Necrotizing Pancreatitis: Medical Management

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Scope of This Talk

Will focus on

- Fluid resuscitation
- Nutritional therapy
- Pain management
- Antibiotic strategy
- Infectious and vascular complications
- Severe pancreatitis prophylaxis

Why Medical Therapy Matters

“In necrotizing pancreatitis, survival is determined by medical management long before any intervention is considered.”

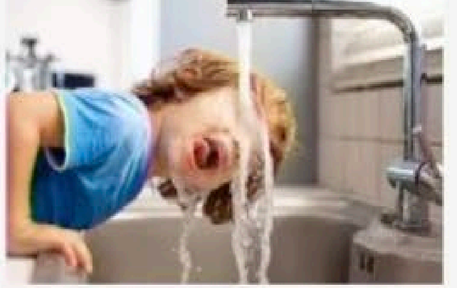
Early deaths are driven by SIRS and organ failure, not by necrosis itself.

Who Benefits From ICU Treatment

- **Patients with severe acute pancreatitis**
- **Patients who do not meet criteria for severe disease but have one or more of the following parameters:**
  - PR <40 or >150 beats/minute
  - SBP <80 mmHg or MAP <60 mmHg or DBP>120 mmHg
  - RR>35 breaths/minute
  - Serum sodium <110 mEq/L or >170 mEq/L
  - Serum potassium <2.0 mEq/L or >7.0 mEq/L
  - PaO2 <50 mmHg
  - pH <7.1 or >7.7
  - Serum glucose >800 mg/dL
  - Serum calcium >15 mg/dL
  - Anuria
  - Coma

IAP/APA/EPC/IPC/JPS Working Group.2025; 25:770.

Fluids

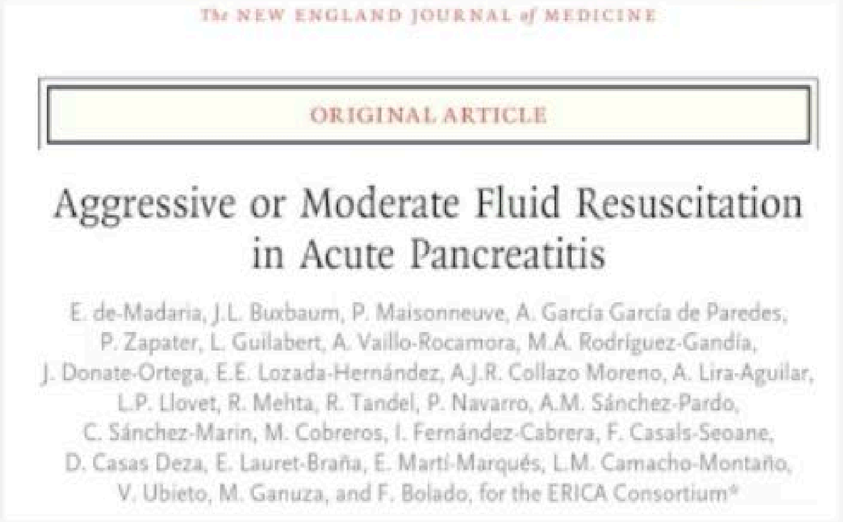


Why? Cytokine cascade -> vascular endothelial damage -> vascular permeability -> fluid mobilisation 3rd space -> organ perfusion ⬇️ + pancreatic microcirculation ⬇️ -> organ failure + chock

WATERFALL trial 2022

Aggressive	Bolus 20mL/kg + 3 mL/kg/h
Moderate	Bolus 10 mL/kg + 1,5 L/kg/h

Planned sample size: 744 patients
Interrim analysis at 249 patients



⬇️

👉 **NO** significant difference in the development of MSAP and SAP

➡️

Significantly **MORE** fluid overload in the aggressive fluid group
20.5% vs 6.3%
aRR 2.85, CI 1.36 – 5.94, p = 0.004
➡️ Study halted

Fluids

2 metaanalysis support less aggressive fluid management [1,2]

Guideline recommendations[3]

Moderate goal-directed fluid resuscitation

Ringers Lactate 1.5 ml/kg/h

Evaluation at least ever 6 hours (more often -> less risk of hypervolemia)

Goal-directed checkpoints:

- Mean arterial pressure 65-85 mm Hg
- Urinary output >0.5 ml/kg/h
- Pulse <100/min

Signs of hypovolemia -> Bolus dose of 10 mL/kg

Signs of hypervolemia -> decrease/stop infusion

Deterioration?

Consider a higher level of care !!

› Trials. 2024 Oct 21;25(1):699. doi: 10.1186/s13063-024-08539-2.

Normal saline versus lactated Ringer's solution for acute pancreatitis resuscitation, an open-label multicenter randomized controlled trial: the WATERLAND trial study protocol

Lucía Guilabert [1], Karina Cárdenas-Jaén [1], Alicia Vaillo-Rocamora [1], Ana García García de Paredes [2 3], Ankit Chhoda [4], Sunil G Sheth [4], Carlos López-Valero [1], Pedro Zapater [3 5 6], Eva M Navarrete-Muñoz [7 8], Patrick Maisonneuve [9], Yasmin G Hernández-Barco [10], Gabriele Capurso [11], James L Buxbaum [12], Enrique de-Madaria [13 14]; ERICA consortium

Abstract Session
Room A4

Monday, October 6, 10:00 - 11:00

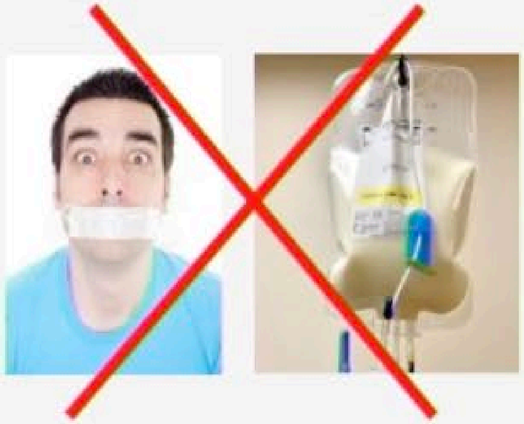
Topics: Pancreas

From The Lion King to Waterland: A journey through pancreatitis

OP074 NORMAL SALINE VERSUS LACTATED RINGER'S SOLUTION FOR ACUTE PANCREATITIS RESUSCITATION, AN OPEN-LABEL MULTICENTER RANDOMIZED CONTROLLED TRIAL: THE WATERLAND TRIAL
Enrique de-Madaria (Spain)

[1] Dawson, HPB 2013; [2] Ding, Pancreas 2023; [3]IAP/APA Guidelines 2025

Nutrition



Enteral nutrition[1]:
Protects intestinal mucosa 👍
-> Bacterial translocation ⬇️
-> Overall inflammatory response ⬇️
-> Morbidity ⬇️

IAP Guidelines[2]

Mild AP

Let them eat!

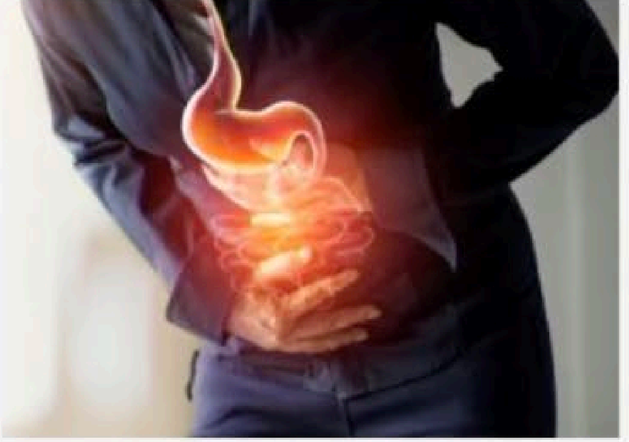


Moderately & Severe AP

Oral feeding is safe!
If not feasible: enteral tube is better than TPN (within 72h)

[1] Peery, Gastroenterology 2012; [2]IAP/APA Guidelines 2025

Pain



Important to treat the patients with adequate analgesia - pain difficult to quantify

World-wide there's no consensus but instead substantial intercontinental differences in the use of opiods[1]

Observational Study > United European Gastroenterol J. 2024 Oct;12(8):1114-1127.
doi: 10.1002/ueg2.12641. Epub 2024 Aug 14.

Global trends in opioid use for pain management in acute pancreatitis: A multicentre prospective observational study

2 metaanalysis[2,3]
Equal efficacy and safety NSAID and opioids for mild AP, less rescue analgesics with opiods
= NSAID or opiods initital choice – also the recommendation in the IAP Guidelines

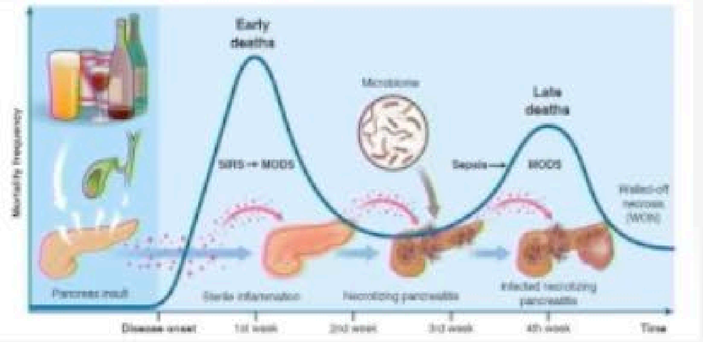
Recent RCT[4]
In moderately and severe AP opiods better than diclofenak

Patient-controlled analgesia (PCA-pump) as rescue
Epidural? Conflicting results, probably effective

Step-up approach WHO [5]
NSAID -> weak opiod -> strong opioids
Step-down?

1 Knoph, UEGJ 2024 ; [2]Thavanesan, World J Surg 2022; [3]Nelson, Gastro Hep Adv 2023; [4] Saini, CGH 2024; [5]Pandanaboyana, Curr Op Gastro 2022;

Antibiotics



Often initiated early (31-82%) without clear indication of infection[1-3]

Large variations globally: 9869 pat, 23 countries:

- ⬆️ Asia, Eastern Europe ~ 80%
- ⬇️ Western Europe ~ 30%
- ➡️ NO difference in morbidity or mortality

How to know about infection?

RCT[4]: Procalcitonin (cut-off 1 ng/mL) can guide the use of antibiotics

-> reduce in ab compare to standard care (45% vs 63%)

- no difference in clinical outcomes

Randomized Controlled Trial > Lancet Gastroenterol Hepatol. 2022 Oct;7(10):913-921. doi: 10.1016/S2468-1253(22)00212-6. Epub 2022 Jul 19.

A procalcitonin-based algorithm to guide antibiotic use in patients with acute pancreatitis (PROCAP): a single-centre, patient-blinded, randomised controlled trial

Ajith K Siriwardena [1], Santhalingam Jegatheeswaran [2], James M Mason [3]; PROCAP investigators

IAP Guidelines: no antibiotics unless proven infection

Prophylactic: 👎 (all guidelines)

Cholangitis? 👍

[1] Timmerhuis. Ann Surg 2023; [2] Barrie, Pancreatology 2018; [3] Parniczky, Pancreatology 2018; [4] Siriwardena, Lancet Gastro Hep 2022; [5] Soreide, BJS 2024

Venous thromboembolism (VTE) prophylaxis

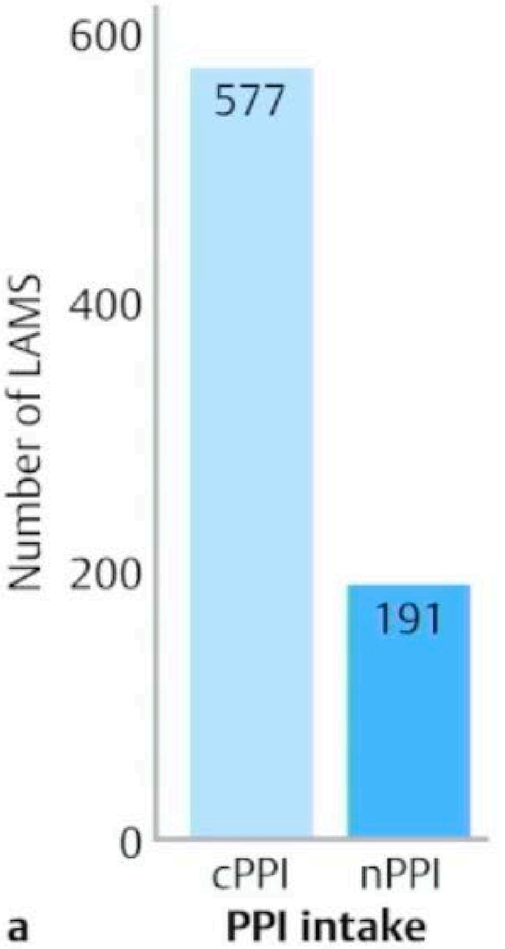
- No formal guidelines about VTE prophylaxis in admitted pancreatitis patients[1]
- **6.5%** of patients with pancreatitis develop VTE[1]
- VTE are associated with
  1. **higher mortality** (27% vs. 13%, $p<0.01$)[1]
  2. **more readmissions** (1.7 vs. 1.3, $p<0.01$)[1]
  3. **Longer length of hospital stay** (16 vs. 5.5 days, $p<0.01$)[1]
- Refer to other guidelines for hospital acquired deep vein thrombosis/pulmonary embolism[2,3]
  - **If at risk for VTE/PE and no considerable bleeding risk: thromboprophylaxis**

[1]Robbins, A. J. et al. (2021), *Pancreas*, [2]NICE guideline: Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism (2018), [3]Encke et al. (2015). *S3-Leitlinie Prophylaxe der venösen Thromboembolie (VTE)*

Do we need PPIs in patients with (necrotizing) AP?

… the answer is **NO!**

- **75%** of patients with complicated acute necrotizing pancreatitis and a Lumen apposing metal stent (LAMS) **received PPIs** (!)
- Common rationale: stress ulcer prophylaxis, bleeding risk
- Is there any evidence for this?
  - ACG[1]/AGA[2] guidelines: **no**
  - IAP[3]/APA[4] guidelines: **no**
  - DGVS[5] guidelines: **no**



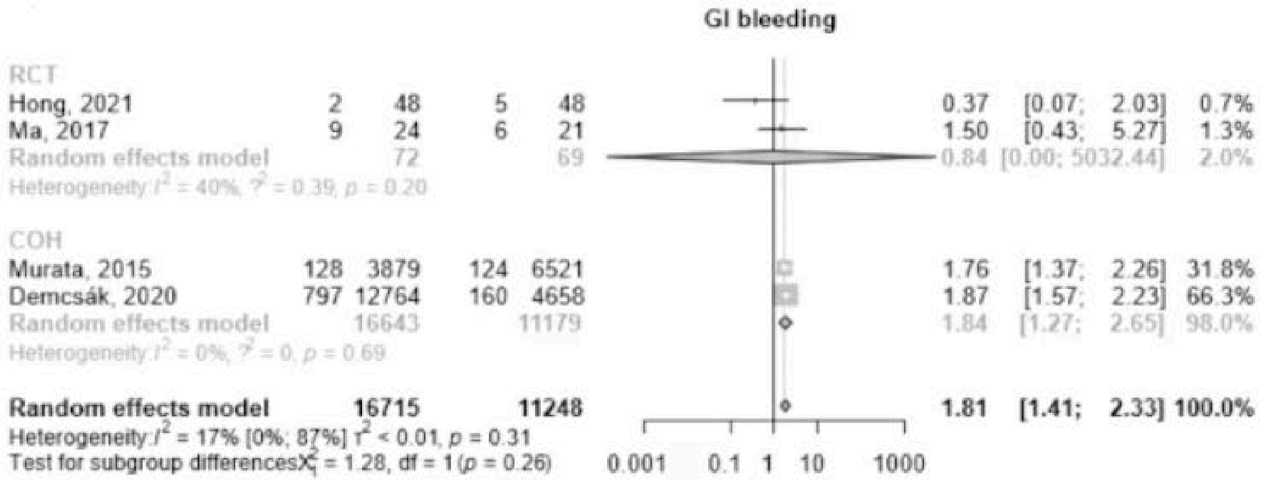
[1]ACG = American College of Gastroenterology, [2]AGA = American Gastroenterological Association
[3]IAP = International Association of Pancreatology, [4]APA = American Pancreatic Association
[5]DGVS = Deutsche Gesellschaft für Gastroenterologie, Viszeralmedizin und Stoffwechselkrankheiten (German Society for Gastroenterology)

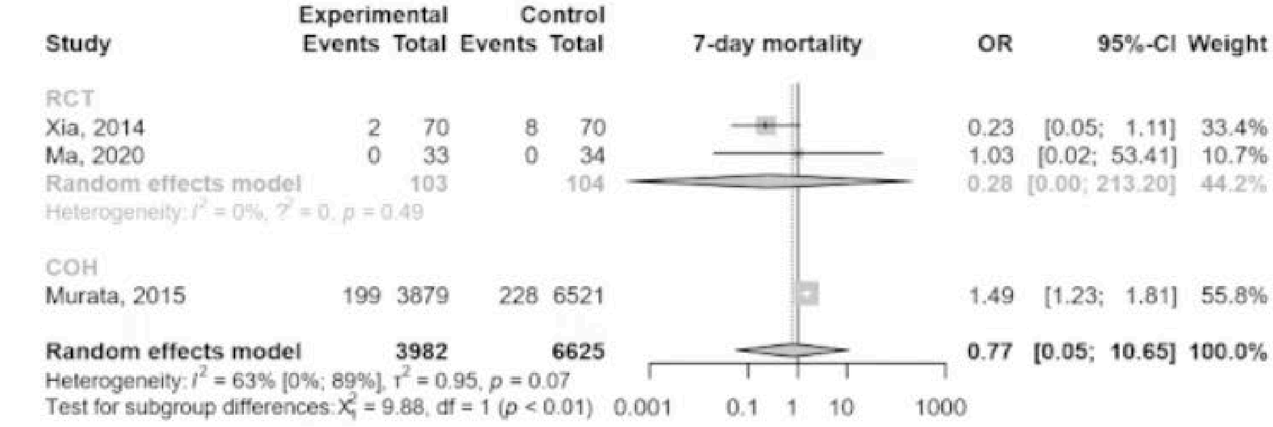
Hamm, J. et al. (2025), *Endoscopy*

Do we need PPIs in patients with (necrotizing) AP?

… the answer is **NO!**

- **Meta-analysis, 6 RCTs, 3 cohort studies**
  - 28,834 patients
  - PPI vs. no PPI
  - PPI group:
    lower rate of pseudocysts [OR 0.39]
  - **PPI group:**
    higher bleeding risk [OR 1.81]
  - No significant differences in mortality
    [OR 0.77]

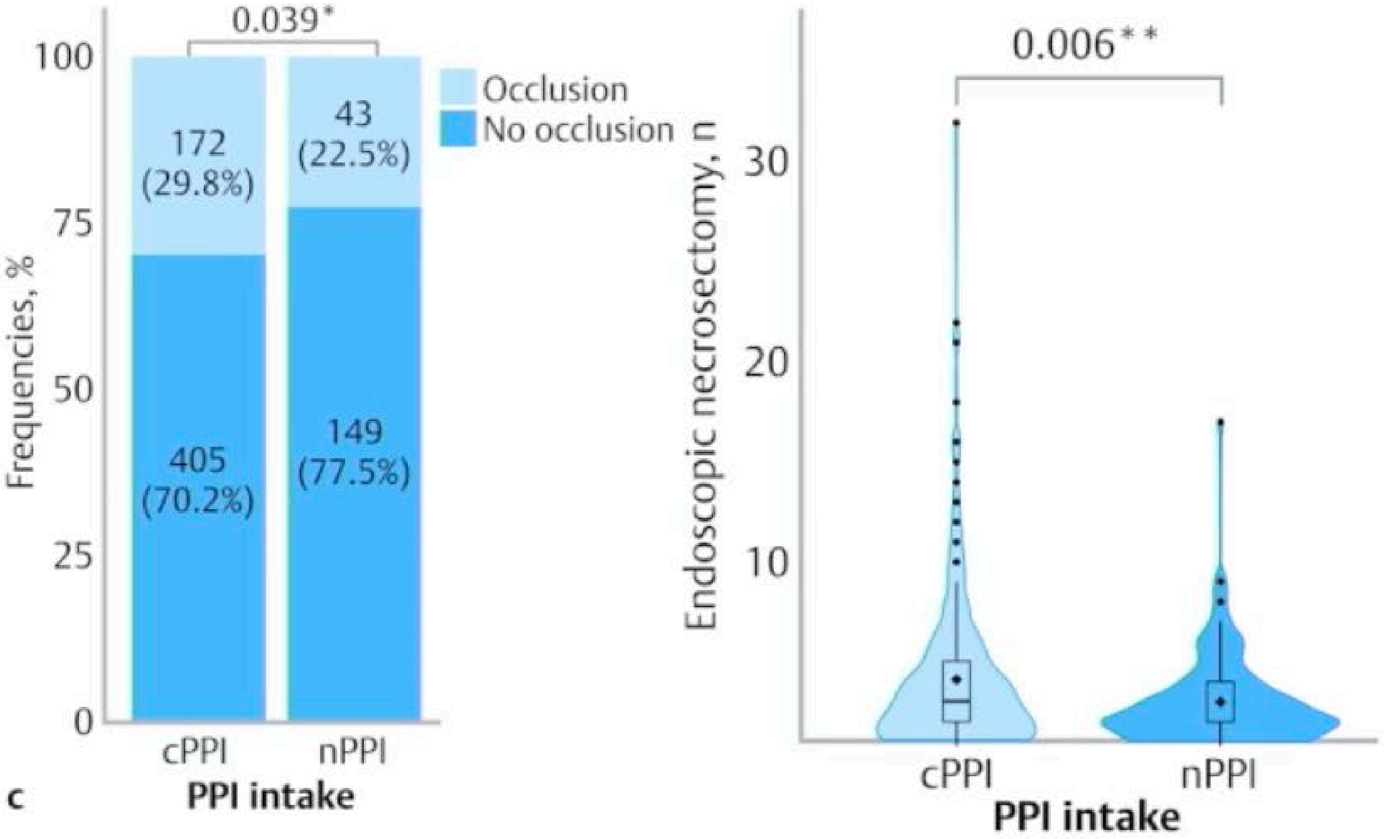




Horváth, I. L. et al. (2023), *Scientific Reports*

PPIs are associated with higher LAMS occlusion rate and higher rates of endoscopic necrosectomies

- **Retrospective cohort study**
- Patients with necrotizing pancreatitis and LAMS
- Multivariable analysis factoring in potential confounding variables
- PPI group:
  - **Higher LAMS occlusion rate (p=0.039)**
  - **More endoscopic necrosectomy sessions (p=0.006)**



Hamm, J. et al. (2025), *Endoscopy*

Do we need PPIs in patients with (necrotizing) AP?

… the answer is **NO!**

Do not start to prescribe PPIs <u>because of</u> acute (necrotizing) pancreatitis!

<u>If not otherwise indicated</u>, **discontinue!**

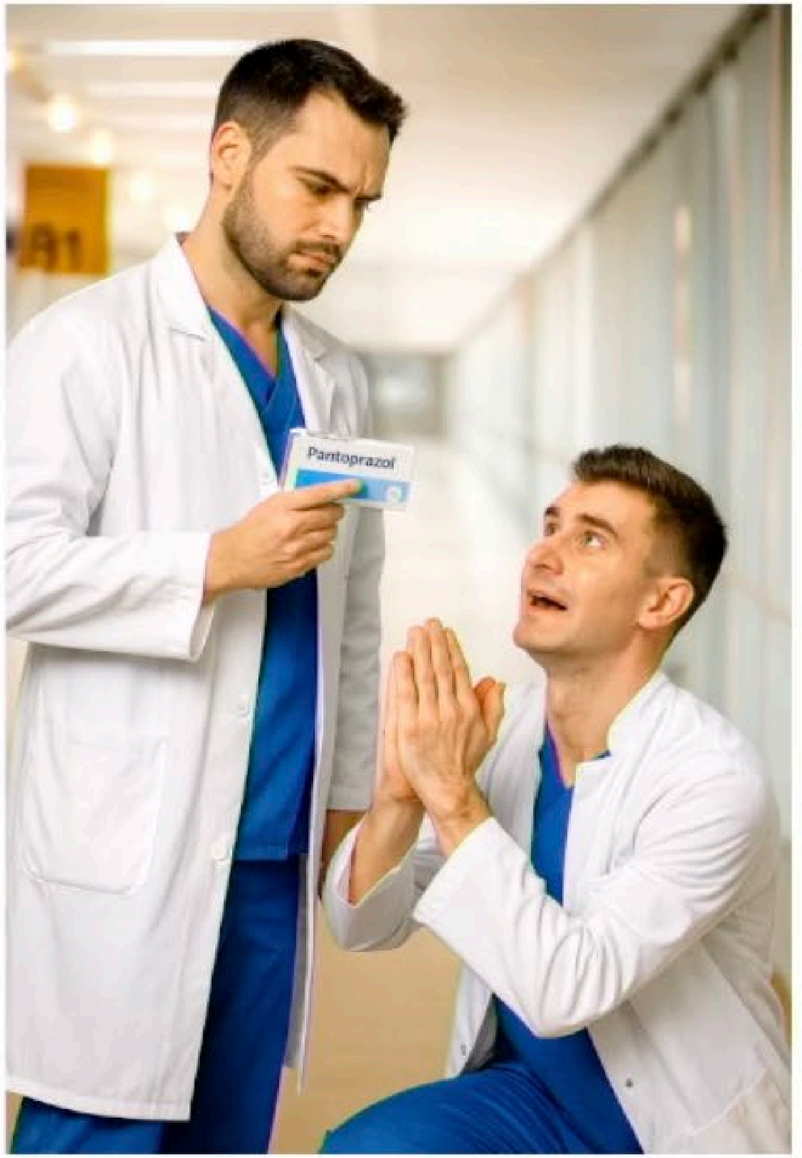
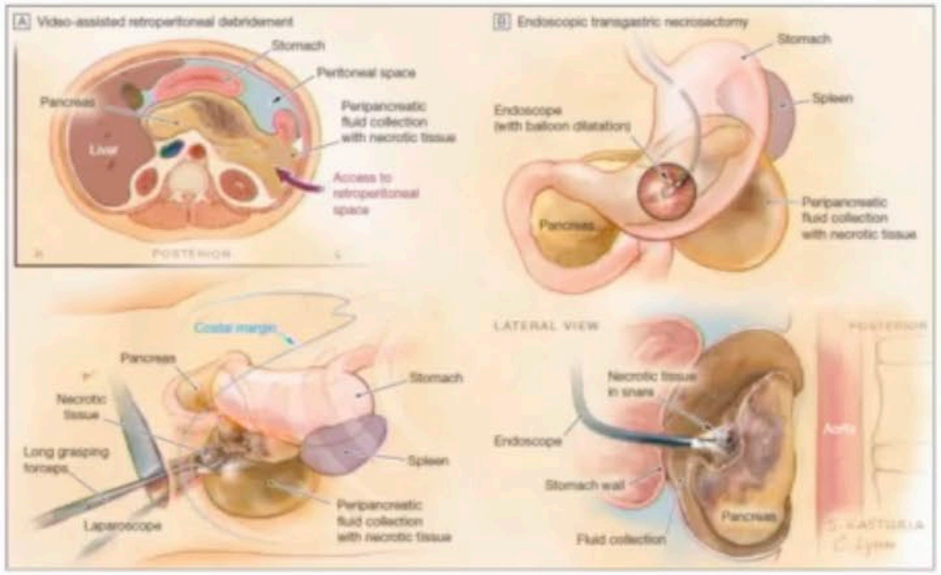


Image generated using ChatGPT

Infectious complications

Treatment strategies for infected necrosis



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Step-up Approach or Open Necrosectomy for Necrotizing Pancreatitis

ORIGINAL ARTICLE

Immediate versus Postponed Intervention for Infected Necrotizing Pancreatitis

Endoscopic Transgastric vs Surgical Necrosectomy for Infected Necrotizing Pancreatitis
A Randomized Trial

Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial

An Endoscopic Transluminal Approach, Compared With Minimally Invasive Surgery, Reduces Complications and Costs for Patients With Necrotizing Pancreatitis

Ji Young Bang,[1] Juan Pablo Arnoletti,[2] Bronte A. Holt,[1] Bryce Sutton,[1] Muhammad K. Hasan,[1] Udayakumar Navaneethan,[1] Nicholas Feranec,[3] C. Mel Wilcox,[4] Benjamin Tharian,[1] Robert H. Hawes,[1] and Shyam Varadarajulu[1]

„Do as much nothing as possible"!

Treat sepsis, delay interventions, use minimally invasive access for drainage!

Step-up approach saves lifes!

1/3 of patients no intervention needed!

van Santvoort HC, N Engl J Med. 2010
Hollemans A Gastroenterology 2019
Bakk OJ et al. JAMA. 2012
van Brunschot S et al. Lancet. 2018
Bang JY et al. Gastroenterology. 2019
Boxhoorn L et al. N Engl J Med. 2021

ACG Guidelines Recommendations/ Key Concepts

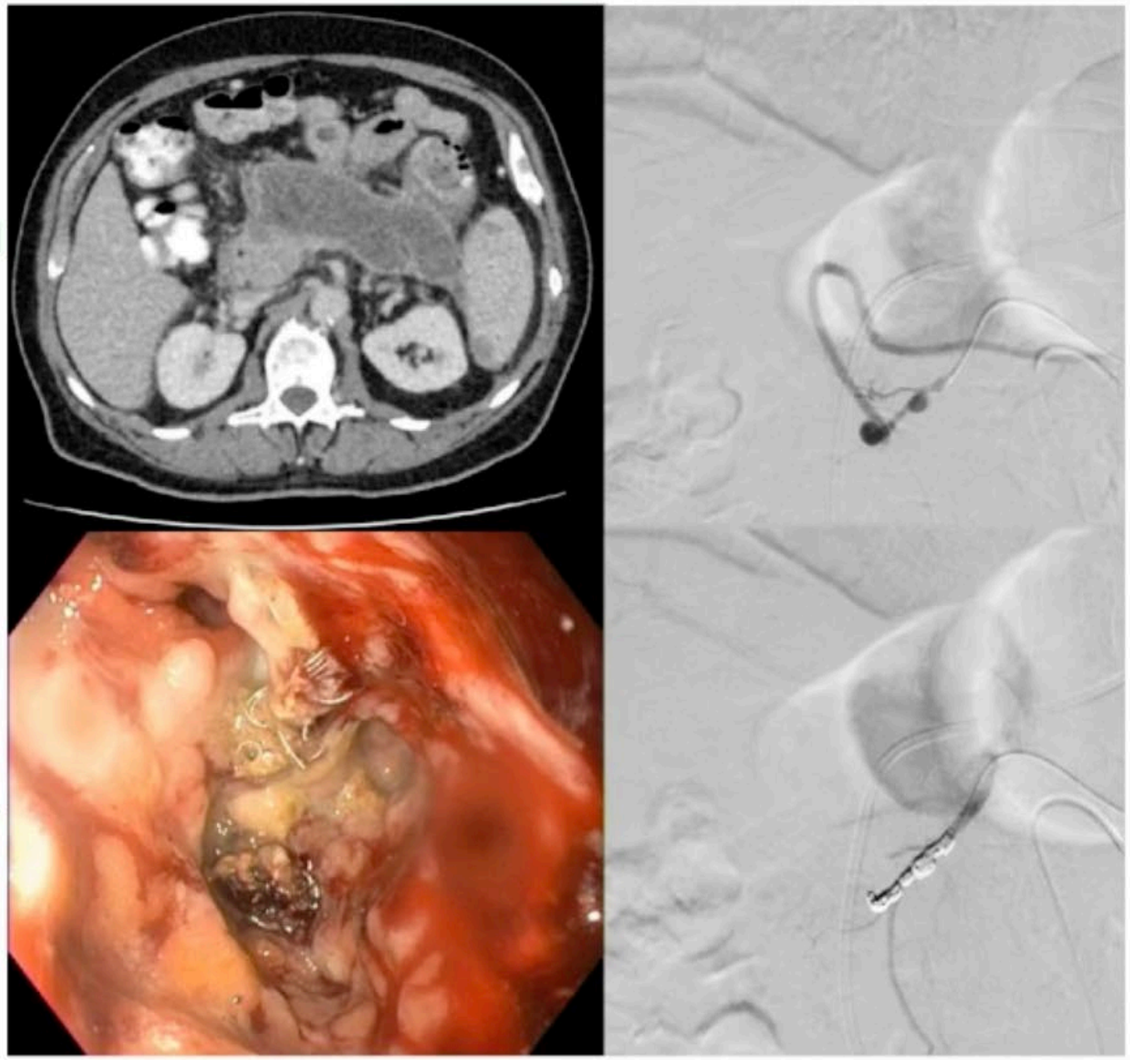
- *ACG suggests against prophylactic antibiotics in pts with severe AP*
- *ACG suggests against FNA in pts with suspected infected PNec*

- Delay any intervention in stable pts with PNec preferably beyond 4 weeks
- In pts with infected PNec, administer antibiotics with good penetrance first to delay minimally invasive drainage beyond 4 weeks
- Some pts may avoid intervention altogether because the infection may completely resolve with Abxs
- Minimally invasive methods preferred to open surgery for debridement in stable patients with symptomatic PNec

Tenner S et al. Am J Gastroenterol 2024

Vascular complications
Arterial Pseudoaneurysm

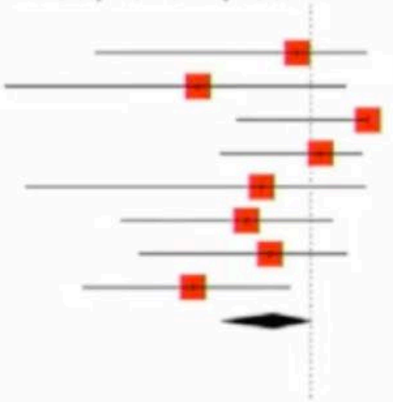
Rare event in AP (<0.1% of cases)
Patients with non-resolving necrotic collections at risk
Splenic artery most commonly affected 37%



Angioembolization is recommended to treat arterial pseudoaneurysms and other arterial bleeding complications …

Study or Subgroup	Events	Total	GLMM, Random, 95% CI
group = AP			
Beattie GC et al	5	6	0.83 [0.36; 1.00]
Bergert H et al	3	5	0.60 [0.15; 0.95]
Czernik M et al	10	10	1.00 [0.69; 1.00]
Duan XH et al	16	18	0.89 [0.65; 0.99]
Gebelmann A et al	3	4	0.75 [0.19; 0.99]
Mallick B et al	10	14	0.71 [0.42; 0.92]
Mansueto G et al	10	13	0.77 [0.46; 0.95]
Zhou F et al	10	17	0.59 [0.33; 0.82]
Total (95% CI)		87	0.78 [0.66; 0.87]

Heterogeneity: $Tau^2 = 0.1435$; $Chi^2 = 4.6$, df = 7 (P = 0.71); $I^2 = 19\%$



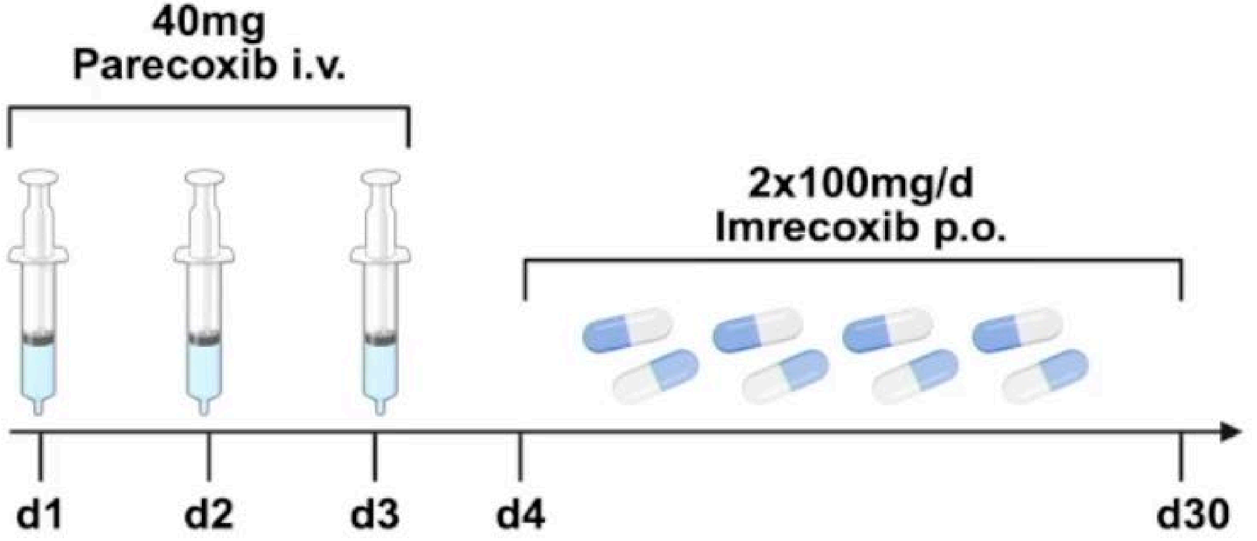
Sagar S et al. Pancreatology. 2021
International Association of Pancreatology Revised Guidelines on Acute Pancreatitis 2025. Pancreatology. 2025.

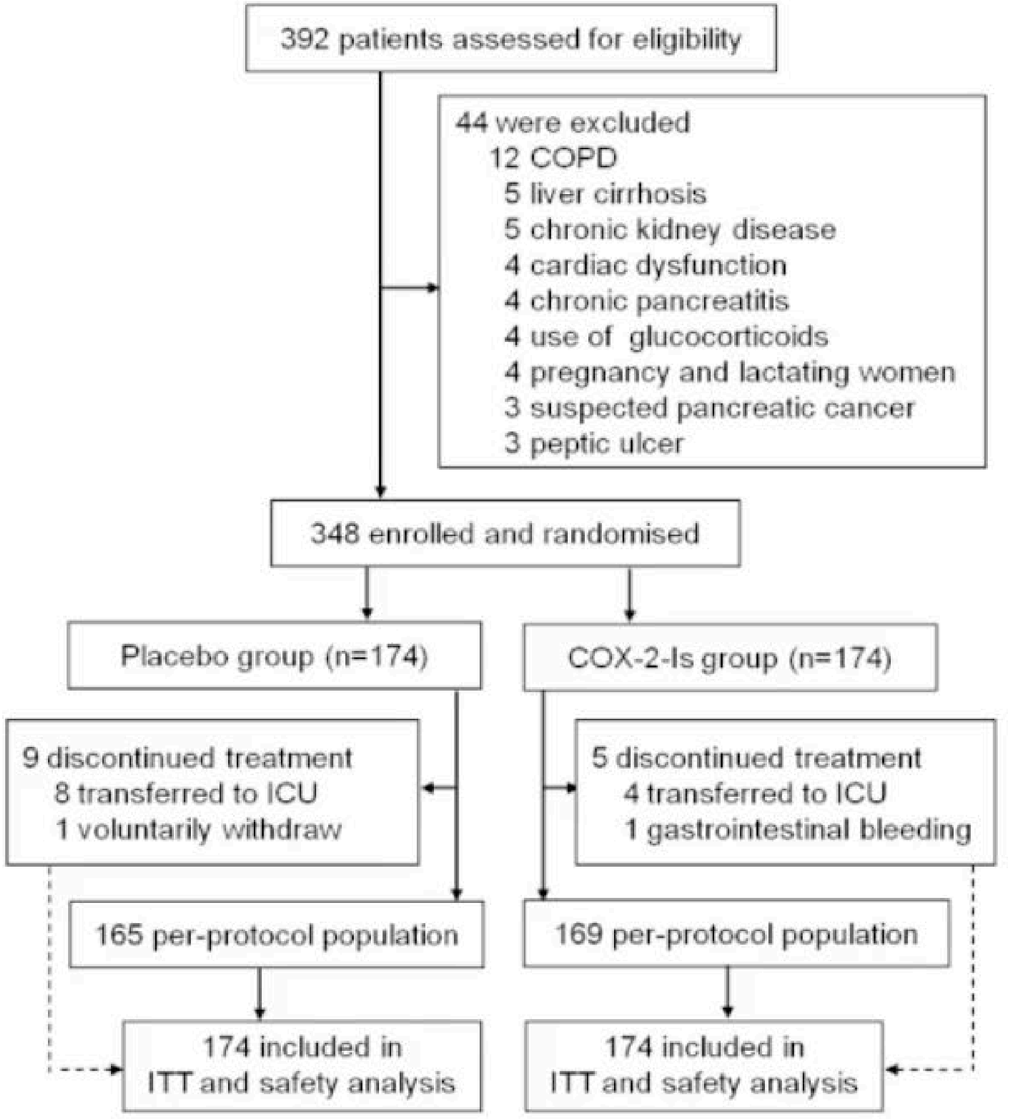
Prevention of severe acute pancreatitis (SAP)

Novel role for COX-2 inhibitors?

- **10 centers, 348 patients**
- Symptom onset within 1 week
- APACHE II ≥7 or modified Marshall Score ≥2

- **Randomized, controlled, double-blind**



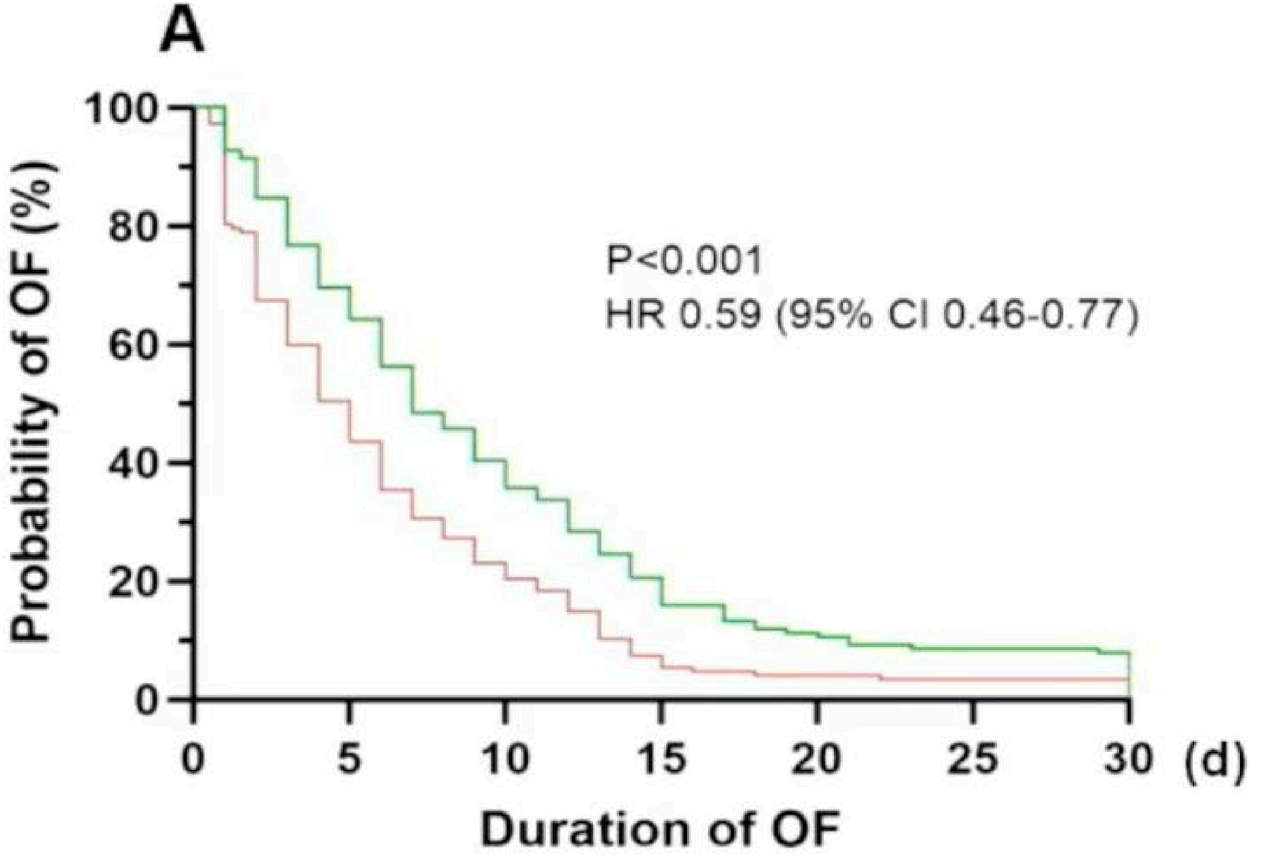


Huang, L. et al. (2025), *Gut*.

Prevention of severe acute pancreatitis (SAP)

Novel role for COX-2 inhibitors?

- Primary EP: organ failure duration
  - **COX-2i** group: median **4** days
  - **Placebo**: median **7** days (p<0.001)
- Severe acute pancreatitis occurrence:
  - **COX-2i** group: **61.5%**
  - Placebo: **77.6%** (p=0.001)
- 30-day mortality rate:
  - **COX-2i** group: **3.4%**
  - **Placebo**: **8.6%** (p=0.043)
- Adverse events:
  - **No differences** between groups



Huang, L. et al. (2025), *Gut*.

Conclusion

Standard of care

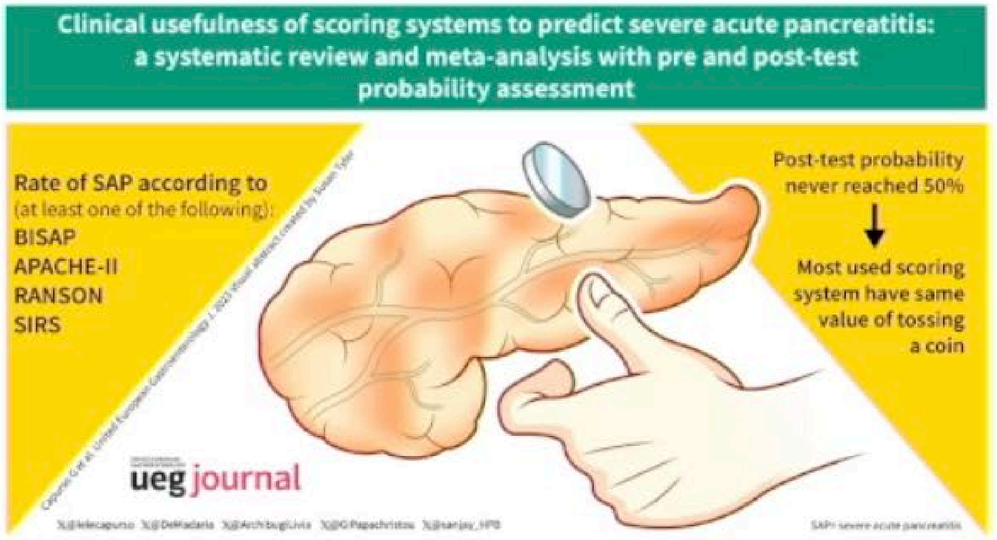
1. **Pain** management: **treat to target** (=pain relief) using **WHO step up** principle
2. **Antibiotics**: only if infectious complications, **PCT-directed**!
3. **Thromboprophylaxis**

Please avoid

1. **No PPIs** if not indicated for other comorbidities!
2. Antibiotics without a clear source of infection!

The future?

- COX-2 inhibitors for patients at risk for severe acute pancreatitis (SAP)?
  - BUT: not for pat. w/ heart/kidney diseases
  - BUT: we cannot predict who will develop SAP



Capurso, G. et al. (2023), *United European Gastroenterology Journal*

