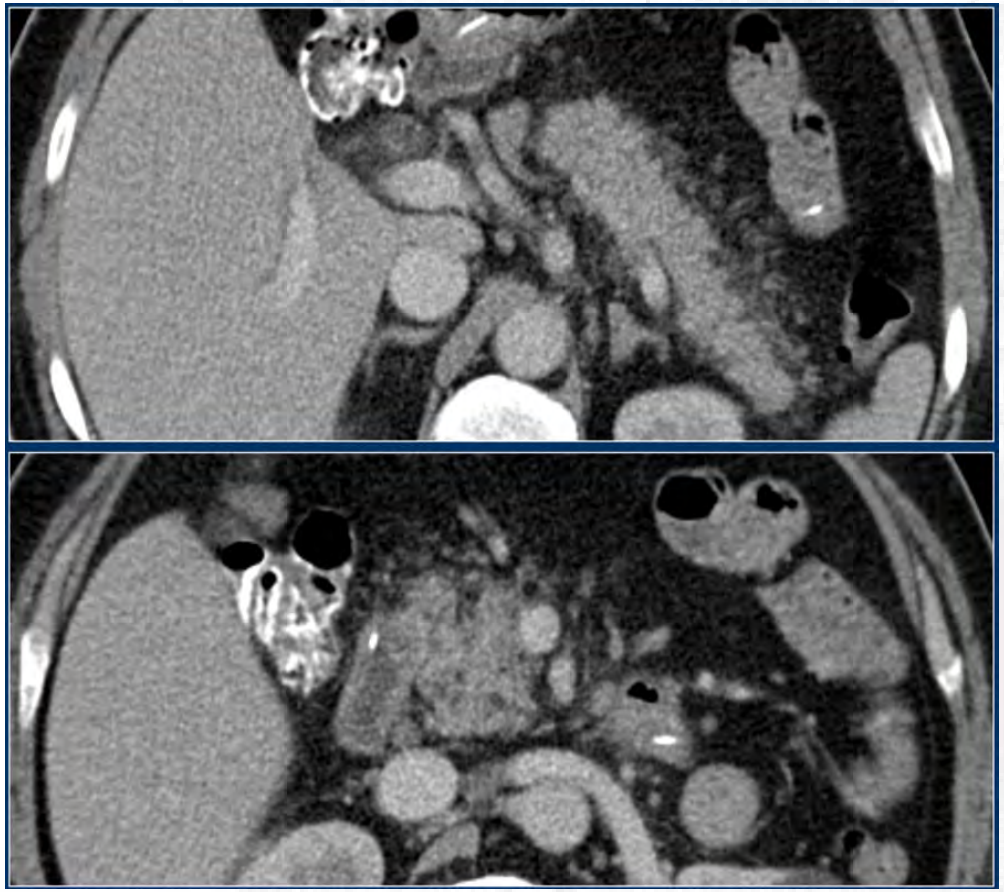
# Interstitial Pancreatitis



- There is normal enhancement of the entire pancreatic gland with only mild surrounding fatty infiltration.
- There are no fluid collections and there is no necrosis of the pancreatic parenchyma.

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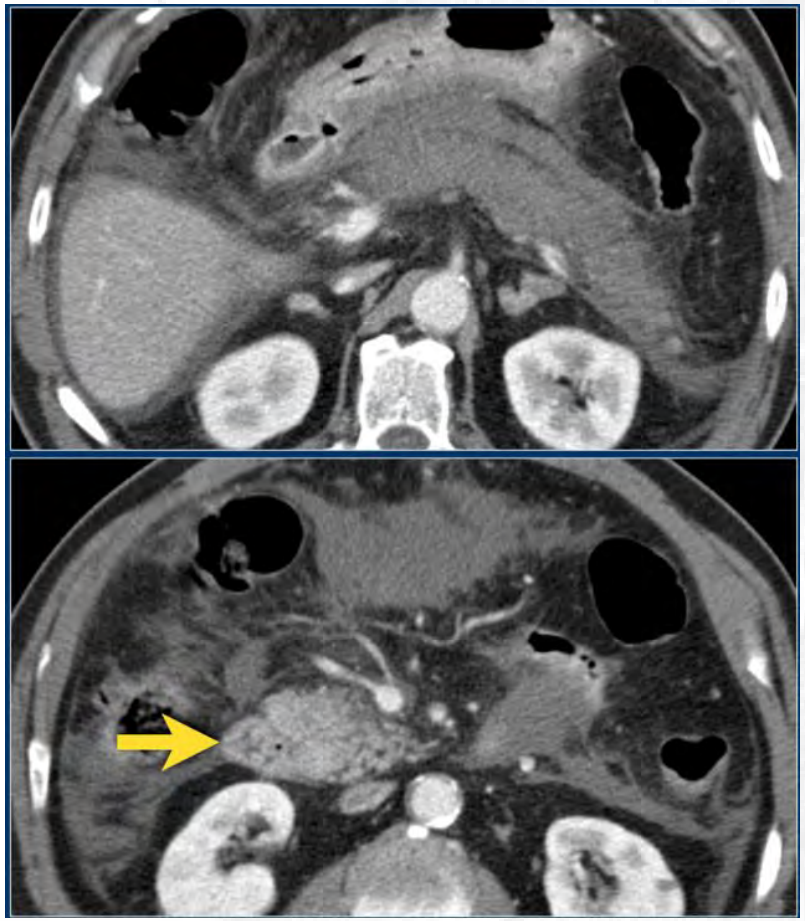
# Necrotizing Pancreatitis



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Necrosis of pancreatic parenchyma or peripancreatic tissues occurs in 10-15 % of patients. It is characterized by a protracted clinical course, a high incidence of local complications, and a high mortality rate.

There are 3 subtypes of necrotizing pancreatitis:

1. Necrosis of *both* pancreatic parenchyma and peripancreatic tissues (most common).
2. Necrosis of *only* extrapancreatic tissue without necrosis of pancreatic parenchyma (less common).
3. Necrosis of pancreatic parenchyma without surrounding necrosis of peripancreatic tissue (very rare).

Necrosis of the pancreatic parenchyma can be diagnosed on a contrast-enhanced CT $\geqslant$ 72 hours.
Necrosis of peripancreatic tissue can be vary difficult to diagnose, but is suspected when the collection is inhomogeneous, i.e. various densities on CT..

The CT shows an acute necrotizing pancreatitis.
The body and tail of the pancreas do not enhance.
There is normal enhancement of the pancreatic head.

More than 50% of the pancreas is necrotic and there are at least two collections.

## Acute Peripancreatic Collection

- < 4 weeks
- In interstitial pancreatitis
- Homogeneous - fluid density
- *No fully definable wall*
- Adjacent to pancreas
- Confined by normal fascial planes

## Acute Necrotic Collection

- < 4 weeks
- In necrotizing pancreatitis
- Heterogeneous collection
- *No fully definable wall*
- Intra- or extrapancreatic

## Pseudocyst

- > 4 weeks
- In interstitial pancreatitis
- Homogeneous - fluid density
- *Well defined wall*
- Adjacent to pancreas
- No non-liquid component

## Walled-off Necrosis

- > 4 weeks
- In necrotizing pancreatitis
- Heterogeneous collection
- *Well-defined wall*
- Intra- or extrapancreatic

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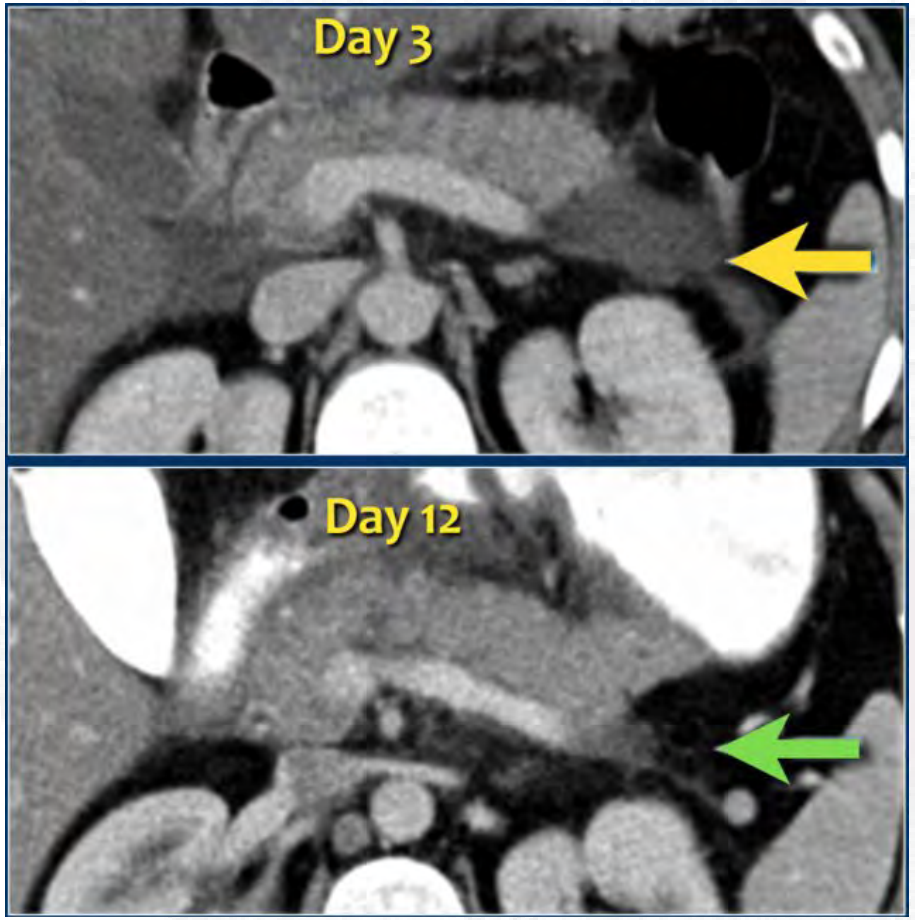
# Acute Peripancreatic Fluid Collection( APFC)

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- Intraabdominal fluid collections and collections of necrotic tissue are common in acute pancreatitis.
- These collections develop early in the course of acute pancreatitis.
  In the early stage, such a collection does not have a wall or capsule.
  Preferred locations of fluid collections are:
  - Lesser sac
  - Anterior and posterior pararenal space of the retroperitoneum.
  - Transverse mesocolon
  - Small bowel mesentery.
- These collections are the result of the release of activated pancreatic enzymes which also cause necrosis of the surrounding tissues.
  This explains why many of these collections harbor solid necrotic debris.
- About 50% of these collections show spontaneous regression
  The remaining 50% either remain stable or increase and undergo organization and demarcation with liquefaction.
  They may remain sterile or develop infection.

## Acute Peripancreatic Collection

- < 4 weeks
- In interstitial pancreatitis
- Homogeneous - fluid density
- *No fully definable wall*
- Adjacent to pancreas
- Confined by normal fascial planes

## Acute Necrotic Collection

- < 4 weeks
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## Pseudocyst

- > 4 weeks
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- *Well defined wall*
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- No non-liquid component

## Walled-off Necrosis

- > 4 weeks
- In necrotizing pancreatitis
- Heterogeneous collection
- *Well-defined wall*
- Intra- or extrapancreatic

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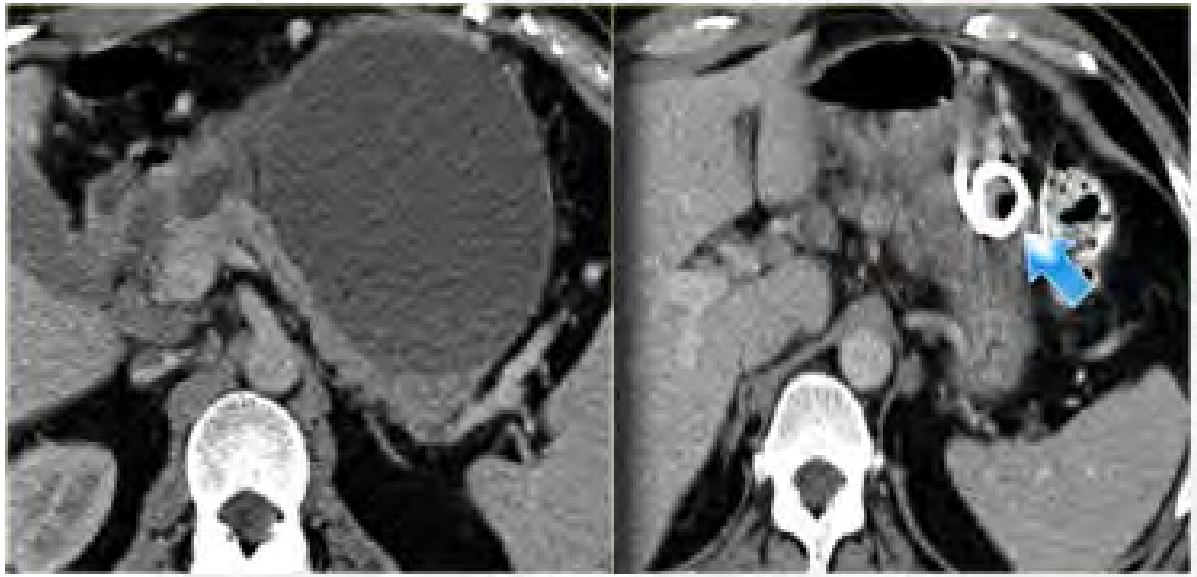
# Pseudocyst



- A Pseudocyst is a collection of pancreatic juice or fluid enclosed by a complete wall of fibrous tissue
  It occurs in interstitial pancreatitis and the absence of necrotic tissue is imperative for its diagnosis.
- Communication with the pancreatic duct may be present.
  A pseudocyst requires 4 or more weeks to develop.
- The differential diagnosis includes walled-off necrosis and sometimes a pseudoaneurysm or even a cystic tumor.
  Most often, they occur in the lesser sac.
- Most collections that persist after 4 weeks are walled-of-necrosis.
  True pseudocysts are uncommon, since most acute peripancreatic fluid collections resolve within 4 weeks.

*The Radiology Assistant : Acute Pancreatitis.* (2015, May https://radiologyassistant.nl/abdomen/pancreas/acute-pancreatitis

## Acute Peripancreatic Collection

- < 4 weeks
- In interstitial pancreatitis
- Homogeneous - fluid density
- *No fully definable wall*
- Adjacent to pancreas
- Confined by normal fascial planes

## Acute Necrotic Collection

- < 4 weeks
- In necrotizing pancreatitis
- Heterogeneous collection
- *No fully definable wall*
- Intra- or extrapancreatic

## Pseudocyst

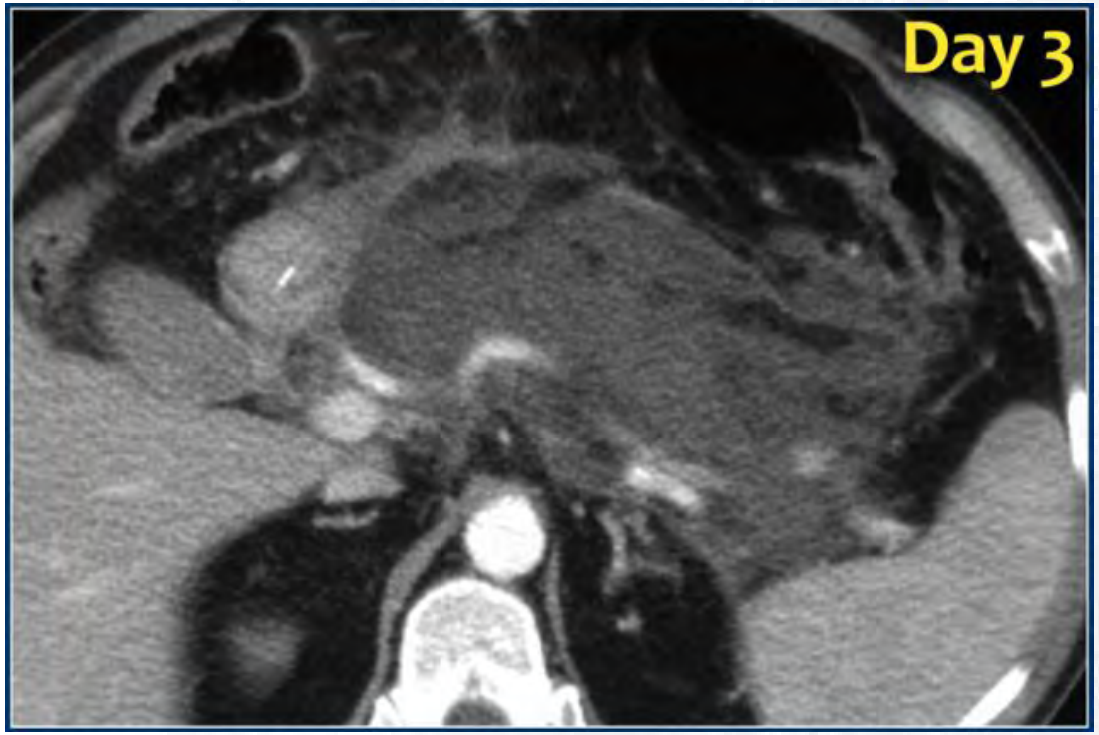
- > 4 weeks
- In interstitial pancreatitis
- Homogeneous - fluid density
- *Well defined wall*
- Adjacent to pancreas
- No non-liquid component

## Walled-off Necrosis

- > 4 weeks
- In necrotizing pancreatitis
- Heterogeneous collection
- *Well-defined wall*
- Intra- or extrapancreatic

*The Radiology Assistant : Acute Pancreatitis*. (2015, May https://radiologyassistant.nl/abdomen/pancreas/acute-pancreatitis

# Acute Necrotic Collection




- Necrosis of the pancreas
- Inhomogeneous collection in the peripancreatic tissue
- No wall

We can conclude that this is an acute necrotic collection - ANC.

*The Radiology Assistant : Acute Pancreatitis.* (2015, May https://radiologyassistant.nl/abdomen/pancreas/acute-pancreatitis

## Acute Peripancreatic Collection

- < 4 weeks
- In interstitial pancreatitis
- Homogeneous - fluid density
- *No fully definable wall*
- Adjacent to pancreas
- Confined by normal fascial planes

## Acute Necrotic Collection

- < 4 weeks
- In necrotizing pancreatitis
- Heterogeneous collection
- *No fully definable wall*
- Intra- or extrapancreatic

## Pseudocyst

- > 4 weeks
- In interstitial pancreatitis
- Homogeneous - fluid density
- *Well defined wall*
- Adjacent to pancreas
- No non-liquid component

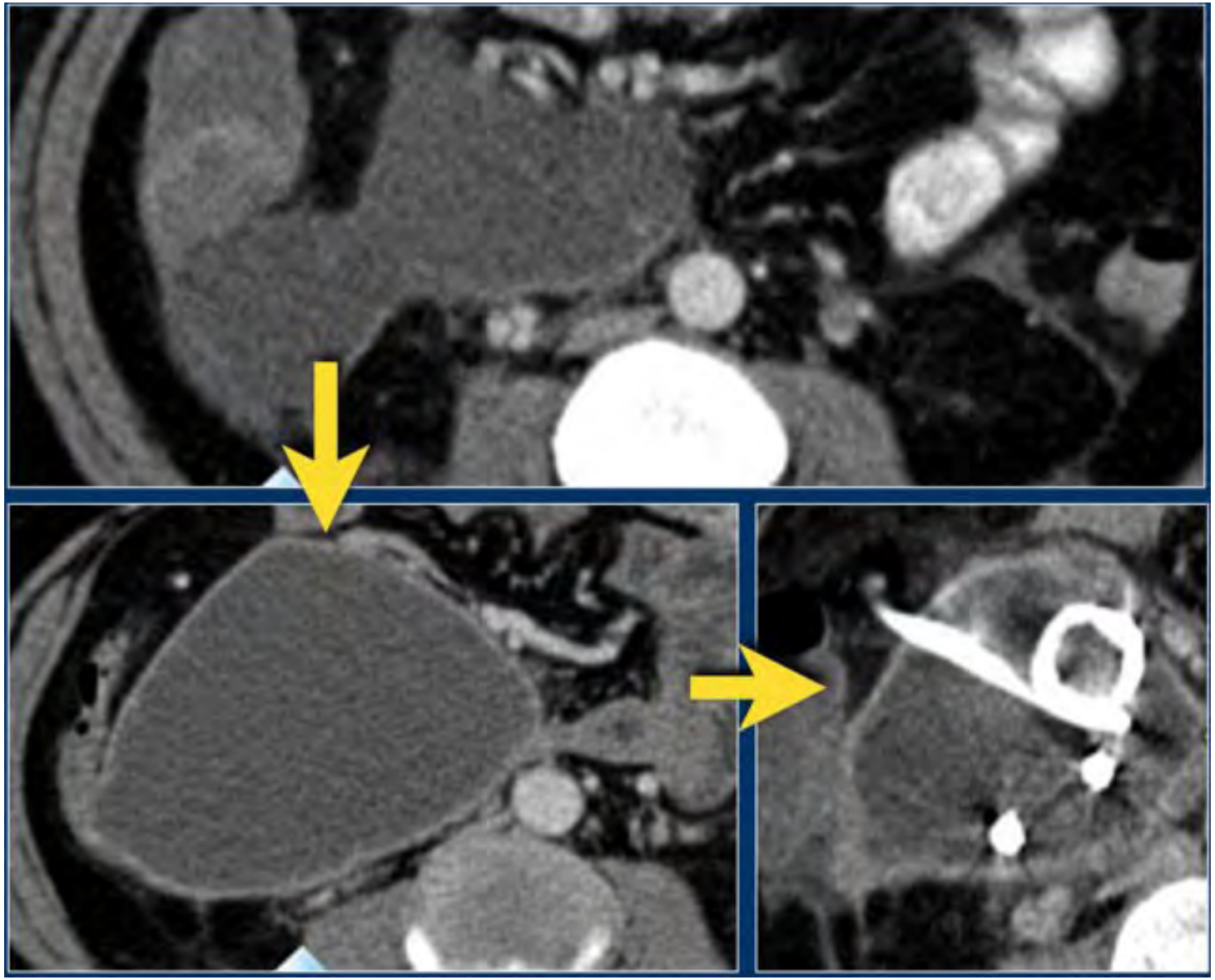
## Walled-off Necrosis

- > 4 weeks
- In necrotizing pancreatitis
- Heterogeneous collection
- *Well-defined wall*
- Intra- or extrapancreatic

*The Radiology Assistant : Acute Pancreatitis*. (2015, May https://radiologyassistant.nl/abdomen/pancreas/acute-pancreatitis

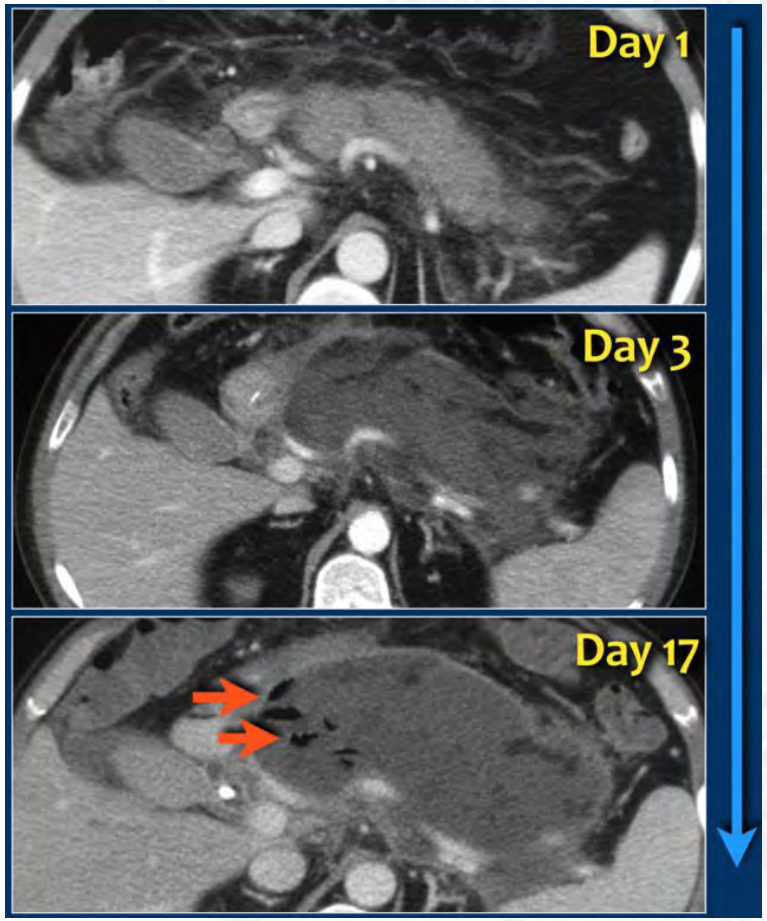
# Walled of Necrosis

- 
- .
- .



*The Radiology Assistant : Acute Pancreatitis.* (2015, May https://radiologyassistant.nl/abdomen/pancreas/acute-pancreatitis

# Infected Necrosis




Usually occurs in the 2nd-4th week and rarely in the first week.

Most severe local complication of acute necrotizing pancreatitis.

- Most common cause of death in patients with acute pancreatitis.
- Diagnose infected necrosis when there are gas bubbles on CT (seen in 40%) or when FNA is positive for bacteria
- On day 1 there is enhancement of the pancreas and it just looks like a mild interstitial pancreatitis.
- On day 3 there is no enhancement of the pancreas, consistent with necrosis.
- The necrosis also involves the peripancreatic tissue. So this is an ANC - acute necrotic collection.
- On day 17 there are gas bubbles in the necrotic collection consistent with infected pancreatic and peripancreatic necrosis.

*The Radiology Assistant : Acute Pancreatitis.* (2015, May https://radiologyassistant.nl/abdomen/pancreas/acute-pancreatitis

# Management of Interstitial Oedematous Pancreatitis

- Acute pancreatic or peripancreatic fluid collections in interstitial oedematous pancreatitis resolve spontaneously in the first few weeks after onset of disease and rarely require intervention
- Development of a pancreatic pseudocyst is rare after acute pancreatitis
- Indication for the intervention of pancreatic pseudocysts is determined by the presence of symptoms, such as gastric outlet obstruction or abdominal pain.
- Pseudocyst larger that 6cm often cause symptoms
- Drainage of pancreatic pseudocysts is preferably done after the collection is encapsulated to reduce the risk of complications, which takes approximately 4–6 weeks from the onset of the disease.

*Diagnosis and Management of Acute Pancreatitis Trikudanathan, Guru et al. Gastroenterology, Volume 167, Issue 4, 673 - 688*

# Intervention strategies

- Drainage modalities :
  - Endoscopic trans-luminal drainage is preferred when a pseudocyst can be reached endoscopically.
  - If a pseudocyst communicates with the main pancreatic duct, additional transpapillary drainage might be needed.
- Role of combined endoscopic transluminal drainage and trans-papillary drainage for pancreatic pseudocysts remains debated, because no additional benefit in reducing reoccurrence

*Diagnosis and Management of Acute Pancreatitis Trikudanathan, Guru et al. Gastroenterology, Volume 167, Issue 4, 673 - 688*

# Management of Necrotizing Pancreatitis

- The majority of patients with sterile pancreatic or peripancreatic necrosis can be treated conservatively , regardless of size and extension
- Drainage of sterile pancreatic or peripancreatic necrosis can introduce iatrogenic infection, with consequent exposure to additional interventions and procedure-related risks.
- Intervention should only be considered in the small subgroup of patients with persistent symptoms, such as abdominal pain, gastric outlet obstruction, jaundice, or failure to thrive at least 4–8 weeks after onset of the disease
- In contrast, secondary infection of peripancreatic necrosis nearly always requires invasive intervention.
- Secondary infection becomes apparent by gas configurations in the necrotic collection on CECT 50% patients
- The other 50% of patients , clinical signs of infection are often sufficient to diagnose secondary infection of pancreatic or peripancreatic necrosis
- A positive gram stain or culture of the necrotic collection, obtained by transabdominal fine-needle aspiration, can be required in case of diagnostic uncertainty  but has a 25% false negative rate

*Diagnosis and Management of Acute Pancreatitis Trikudanathan, Guru et al. Gastroenterology, Volume 167, Issue 4, 673 - 688*

# Management of Necrotizing Pancreatitis

- The first step in treating patients with infected necrotising pancreatitis is the administration of broad-spectrum antibiotic therapy.
- A small proportion of patients can be managed with supportive care and antibiotics alone, without the need for additional invasive interventions.

*Diagnosis and Management of Acute Pancreatitis Trikudanathan, Guru et al. Gastroenterology, Volume 167, Issue 4, 673 - 688*

# Management of Necrotizing Pancreatitis

1.Indications for intervention in necrotizing pancreatitis are:

- Clinical suspicion or documented infected necrotizing pancreatitis with clinical deterioration
- Ongoing organ failure for several weeks after disease onset in the absence of documented infected necrotizing pancreatitis.

2. Indications for intervention in sterile necrotizing pancreatitis are:

- Ongoing gastric outlet, intestinal, or biliary obstruction due to mass effect of walled-off necrosis (i.e. arbitrarily >4-8 weeks after onset of acute pancreatitis)
- Persistent debilitating symptoms in patients with walled-off necrosis without signs of infection (i.e. arbitrarily >8 weeks after onset of acute pancreatitis)
- Disconnected duct syndrome with persisting symptoms (e.g. pain, obstruction) collection(s) with walled-off necrosis

*Diagnosis and Management of Acute Pancreatitis Trikudanathan, Guru et al. Gastroenterology, Volume 167, Issue 4, 673 - 688*

# Management of Necrotizing Pancreatitis

3.Proven or suspected infected necrotizing pancreatitis

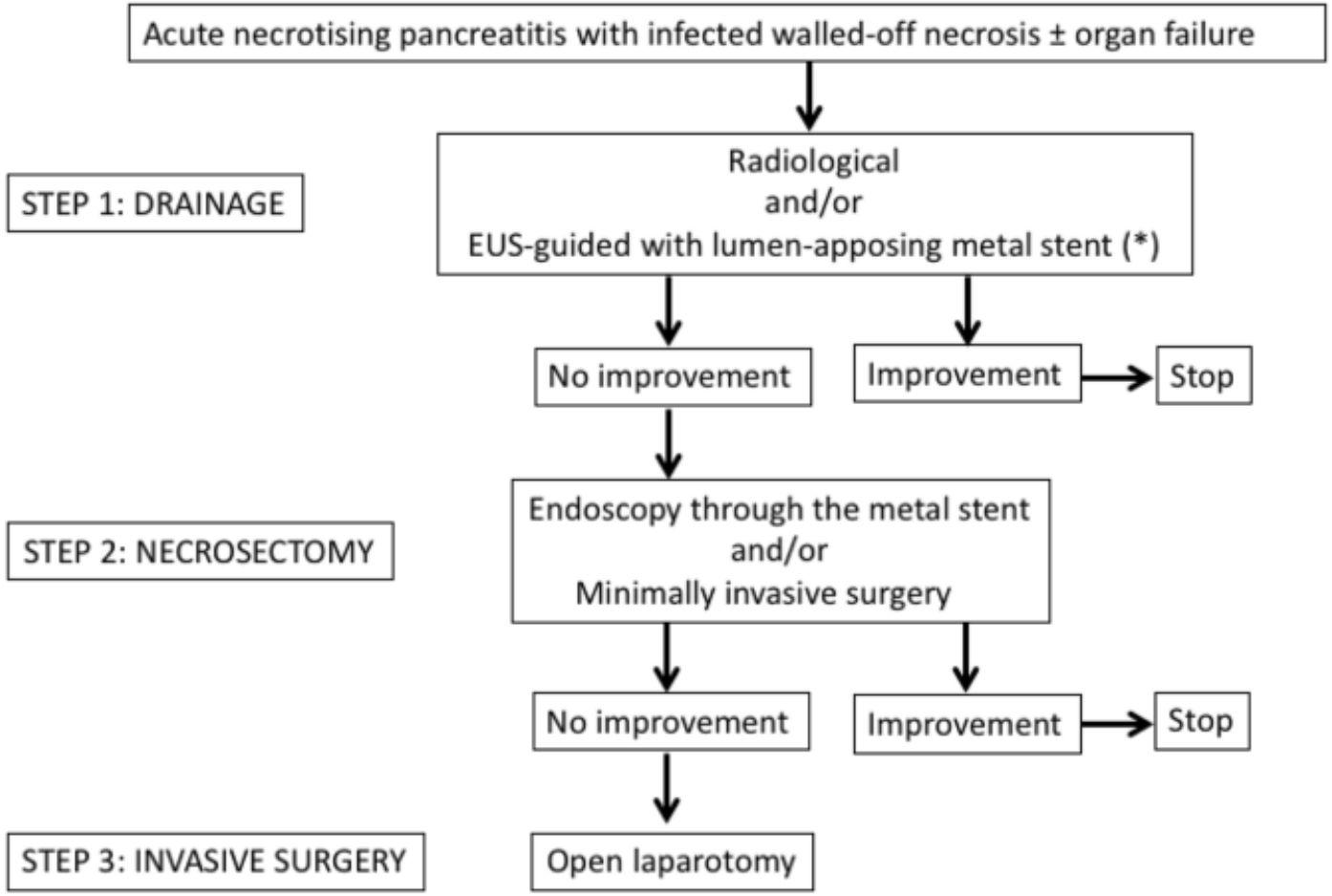
Invasive intervention should be preferably delayed until at least 4 weeks after initial presentation to allow collections to become 'walled-off’.

4. Interventional strategy for patients with suspected or confirmed infected necrotizing pancreatitis is

- initial image-guided percutaneous (retroperitoneal) catheter drainage
- Or endoscopic transluminal drainage
- Followed, if necessary, by endoscopic or surgical necrosectomy.

*Diagnosis and Management of Acute Pancreatitis Trikudanathan, Guru et al. Gastroenterology, Volume 167, Issue 4, 673 - 688*

# The Step-up Approach



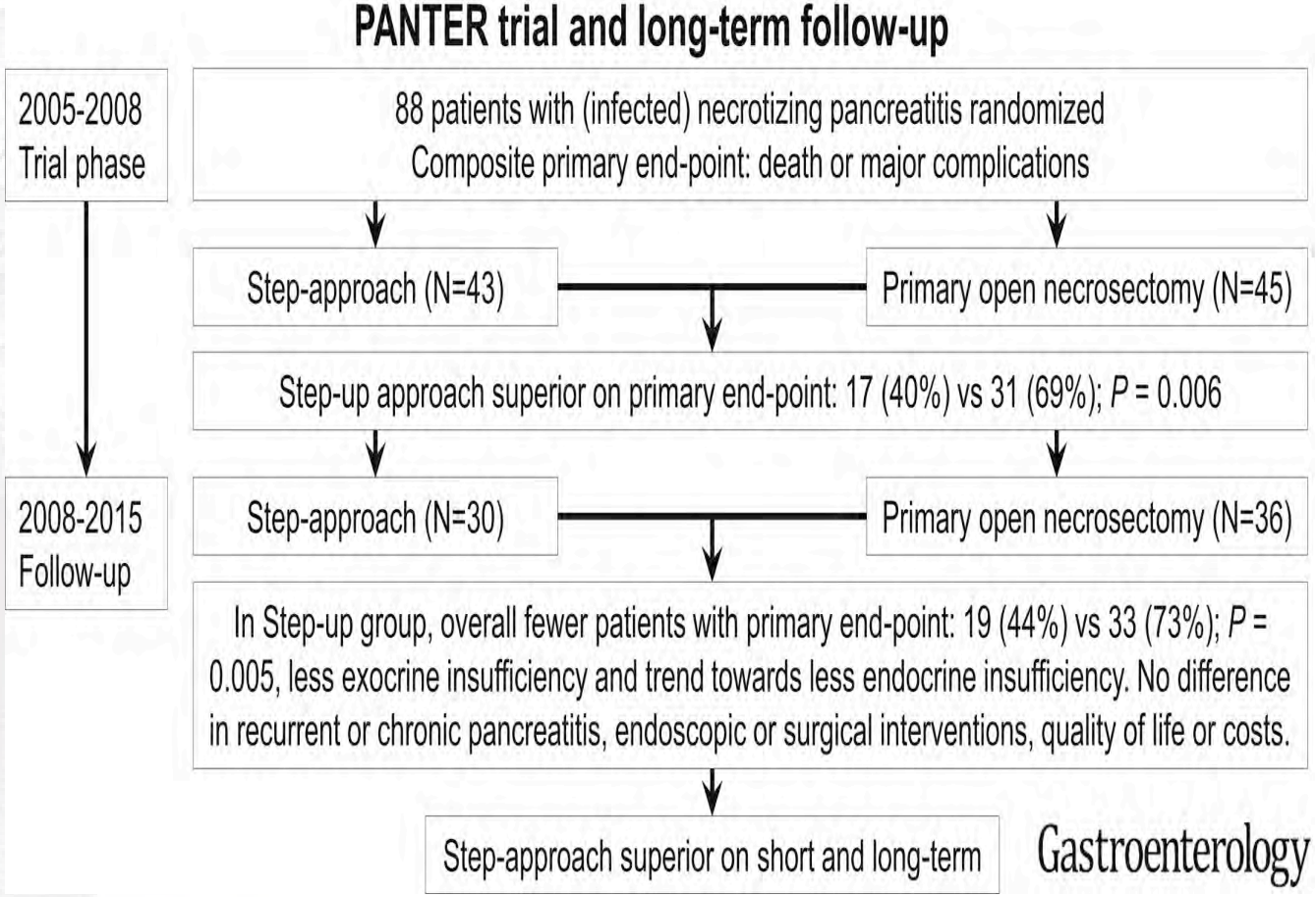

Valentin, C., Le Cosquer, G., Tuyeras, G. *et al.* Step-up approach for the treatment of infected necrotising pancreatitis: real life data from a single-centre experience with long-term follow-up. *BMC Gastroenterol* **24**, 213 (2024)

# PANTER TRIAL

Table 3. Primary and Secondary End Points.*

| Outcome | Minimally Invasive Step-up Approach (N=43) | Primary Open Necrosectomy (N=45) | Risk Ratio (95% CI) | P Value |
|---|---|---|---|---|
| Primary composite end point: major complications or death — no. (%)† | 17 (40) | 31 (69) | 0.57 (0.38–0.87) | 0.006 |
| Secondary end points | | | | |
| Major complication — no. (%) | | | | |
| New-onset multiple-organ failure or systemic complications‡ | 5 (12) | 19 (42) | 0.28 (0.11–0.67) | 0.001 |
| Multiple-organ failure | 5 (12) | 18 (40) | | |
| Multiple systemic complications | 0 | 1 (2) | | |
| Intraabdominal bleeding requiring intervention | 7 (16) | 10 (22) | 0.73 (0.31–1.75) | 0.48 |
| Enterocutaneous fistula or perforation of a visceral organ requiring intervention | 6 (14) | 10 (22) | 0.63 (0.25–1.58) | 0.32 |
| Death — no. (%) | 8 (19) | 7 (16) | 1.20 (0.48–3.01) | 0.70 |
| Other outcome — no. (%) | | | | |
| Pancreatic fistula | 12 (28) | 17 (38) | 0.74 (0.40–1.36) | 0.33 |
| Incisional hernia§ | 3 (7) | 11 (24) | 0.29 (0.09–0.95) | 0.03 |
| New-onset diabetes§ | 7 (16) | 17 (38) | 0.43 (0.20–0.94) | 0.02 |
| Use of pancreatic enzymes§ | 3 (7) | 15 (33) | 0.21 (0.07–0.67) | 0.002 |
| Health care resource utilization | | | | |
| Necrosectomies (laparotomy or VARD) — no. (%) | | | | <0.001 |
| 0 | 17 (40) | 0 | | |
| 1 | 19 (44) | 31 (69) | | |
| 2 | 6 (14) | 8 (18) | | |
| ≥3 | 1 (2) | 6 (13) | | |
| Total no. of operations¶ | | | | 0.004 |
| Per study group | 53 | 91 | | |
| Range per patient | 0–6 | 1–7 | | |
| Total no. of drainage procedures‖ | | | | <0.001 |
| Per study group | 82 | 32 | | |
| Range per patient | 1–7 | 0–6 | | |
| New ICU admission at any time after first intervention — no. (%)** | 7 (16) | 18 (40) | 0.41 (0.19–0.88) | 0.01 |
| Days in ICU | | | | 0.26 |
| Median | 9 | 11 | | |
| Range | 0–281 | 0–111 | | |
| Days in hospital | | | | 0.53 |
| Median | 50 | 60 | | |
| Range | 1–287 | 1–247 | | |

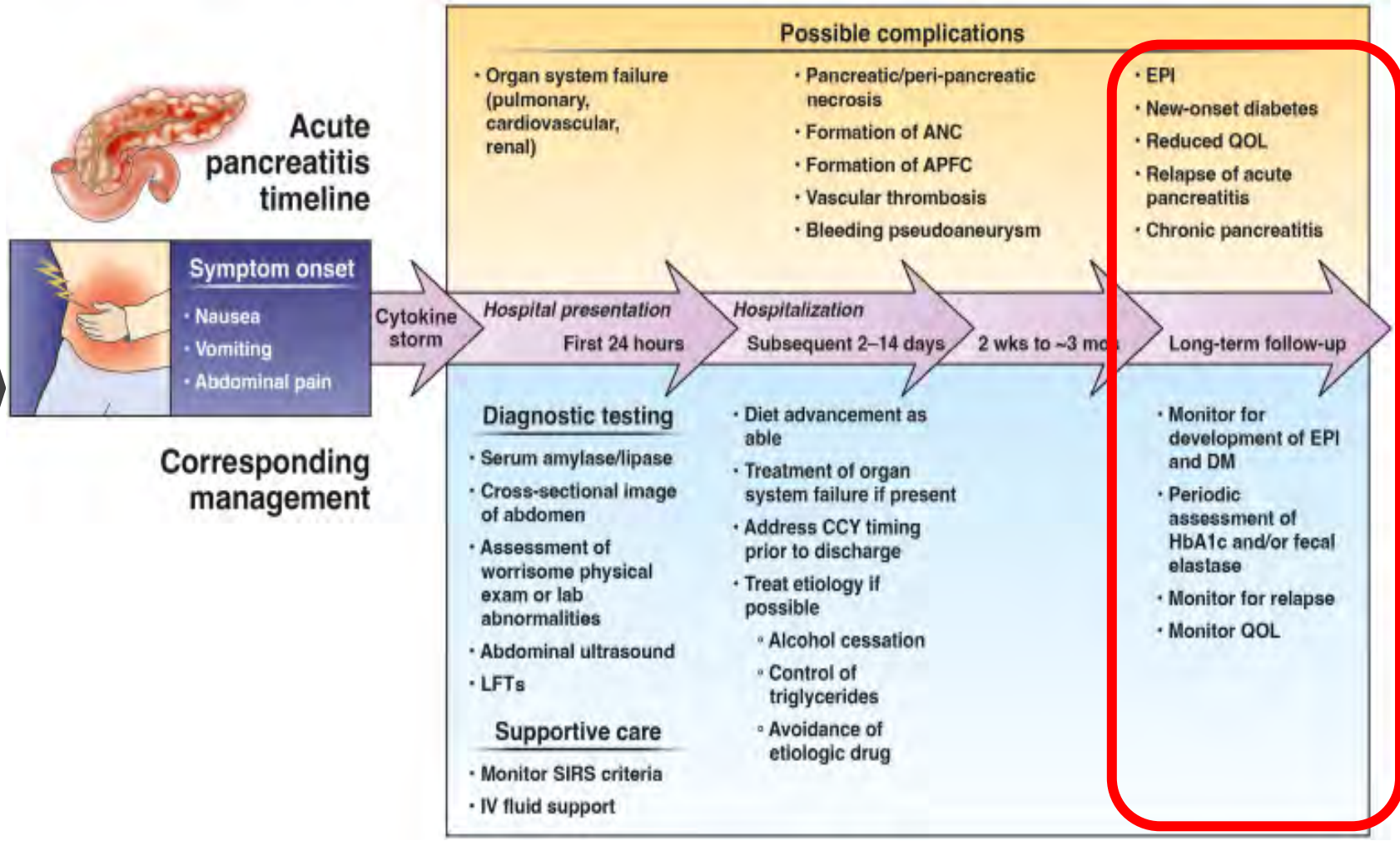
* ICU denotes intensive care unit, and VARD video-assisted retroperitoneal debridement.
† Multiple events in the same patient were considered as one end point.
‡ This category included only patients without multiple-organ failure or multiple systemic complications at any time in the 24 hours before the first intervention.
§ Patients were assessed 6 months after discharge from the index admission (readmission within 10 days was considered the same admission).
¶ This category included necrosectomies (laparotomy or VARD procedure) and additional operations to treat complications (e.g., repeated laparotomy for abdominal bleeding) during the index admission.
‖ This category included primary drainage procedures as part of the minimally invasive step-up approach and additional drainage procedures after necrosectomy in both treatment groups during the index admission.
** This category included only patients who were not admitted to the ICU at any time in the 24 hours before the first intervention.



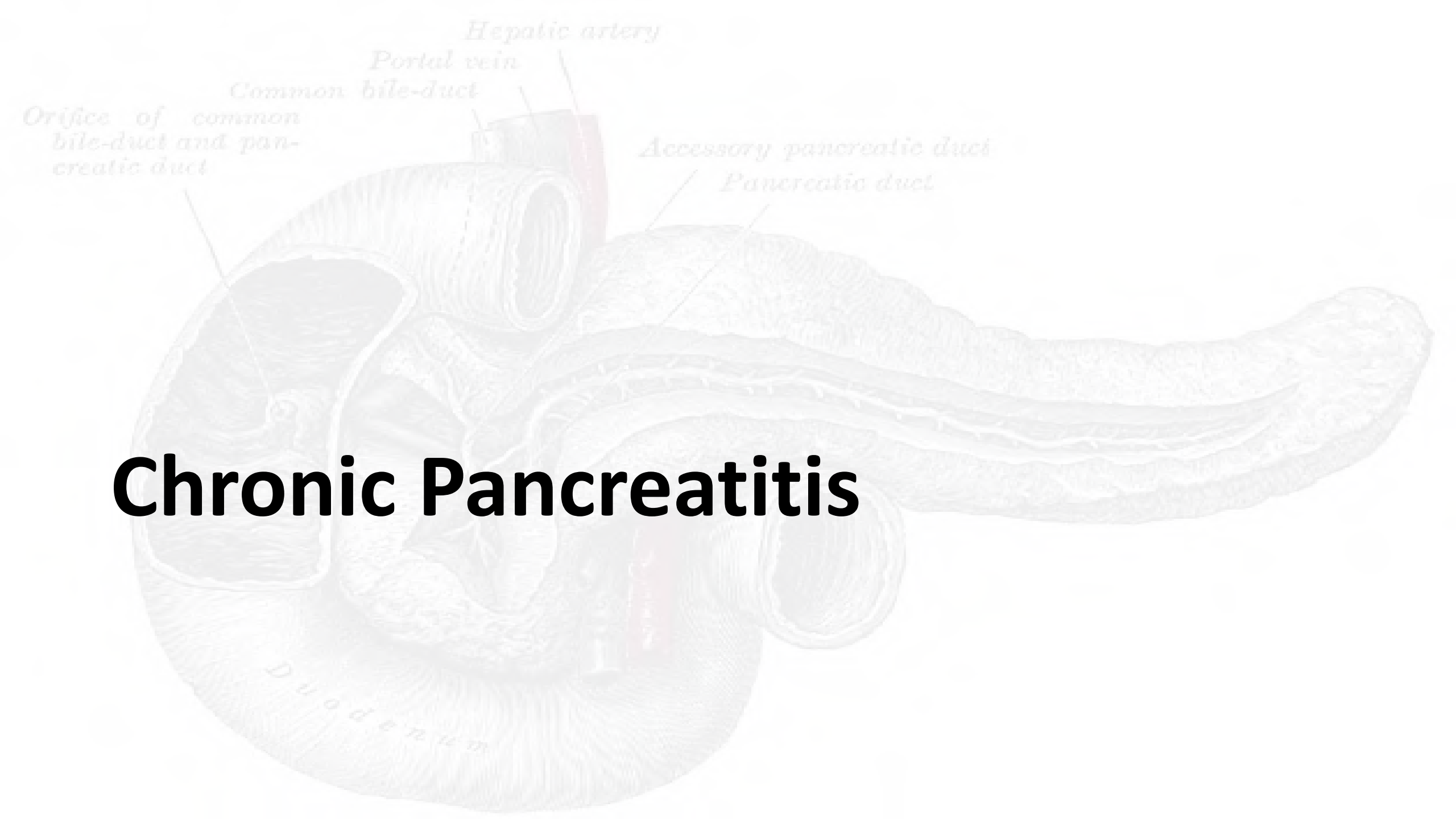

van Santvoort HC, Besselink MG, Bakker OJ, Hofker HS, Boermeester MA, Dejong CH, van Goor H, Schaapherder AF, van Eijck CH, Bollen TL, van Ramshorst B, Nieuwenhuijs VB, Timmer R, Laméris JS, Kruyt PM, Manusama ER, van der Harst E, van der Schelling GP, Karsten T, Hesselink EJ, van Laarhoven CJ, Rosman C, Bosscha K, de Wit RJ, Houdijk AP, van Leeuwen MS, Buskens E, Gooszen HG; Dutch Pancreatitis Study Group. A step-up approach or open necrosectomy for necrotizing pancreatitis. N Engl J Med. 2010 Apr 22;362(16):1491-502.

Superiority of Step-up Approach vs Open Necrosectomy in Long-term Follow-up of Patients With Necrotizing Pancreatitis
Hollemans, Robbert A. et al.
Gastroenterology, Volume 156, Issue 4, 1016 - 1026

# Summary




*Diagnosis and Management of Acute Pancreatitis Trikudanathan, Guru et al. Gastroenterology, Volume 167, Issue 4, 673 - 688*



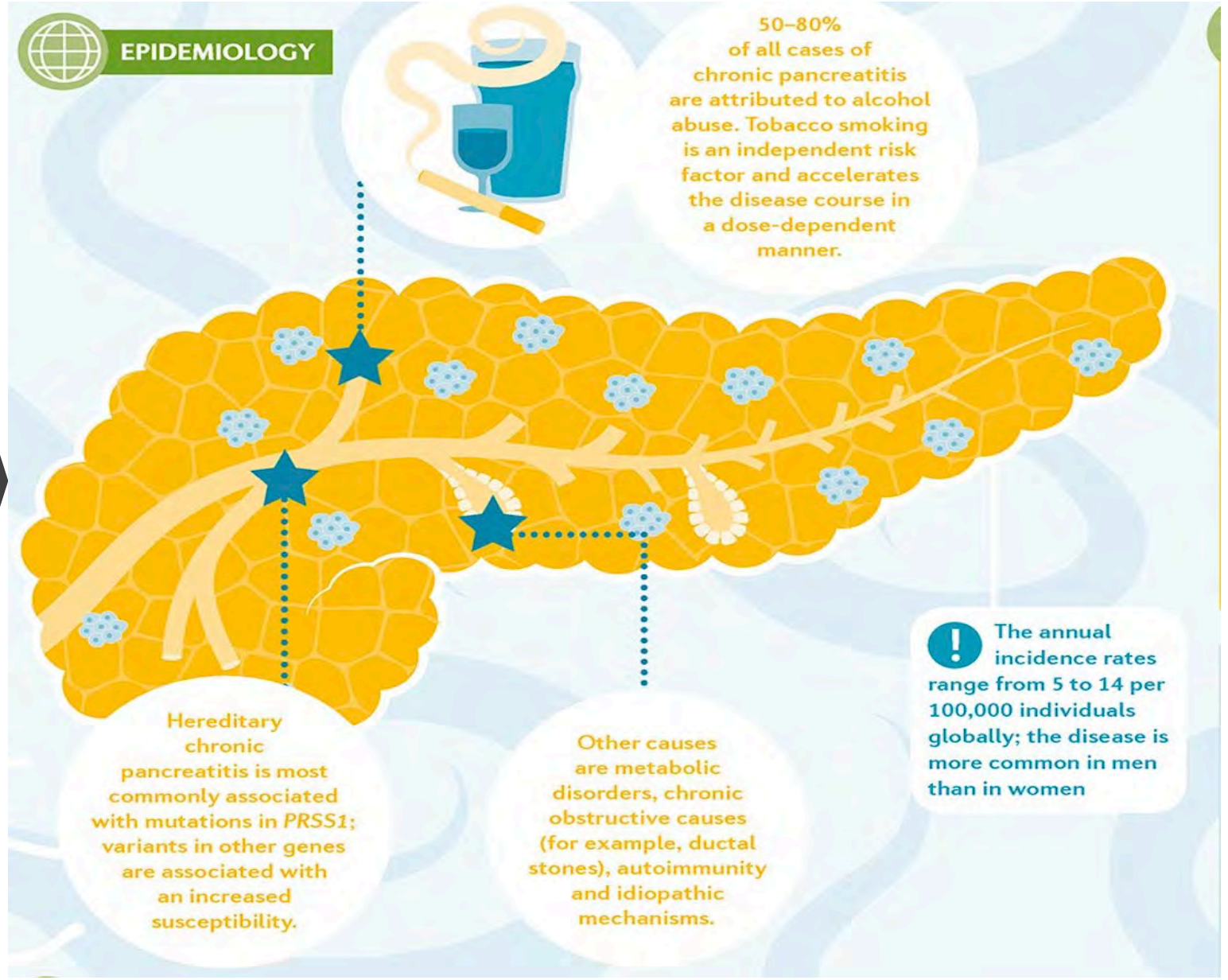

# Chronic Pancreatitis

# Definition

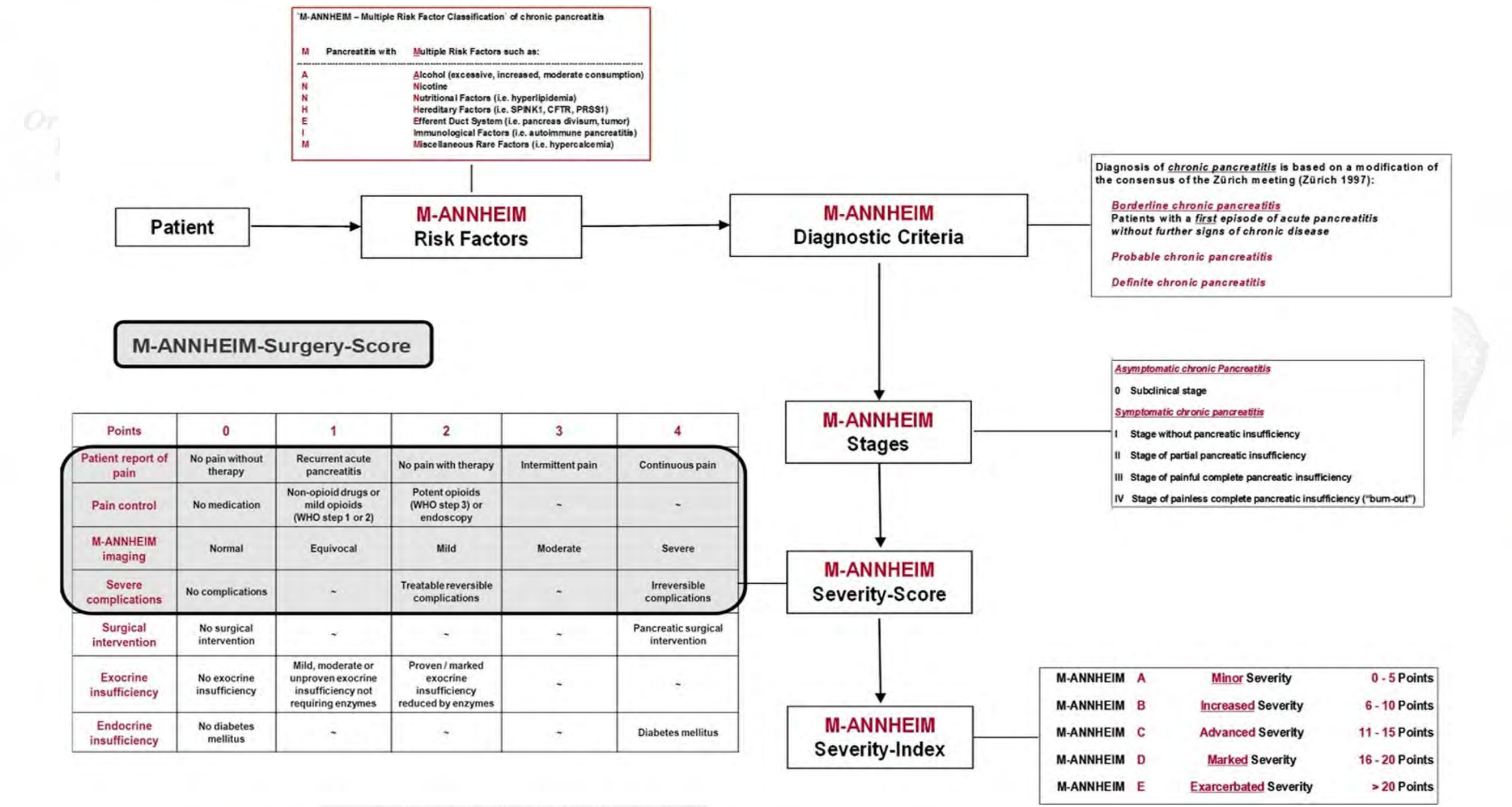
- Chronic Pancreatitis
  - Pathological fibroinflammatory syndrome of the pancreas in
  - Individuals with genetic, environmental, or other risk factors
  - who develop persistent, pathological responses to parenchymal injury or stress
  - causing loss of function, local complications, and pain
- Often multifactorial, but the precise pathophysiology is not fully understood.
- Common features of established and advanced chronic pancreatitis include:
  - Pancreatic atrophy
  - Fibrosis
  - Pain syndromes
  - Pancreatic duct distortion and strictures, calcifications
  - Pancreatic exocrine and endocrine dysfunction
  - Dysplasia

*Thierens N, Verdonk RC, Löhr JM, van Santvoort HC, Bouwense SA, van Hooft JE. Chronic pancreatitis. Lancet. 2025 Dec 21;404(10471):2605-2618.*

# Epidemiology




Chronic pancreatitis. *Nat Rev Dis Primers* **3**, 17061 (2017)




| Points | 0 | 1 | 2 | 3 | 4 |
|---|---|---|---|---|---|
| Patient report of pain | No pain without therapy | Recurrent acute pancreatitis | No pain with therapy | Intermittent pain | Continuous pain |
| Pain control | No medication | Non-opioid drugs or mild opioids (WHO step 1 or 2) | Potent opioids (WHO step 3) or endoscopy | ~ | ~ |
| M-ANNHEIM imaging | Normal | Equivocal | Mild | Moderate | Severe |
| Severe complications | No complications | ~ | Treatable reversible complications | ~ | Irreversible complications |
| Surgical intervention | No surgical intervention | ~ | ~ | ~ | Pancreatic surgical intervention |
| Exocrine insufficiency | No exocrine insufficiency | Mild, moderate or unproven exocrine insufficiency not requiring enzymes | Proven / marked exocrine insufficiency reduced by enzymes | ~ | ~ |
| Endocrine insufficiency | No diabetes mellitus | ~ | ~ | ~ | Diabetes mellitus |

Schneider, A., Hirth, M. Pain Management in Chronic Pancreatitis: Summary of Clinical Practice, Current Challenges and Potential Contribution of the M-ANNHEIM Classification. *Drugs* **81**, 533–546 (2021)

# Risk Factors



**Table 2.** The M-ANNHEIM multiple risk factor classification of chronic pancreatitis

| | M Pancreatitis with Multiple risk factors |
|---|---|
| A | Alcohol consumption |
| | Excessive consumption (>80 g/day) |
| | Increased consumption (20–80 g/day) |
| | Moderate consumption (<20 g/day) |
| N | Nicotine consumption |
| | (In cigarette smokers: description of nicotine consumption by pack-years) |
| N | Nutritional factors |
| | Nutrition (e.g., high caloric proportion of fat and protein) |
| | Hyperlipidemia |
| H | Hereditary factors[a] |
| | Hereditary pancreatitis (defined according to Whitcomb[96]) |
| | Familial pancreatitis (defined according to Whitcomb[96]) |
| | Early-onset idiopathic pancreatitis |
| | Late-onset idiopathic pancreatitis |
| | Tropical pancreatitis |
| | (possible mutations in the *PRSS1*, *CFTR*, or *SPINK1* genes) |
| E | Efferent duct factors |
| | Pancreas divisum |
| | Annular pancreas and other congenital abnormalities of the pancreas |
| | Pancreatic duct obstruction (e.g., tumors) |
| | Posttraumatic pancreatic duct scars |
| | Sphincter of Oddi dysfunction |
| I | Immunological Factors |
| | Autoimmune pancreatitis |
| | Sjögren syndrome-associated chronic pancreatitis |
| | Inflammatory bowel disease-associated chronic pancreatitis |
| | Chronic pancreatitis with autoimmune diseases |
| | (e.g., primary sclerosing cholangitis, primary biliary cirrhosis) |
| M | Miscellaneous and rare metabolic factors |
| | Hypercalcemia and hyperparathyroidism |
| | Chronic renal failure |
| | Drugs |
| | Toxins |

The M-ANNHEIM classification is based on the assumption that, in the majority of patients, chronic pancreatitis results from the interaction of multiple risk factors (M). The different risk factors are grouped into the major subcategories of alcohol consumption (A), nicotine consumption (N), nutritional factors (N), hereditary factors (H), efferent pancreatic duct factors (E), immunological factors (I), and various rare miscellaneous and metabolic factors (M)

[a] Hereditary and familial pancreatitis are defined according to Whitcomb.[96] Hereditary pancreatitis refers to otherwise unexplained pancreatitis in an individual from a family in which the pancreatitis phenotype appears to be inherited through a disease-causing gene mutation expressed in an autosomal dominant pattern.[96] Familial pancreatitis refers to pancreatitis due to any cause that occurs in a family with an incidence higher

**Table 4.** M-ANNHEIM diagnostic criteria of chronic pancreatitis (modified from Ammann[32])

The diagnosis of chronic pancreatitis requires a typical clinical history of chronic pancreatitis (such as recurrent pancreatitis or abdominal pain, except for primary painless pancreatitis)
Based on these features, three forms of chronic pancreatitis

***Definite chronic pancreatitis*** is established by one or more of the following additional criteria:

1. Pancreatic calcifications
2. Moderate or marked ductal lesions (according to the Cambridge classification)
3. Marked and persistent exocrine insufficiency defined as pancreatic steatorrhea markedly reduced by enzyme supplementation
4. Typical histology of an adequate histological specimen

***Probable chronic pancreatitis*** is established by one or more of the following additional criteria:

1. Mild ductal alterations (according to the Cambridge classification)
2. Recurrent or persistent pseudocysts
3. Pathological test of pancreatic exocrine function (such as fecal elastase-1 test, secretin test, secretin–pancreozymin test)
4. Endocrine insufficiency (i.e., abnormal glucose tolerance test)

***Borderline chronic pancreatitis*** is already established and is defined by a typical clinical history of the disease but without any of the additional criteria required for definite or probable chronic pancreatitis. This form is also established as a first episode of acute pancreatitis with or without (1) a family history of pancreatic disease (i.e., other family members with acute pancreatitis or pancreatic cancer) or (2) the presence of M-ANNHEIM risk factors

***Pancreatitis associated with alcohol consumption*** requires in addition to the above-mentioned criteria for definite, probable, or borderline chronic pancreatitis one of the following features:

1. History of *excessive* alcohol intake (>80 g/day for some years in men, smaller amounts in women) or
2. History of *increased* alcohol intake (20–80 g/day for some years) or
3. History of *moderate* alcohol intake (<20 g/day for some years)

The Zürich workshop on alcoholic chronic pancreatitis proposed a classification of chronic pancreatitis into "probable" or "definite" chronic pancreatitis, depending on the presence of several distinguishing diagnostic features of the disease.[32] We included a subgroup of "borderline" chronic pancreatitis in the M-ANNHEIM classification system, and we introduced a subclassification for the amount of alcohol consumed

**Table 5.** Cambridge classification of pancreatic morphology in chronic pancreatitis[28–30]

| Pancreatic morphology evaluated by ERCP | | | |
|---|---|---|---|
| | Main duct | Abnormal side branches | Additional features |
| Normal | Normal | None | |
| Equivocal | Normal | <3 | |
| Mild changes | Normal | ≥3 | |
| Moderate changes | Abnormal | >3 | |
| Marked changes | Abnormal | >3 | One or more of the following: large cavity, obstruction, filling defects, severe dilatation, or irregularity |

| Pancreatic morphology evaluated by computed tomography and ultrasound | |
|---|---|
| Normal | Main pancreatic duct <2 mm, normal gland size and shape, homogenous parenchyma |
| Equivocal | One only of the following signs: Main pancreatic duct enlarged (between 2 and 4 mm), slight gland enlargement (up to 2 x normal), heterogeneous parenchyma, small cavities (<10 mm), irregular ducts, focal acute pancreatitis, increased echogenicity of the main pancreatic duct wall, irregular head / body contour |
| Mild changes | Two or more of the above listed criteria |
| Moderate changes | As with mild changes (not differentiated) |
| Marked changes | As above, with one or more of the following: large cavities (>10 mm), gross gland enlargement (>2× normal), intraductal filling defects or calculi, duct obstruction, structure or gross irregularity, contiguous organ invasion |

The Cambridge classification established clear-cut criteria for the description of equivocal, mild, moderate, and severe changes of chronic pancreatitis using the imaging technique of ERCP.[28–30] The Cambridge classification also categorized chronic pancreatitis according to pancreatic imaging findings on CT and abdominal US, similar to the grading of ERCP changes.[28–30] However, the grading according to CT and US did not clearly differentiate between mild and moderate changes

**Table 6.** Endoscopic ultrasound criteria of chronic pancreatitis[82,84,85,89]

Parenchymal features
- Gland size
- Cysts
- Echo-poor lesions (focal areas of reduced echogenicity)
- Echo-rich lesions (>3 mm in diameter)
- Accentuation of lobular pattern (e.g., echo-poor normal parenchyma surrounded by hyperechoic strands)

Ductal features
- Increased duct wall echogenicity
- Irregularity of the main pancreatic duct (e.g., with narrowing of the duct)
- Dilation of the main pancreatic duct
- Visible side branches (e.g., with dilation)
- Calcification

**Table 7.** M-ANNHEIM pancreatic imaging criteria for US, CT, MRI/MRCP, and EUS based on imaging features as defined by the Cambridge classification

| Cambridge grading | CT, US, MRI/MRCP[a] | EUS[b] |
|---|---|---|
| Normal | Quality study depicting whole gland without abnormal features (0 points)[c] | |
| Equivocal<br>Mild changes | One abnormal feature (1 point)[c]<br>Two or more abnormal features, but normal main pancreatic duct (2 points)[c] | Four or fewer abnormal features (no differentiation between equivocal and mild) (1 point)[c] |
| Moderate changes | Two or more abnormal features, including minor main pancreatic duct abnormalities (either enlargement between 2 and 4 mm or increased echogenicity of the duct wall) (3 points)[c] | Five or more abnormal features (no differentiation between moderate and marked) (3 points)[c] |
| Marked changes | As above with one or more of the required features of | |

**Table 3.** M-ANNHEIM clinical staging of chronic pancreatitis (modified from Chari and Singer[21])

| | |
|---|---|
| ➢ **Asymptomatic chronic pancreatitis** | |
| 0 | Stage of subclinical chronic pancreatitis |
| a | Period without symptoms (determination by chance, e.g., autopsy) |
| b | Acute pancreatitis—single episode (possible onset of chronic pancreatitis)[a] |
| c | Acute pancreatitis with severe complications[b] |
| ➢ **Symptomatic chronic pancreatitis** | |
| I | Stage without pancreatic insufficiency |
| a | (Recurrent) acute pancreatitis (no pain between episodes of acute pancreatitis)* |
| b | Recurrent or chronic abdominal pain (including pain between episodes of acute pancreatitis) |
| c | I a/b with severe complications[b] |
| II | Stage of partial pancreatic insufficiency |
| a | Isolated exocrine (or endocrine) pancreatic insufficiency (without pain) |
| b | Isolated exocrine (or endocrine) pancreatic insufficiency (with pain) |
| c | II a/b with severe complications[b] |
| III | Stage of painful complete pancreatic insufficiency |
| a | Exocrine and endocrine insufficiency (with pain, e.g., requiring pain medication) |
| b | III a with severe complications[b] |
| IV | Stage of secondary painless disease (burnout) |
| a | Exocrine and endocrine insufficiency without pain and without severe complications[b] |
| b | Exocrine and endocrine insufficiency without pain and with severe complications[b] |

[a] A patient with a single episode of acute pancreatitis (without other symptoms of chronic pancreatitis) and with risk factors for chronic pancreatitis (e.g., a history of increased alcohol consumption) would be classified as "0 b" without morphological or functional signs of chronic pancreatitis. In contrast, the patient would be categorized as "I a" in the presence of chronic pancreatitis features (e.g., calcifications).

[b] Severe complications are defined as severe organ complications not included in the Cambridge classification. Reversible severe complications include development of ascites, bleeding, pseudoaneurysm, obstruction or stricture of the ductus choledochus, pancreatic fistula, and duodenal

# Diagnosis

Although histology remains the gold standard against which all diagnostic approaches are judged, it is not practical in the clinical setting.

Diagnosis currently depends on identifying clinical and morphological features which characterize the final common pathologic pathway of a variety of pancreatic disorders.

**Clinical manifestations**

- The primary clinical manifestations of CP are abdominal pain and pancreatic insufficiency, but patients may also present with the consequences of a complication.
- Abdominal pain
  - The pain is typically epigastric in location, often radiates to the back, is frequently worse after meals
  - May be relieved by sitting upright or leaning forward.
  - Pain is usually but not invariably present; in one series, 20% of patients with CP presented with pancreatic exocrine or endocrine insufficiency, but no pain.

*Bornman PC, Botha JF, Ramos JM, Smith MD, Van der Merwe S, Watermeyer GA, Ziady CC. Guideline for the diagnosis and treatment of chronic pancreatitis. S Afr Med J. 2010 Dec 1;100(12 Pt 2):845-60*

# Diagnosis

Pancreatic exocrine insufficiency

- Clinically significant fat and protein deficiencies do not occur until over 90% of pancreatic function is lost.
- The clinical manifestations of fat malabsorption are steatorrhoea and flatulence.
- Malabsorption of fat-soluble vitamins and vitamin B12 may also occur, but clinically symptomatic vitamin deficiencies are rare.

*Bornman PC, Botha JF, Ramos JM, Smith MD, Van der Merwe S, Watermeyer GA, Ziady CC. Guideline for the diagnosis and treatment of chronic pancreatitis. S Afr Med J. 2010 Dec 1;100(12 Pt 2):845-60*

# Diagnosis

Pancreatic endocrine insufficiency

- Overt diabetes mellitus (DM) typically occurs late in the course of the disease.
- A family history of type 1 or type 2 DM, early pancreatic calcification and distal pancreatectomy increases the risk of developing DM
- .Most patients with DM secondary to CP require insulin.
- Owing to the loss of glucagon-producing α-cells, such patients are at increased risk of spontaneous and treatment-related hypoglycaemia.

*Bornman PC, Botha JF, Ramos JM, Smith MD, Van der Merwe S, Watermeyer GA, Ziady CC. Guideline for the diagnosis and treatment of chronic pancreatitis. S Afr Med J. 2010 Dec 1;100(12 Pt 2):845-60*

# Diagnostic Tests



**Table 1.** Diagnostic Tests for Chronic Pancreatitis

| | |
|---|---|
| Imaging tests | |
| EUS | Two systems of reporting are used: standard terminology and Rosemont criteria.[5] EUS allows detailed examination of both the pancreatic parenchyma and the pancreatic duct. |
| MRI with MRCP | Administration of secretin during MRCP improves the quality of imaging of the pancreatic duct and may allow the pancreatic secretory capacity to be estimated. MRI cannot visualize calcification. |
| CT | CT images the pancreatic parenchyma well, with less ductal detail than MRI. |
| ERCP | ERCP provides the most detailed images of the pancreatic duct but is rarely used for diagnosis. |
| Ultrasonography | Ultrasonography has limited ability to image the pancreas, but it is of low cost and has no ionizing radiation. |
| Functional tests | |
| Secretin test | Administration of a supraphysiologic dose of secretin produces maximal pancreatic stimulation; pancreatic juice is collected with a Dreiling tube or an endoscope and analyzed for bicarbonate concentration. |
| Fecal elastase | Low levels in the stool (<200 $\mu$g/g of stool) are seen in patients with advanced chronic pancreatitis. |
| Serum trypsin | Low levels (<20 mg/dL) are seen in patients with advanced chronic pancreatitis. |

# Rosemont Criteria

**Addendum A**

**Rosemont criteria: Consensus-based parenchymal features of CP[21]**

| A | Definition | Major criteria | Minor criteria | Rank | Histological correlation |
|---|---|---|---|---|---|
| Hyperechoic foci with shadowing | Echogenic structures ≥2 mm in length and width that shadow | Major A | | 1 | Parenchymal-based calcifications |
| Lobularity | Well- circumscribed, ≥5 mm structures, with enhancing rim and relatively echo-poor centre | | | 2 | Unknown |
| A. With honeycombing | Contiguous ≥3 lobules | Major B | | | |
| B. Without honeycombing | Non-contiguous lobules | | Yes | | |
| Hyperechoic foci without shadowing | Echogenic structures foci ≥2 mm in both length and width with no shadowing | | Yes | 3 | Unknown |
| Cysts | Anechoic, rounded/ elliptical structures, with or without septations | | Yes | 4 | Pseudocyst |
| Stranding | Hyperechoic lines ≥3 mm in length in at least 2 different directions with respect to the image plane | | Yes | 5 | Unknown |

**Rosemont criteria: Consensus-based ductal features of CP[21]**

| Feature | Definition | Major criteria | Minor criteria | Rank | Histological correlation |
|---|---|---|---|---|---|
| MPD calculi | Echogenic structure(s) within MPD with acoustic shadowing | Major A | | 1 | Stones |
| Irregular MPD contour | Uneven or irregular outline and ectatic course | | Yes | 2 | Unknown |
| Dilated side branches | ≥3 tubular anechoic structures each measuring ≥1 mm in width, budding from the MPD | | Yes | 3 | Side-branch ectasia |
| MPD dilation | ≥3.5 mm body or >1.5 mm tail | | Yes | 4 | MPD dilation |
| Hyperechoic MPD margin | Echogenic, distinct structure >50% of entire MPD in the body and tail | | Yes | 5 | Ductal fibrosis |

*Bornman PC, Botha JF, Ramos JM, Smith MD, Van der Merwe S, Watermeyer GA, Ziady CC. Guideline for the diagnosis and treatment of chronic pancreatitis. S Afr Med J. 2010 Dec 1;100(12 Pt 2):845-60*

# Rosemont Criteria

**Addendum B**

**EUS diagnosis of CP on the basis of consensus criteria**[21]

**I. Consistent with CP**

A. 1 major A feature (+) ≥3 minor features

B. 1 major A feature (+) major B feature

C. 2 major A features

**II. Suggestive of CP***

A. 1 major A feature (+) <3 minor features

B. 1 major B feature (+) ≥3 minor features

C. ≥5 minor features (any)

**III. Indeterminate for CP†**

A. 3 - 4 minor features, no major features

B. major B feature alone or with <3 minor features

**IV. Normal**

≤2 minor features,‡ no major features

*EUS diagnosis of CP should be made in the appropriate clinical setting.

†Diagnosis requires confirmation by additional imaging study (ERCP, CT, MRI or PFT).

‡Excludes cysts, dilated MPD, hyperechoic non-shadowing foci, dilated side branch.

Bornman PC, Botha JF, Ramos JM, Smith MD, Van der Merwe S, Watermeyer GA, Ziady CC. Guideline for the diagnosis and treatment of chronic pancreatitis. S Afr Med J. 2010 Dec 1;100(12 Pt 2):845-60

# Approach to Management



DISEASE AND THERAPY OF PANCREATIC DISORDER

**Make a correct diagnosis**
- Appropriate history
- Corroborating imaging tests
  - MRI/MRCP
  - EUS
  - CT
- Functional tests if imaging tests equivocal
  - Tube-based secretin test
  - Endoscopic-based secretin test
- Assess for alternative diseases and complications and treat if present
  - Pancreatic cancer or IPMN
  - Pseudocyst
  - Bile duct obstruction
  - Duodenal obstruction

↓

**Medical therapy**
- Measure pain severity, character, and impact on QOL
- Refer for formal structured smoking and alcohol cessation programs
- Counsel on good nutrition and initiate supplementation with vitamin D and calcium
  - Baseline bone mineral density testing
- Provide information on local and national support groups
- Initiate analgesics (starting with Tramadol)
  - Increase dose and potency slowly as required
- Initiate adjunctive agents in those with persistent pain or requiring higher dosages or potency of narcotics
  - Pregabalin, Gabapentin
  - SSRI
  - SSNRI
  - Tricyclic antidepressants
- Assess for evidence of coexistent exocrine or endocrine insufficiency and treat if present
  - Fecal elastase or serum trypsin
  - HgB A1C or GTT
- Initiate steroids if autoimmune pancreatitis

↓

# Approach to Management

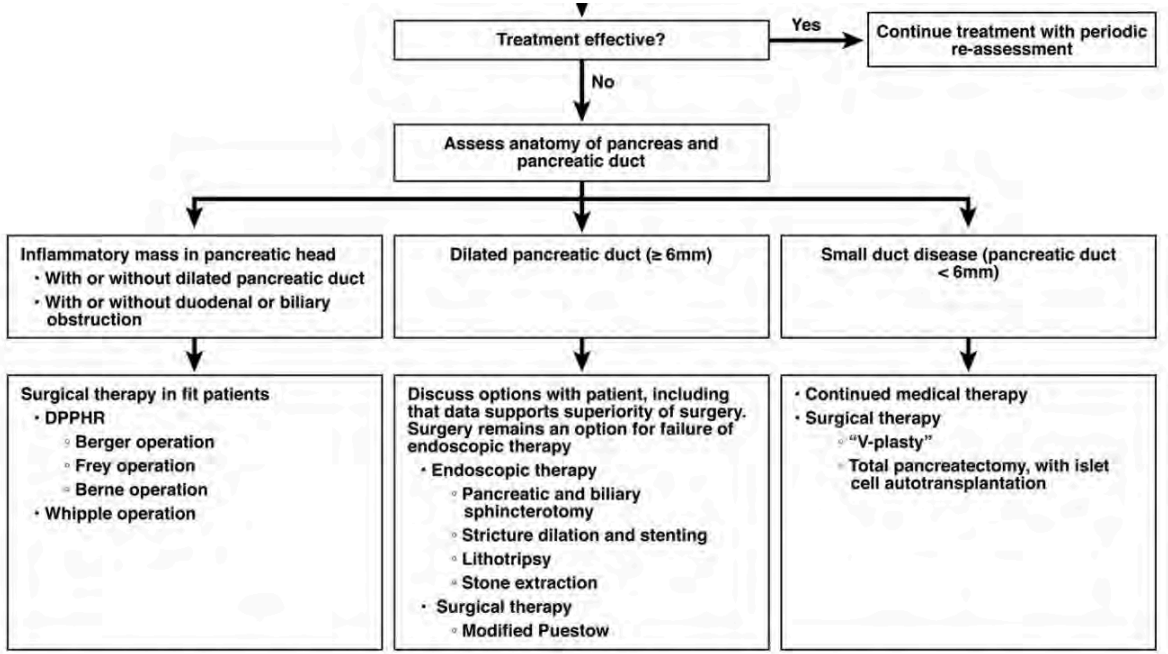
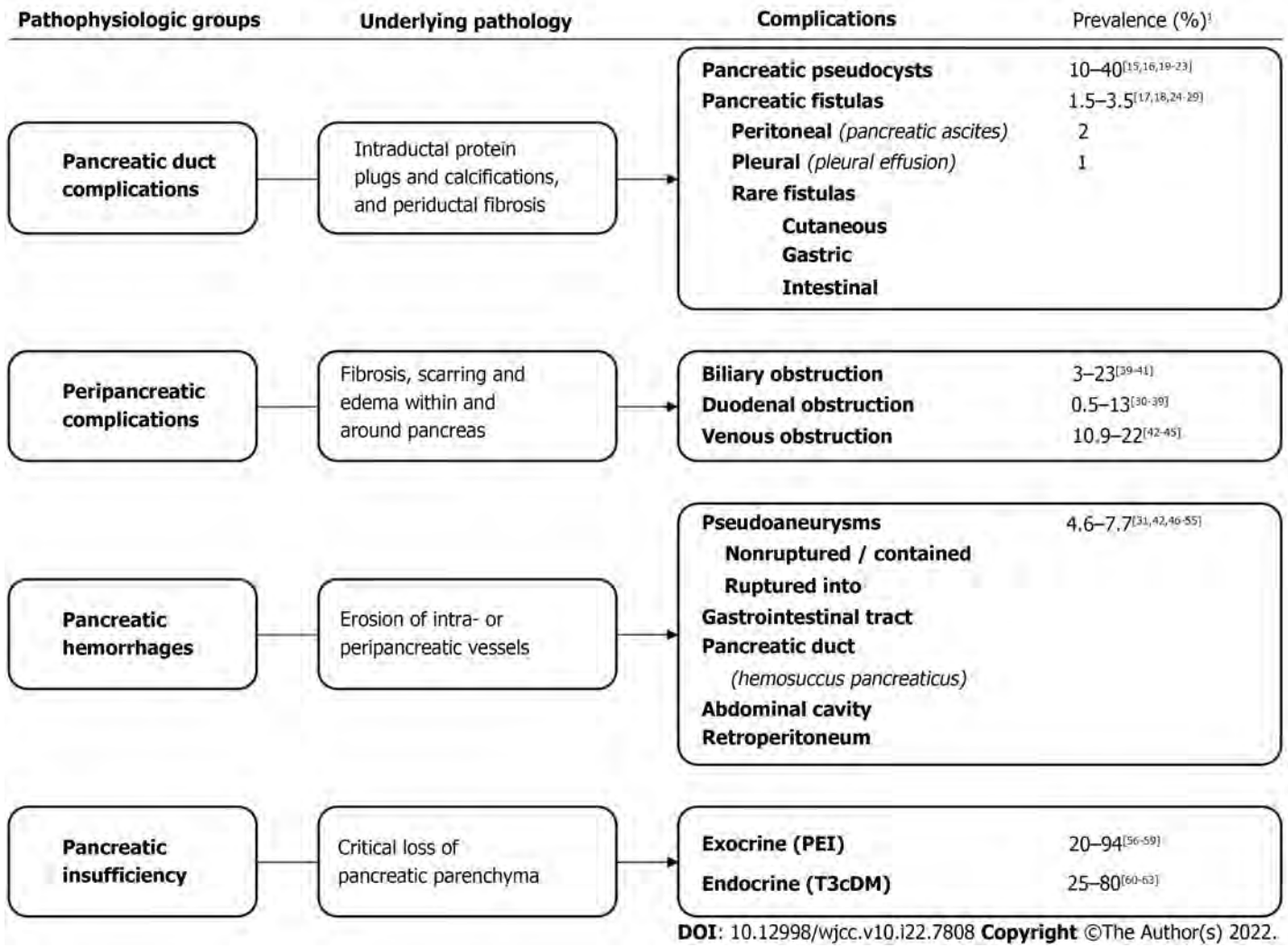



**Figure 3.** Management algorithm for chronic pancreatitis. IPMN, intraductal papillary mucinous neoplasm; QOL, quality of life; SSRI, selective serotonin reuptake inhibitor; SSNRI, serotonin-norepinephrine reuptake inhibitor; GTT, glucose tolerance test.

# Complications of Chronic Pancreatitis

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# Pancreatic Pseudocysts

- **Presentation:** Fluid collections in peripancreatic tissue, occurring in 25-30% (or 20-40%) of CP patients. Can be asymptomatic or cause pain, early satiety, nausea, vomiting
- **Management:**
  - **Observation:** For uncomplicated, asymptomatic pseudocysts, as ~33% resolve spontaneously within 2-6 weeks. Observe for at least 6 weeks if recent acute pancreatitis.
  - **Intervention:** Indicated for symptomatic pseudocysts, complications (infection, hemorrhage, rupture), or asymptomatic cysts >5 cm not resolving within 3-6 months.
  - **Endoscopic Drainage (ED):** Preferred minimally invasive strategy. Modalities include transmural (through GI wall) or transpapillary (via ERCP) drainage.
  - **Surgical Drainage:** Option for mature pseudocysts when endoscopy fails or is not feasible. Procedures include cystogastrostomy, cystoduodenostomy, or Roux-en-Y cystojejunostomy Resection may be used for cystic neoplasia or splenic vein involvement.
  - **Percutaneous Drainage:** Generally *not recommended* as primary treatment due to high complication rates.

United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU). United European Gastroenterol J. 2017 Mar;5(2):153-199

Pan G, Wan MH, Xie KL, Li W, Hu WM, Liu XB, Tang WF, Wu H. Classification and Management of Pancreatic Pseudocysts. Medicine (Baltimore). 2015 Jun;94(24

# Bile Duct Obstruction/Strictures

- **Presentation:** Affects 5-10% of patients. Caused by inflammation, fibrosis, or pseudocyst compression. Can be asymptomatic, transient jaundice, recurrent jaundice, or persistent jaundice. Symptoms include clay-colored stools, dark urine, fever, chills, pruritus, weight loss. Risk of cholangitis and biliary cirrhosis
- **Management:**
  - **Conservative:** For asymptomatic or transient jaundice, monitor with 6-monthly liver function tests and ultrasound.
  - **Interventional:** Recommended for persistent jaundice (>1 month), frequent relapses, or cholangitis.
  - **Endoscopic Biliary Stenting:** Temporary plastic stents or covered self-expandable metallic stents (SEMS) can provide long-term success. Reserved for patients who can comply with repeat ERCPs, are high surgical risk, or have portal hypertension.
  - **Surgical Biliary Drainage:** Indicated when endoscopic methods fail, or for persistent jaundice, cholangitis, or suspicion of malignancy. Choledochojejunostomy (Roux-en-Y) is often preferred. Pancreaticoduodenectomy (Whipple) if malignancy cannot be ruled out

Abdallah AA, Krige JE, Bornman PC. Biliary tract obstruction in chronic pancreatitis. HPB (Oxford). 2007;9(6):421-8 United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU). United European Gastroenterol J. 2017 Mar;5(2):153-199

# Pancreatic Cancer Risk & Surveillance

- **Risk:** Significantly increased risk (15-40%). Chronic pancreatitis is an independent risk factor. Average interval to cancer diagnosis is ~2.4 years.
- **Surveillance:**
  - **General CP Population:** Routine screening is *not recommended* for all CP patients due to cost-effectiveness and accuracy concerns.
  - **High-Risk Groups:** Surveillance *is recommended* for specific high-risk individuals, such as those with PRSS1 mutation-related hereditary CP (consider from age 40, annual screening). Also for inherited mutations in STK11, CDKN2A, ATM, BRCA1, BRCA2 (screening typically starts age 30-50 or 10 years earlier than family's earliest diagnosis).
  - **Imaging:** MRI/MRCP or CT are suitable. Endoscopic Ultrasonography (EUS) is *not recommended* for surveillance in CP due to difficulty distinguishing early tumors from inflammation.
  - **Abnormal Findings:** Shorten observation interval to 3-6 months if main pancreatic duct strictures, solid lesions <1 cm, or new-onset diabetes.

Shin H, Choe JW. Tailored Surveillance Strategies for Pancreatic Cancer in Patients with Chronic Pancreatitis. JDCR 2024;12:102-105