Mistakes in the management of acute pancreatitis

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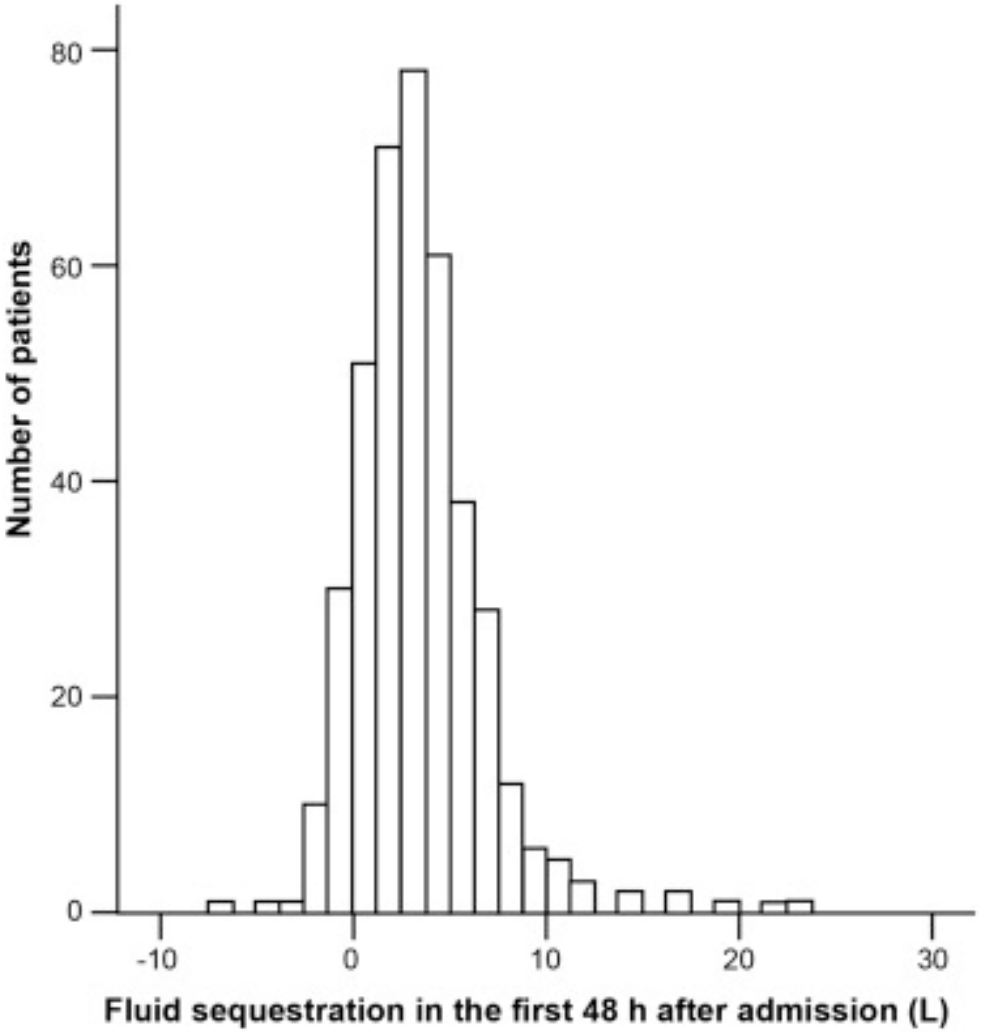
Acute pancreatitis- 2009

- most frequent diagnosis in patients discharged from GI services in the US
- 274,000 discharges
- median LOS 4 days
- fifth leading cause of in-hospital mortality
- mortality 1%

1. Failure to adequately assess fluid status

- fluid sequestration due to third spacing is a common early event in acute pancreatitis
- associated with pancreatic necrosis and organ failure if not treated immediately

The median level of fluid sequestration in the first 48 hours after hospital admission was 3.2 L



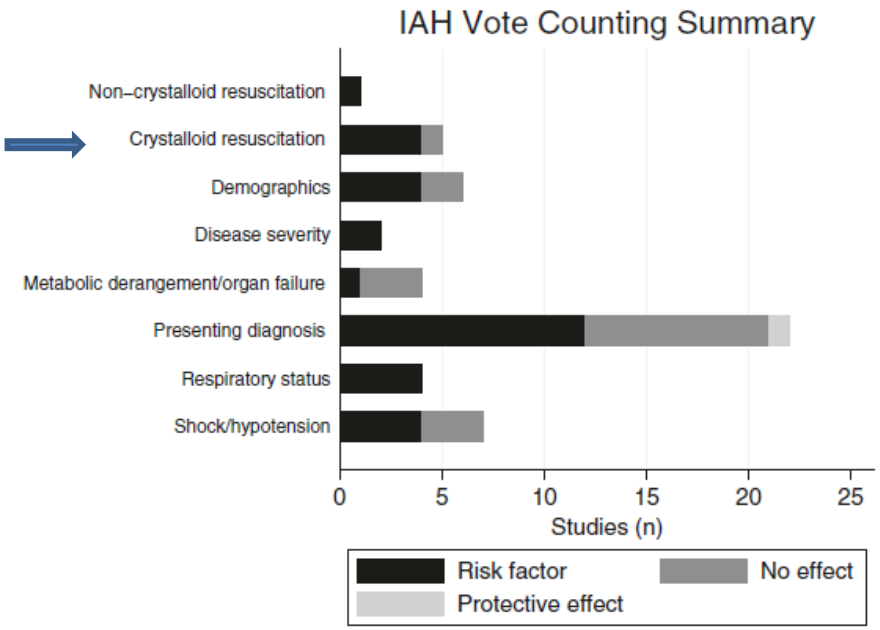
Initial management

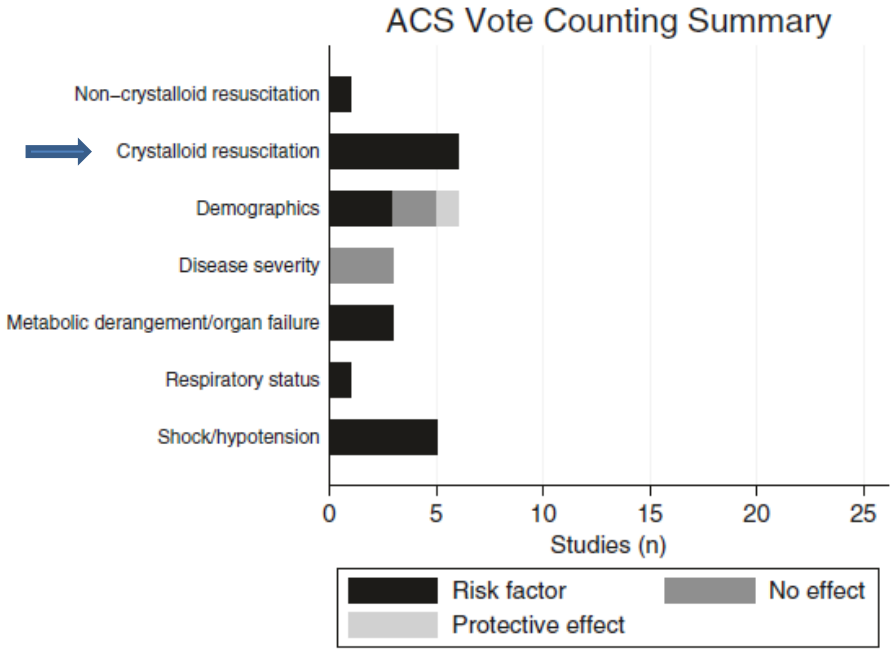
- aggressive early IV hydration (up to 250-500 ml/h with **RL**)
- most beneficial **first 12-24H**
- most critical part of active treatment within **the first 48 hours**

fluid resuscitation

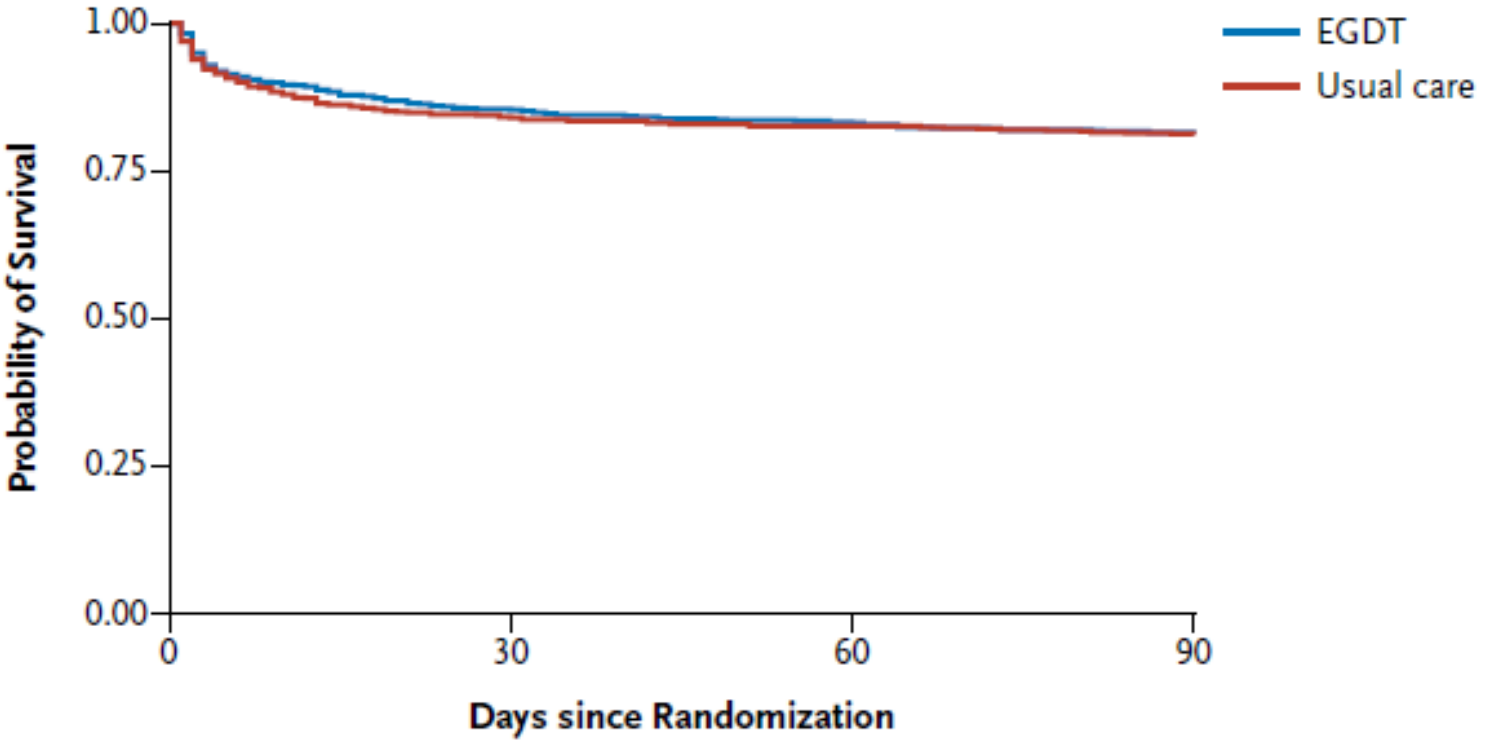
- **overly aggressive** administration is not necessarily beneficial for patients and could even be **harmful**
- *goal-directed fluid resuscitation*, have failed to improve patient outcomes in studies (both pancreatitis and non-pancreatitis patients)

risk factors for IAH and ACS in critically ill patients





probability of death in patients with septic shock



No. at Risk				
EGDT	792	677	660	646
Usual care	796	670	657	646

Fluid Therapy in Acute Pancreatitis

Anybody's Guess

In conclusion, FT is considered an important early intervention in patients with AP, in theory, offering the opportunity to prevent the severity of the disease and improve clinical outcomes. Given the clinical and economical burden of AP, it is an indictment that, despite decades of research into the management of, there is such a lack of quality evidence to guide the most basic aspects of its FT. Furthermore, what data are available remain conflicted, providing the equipoise necessary for further randomized studies. High-quality randomized data are needed to answer the urgent basic clinical management questions of what fluid to give, at what rate, and how best to guide successful FT delivery in AP.

(*Ann Surg* 2013;257: 182–188)

fluid resuscitation

- patients should receive crystalloid fluids, (rather than colloids), at a rate of 5–10ml/kg of BW to reach
- H.R. <120 bpm under adequate analgesic therapy
  - M.A.P 65–85 mmHg
  - urine output >0.5ml/kg BW/h
  - Ht 35–44%

IAP/ APA acute pancreatitis guidelines 2013

- Attention for fluid overload in:

  -pre-existing heart failure, cardiac valve disease or renal disease
- IAP should be monitored in severe disease
- Thermodilution/ stroke volume variation

2. Delaying ERCP in pts with AP and cholangitis

- Inflammation/ oedema can lead to biliary obstruction even without choledocholithiasis.
- Guidelines: ERCP if
  - ❑concurrent **acute cholangitis** (ES in 24h)
  - ❑ongoing **biliary obstruction** (clinical-laboratory)

- In most cases **(95-97%)** of biliary pancreatitis the stone has already passed into the duodenum
- In patients who have no cholangitis but unclear derangement of liver function test results and/or a history of gallstones, **MRCP or EUS** can help to avoid ERCP

Cholangitis definition

- body temperature: **≥ 38.5ºC with chills**, without an obvious other cause (e.g., cystitis, pneumonia, thrombophlebitis, etc), **or 39ºC without chills**, without an obvious cause for fever, **and either:**
- 1) Choledocholithiasis on abdominal US, CT, EUS or MRI, **or**
- 2) A dilated common bile duct on imaging defined as >8mm in patients ≤75 years or >10mm in patients >75 years **or**
- 3) Progressive cholestasis for at least two consecutive days and a bilirubin **>2.3 mg/dL** (40 µmol/L).

cholestasis definition

- serum bilirubin level: >2.3 mg/dL
- and/or dilated CBD
- temperature: < 38.5°C

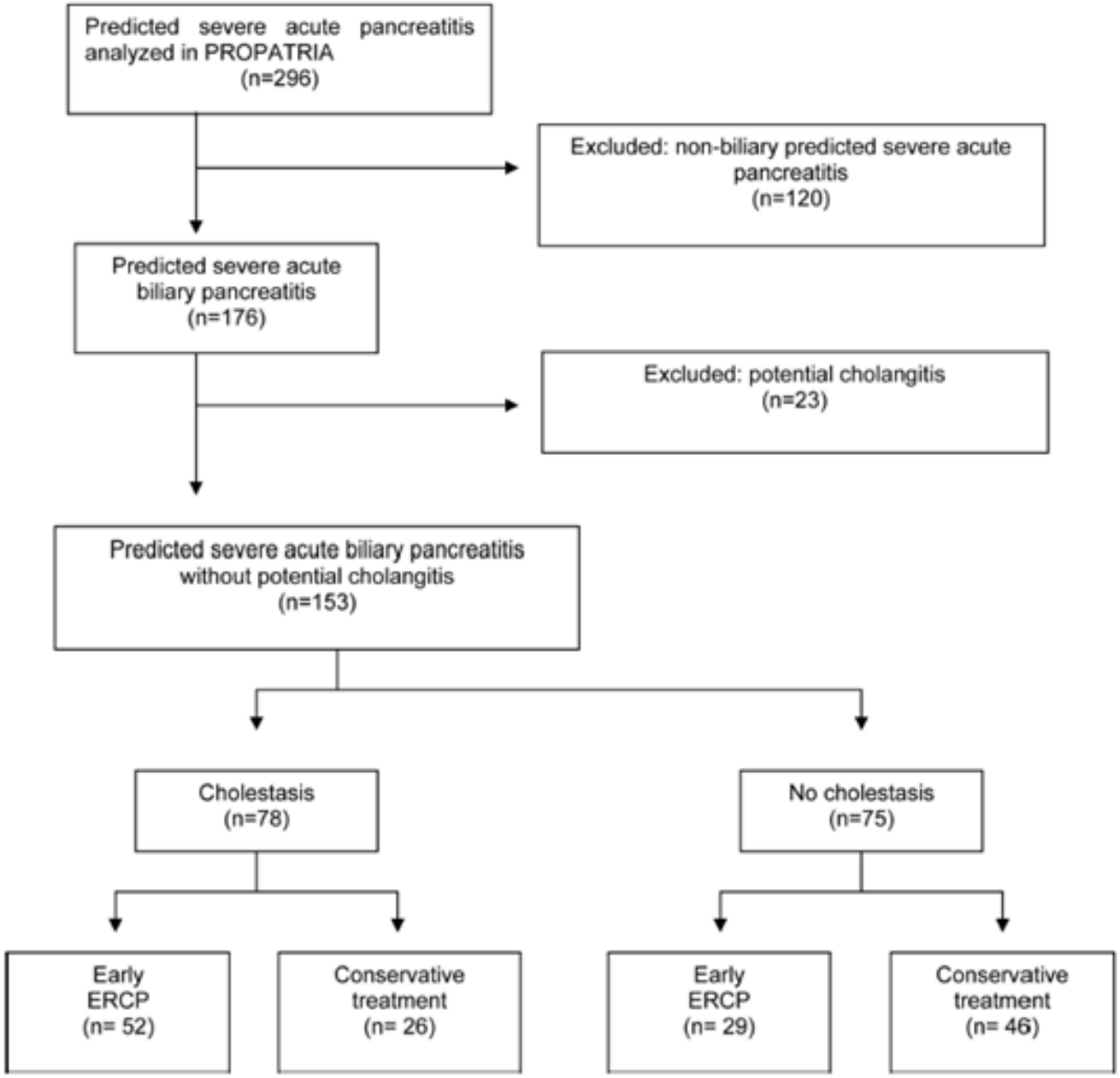

Predicted severe acute pancreatitis analyzed in PROPATRIA (n=296)
Excluded: non-biliary predicted severe acute pancreatitis (n=120)
Predicted severe acute biliary pancreatitis (n=176)
Excluded: potential cholangitis (n=23)
Predicted severe acute biliary pancreatitis without potential cholangitis (n=153)
Cholestasis (n=78)
No cholestasis (n=75)
Early ERCP (n= 52)
Conservative treatment (n= 26)
Early ERCP (n= 29)
Conservative treatment (n= 46)

TABLE 2. Outcome of 153 Patients With Predicted Severe Acute Biliary Pancreatitis Undergoing Early ERCP or Conservative Treatment

Characteristics	Patients With Cholestasis (n = 78)			Patients Without Cholestasis (n = 75)		
	Early ERCP (n = 52)	Conservative Treatment (n = 26)	*P*	Early ERCP (n = 29)	Conservative Treatment (n = 46)	*P*
Primary endpoints						
Overall complications	13 (25%)	14 (54%)	0.020	13 (45%)	19 (41%)	0.814
Pancreatic necrosis	8 (17%)	9 (38%)	0.076	10 (36%)	13 (30%)	0.796
<30% pancreatic necrosis	4 (8%)	1 (4%)	0.660	4 (14%)	7 (15%)	0.999
>30% pancreatic necrosis	4 (8%)	8 (31%)	0.010	6 (21%)	6 (13%)	0.519
Infected pancreatic necrosis	4 (8%)	5 (20%)	0.151	5 (17%)	5 (11%)	0.496
Bacteremia	6 (12%)	6 (23%)	0.200	7 (24%)	6 (13%)	0.230
Infected ascites	0 (0%)	1 (4%)	0.333	1 (3%)	1 (2%)	0.999
Pneumonia	4 (8%)	4 (16%)	0.430	3 (10%)	4 (9%)	0.999
New onset organ failure	6 (12%)	4 (16%)	0.723	6 (20%)	7 (15%)	0.549
New onset multi-organ failure	6 (12%)	3 (12%)	0.999	6 (20%)	9 (20%)	0.999
Bowel ischaemia*	1 (2%)	0 (0%)	0.999	1 (4%)	1 (2%)	0.999
Mortality	3 (6%)	4 (15%)	0.213	4 (14%)	8 (17%)	0.754
Secondary endpoints						
CTSI†	3.0 (0.0–10.0)	3.5 (0.0–10.0)	0.462	4.0 (0.0–10.0)	4.0 (0.0–10.0)	0.812
Percutaneous drainage	4 (8%)	2 (8%)	0.999	3 (10%)	2 (4%)	0.369
Operative necrosectomy	4 (15%)	4 (8%)	0.430	6 (21%)	4 (9%)	0.171
Intensive care admission	12 (23%)	7 (27%)	0.782	9 (31%)	8 (17%)	0.257
Total intensive care stay in days	0 (0–89)	0 (0–110)	0.763	0 (0–30)	0 (0–40)	0.163
Total hospital stay in days	14 (3–140)	20 (5–112)	0.218	13 (5–155)	16 (3–85)	0.931

3. Delaying cholecystectomy in biliary pancreatitis

- Patients with biliary pancreatitis are at **high risk of recurrence** if the the gallbladder is not removed
- In patients who have mild biliary pancreatitis, cholecystectomy can safely be performed during the index hospital admission
- Delaying removal of the gallbladder **beyond 6 weeks** from admission increases the risk of recurrent biliary events

PONCHO RTC (2015) [3 days vs. 30 days]

	Interval cholecystectomy (n=136)	Same-admission cholecystectomy (n=128)	Risk ratio (95% CI)	p value
Primary endpoint				
Mortality or readmission for gallstone-related complications	23 (17%)	6 (5%)	0·28 (0·12–0·66)	0·002
Secondary endpoints				
Readmission for gallstone-related complications				
Recurrent pancreatitis	12 (9%)	3 (2%)	0·27 (0·08–0·92)	0·03
Cholecystitis	2 (2%)	0		0·50
Choledocholithiasis needing ERCP	2 (2%)	1 (1%)	0·53 (0·05–5·79)	1·00
Gallstone colic	7 (5%)	2 (2%)	0·30 (0·06–1·43)	0·17
Mortality	0	1 (1%)		0·48
Patients reporting colics during waiting period*	62 (51%)	3 (3%)	0·06 (0·02–0·19)	<0·0001
Difficulty of cholecystectomy (assessed on a 0–10 visual analogue scale)	6 (4–7)	6 (4–7)		0·70
Conversion to open cholecystectomy†	4 (3%)	5 (4%)	1·31 (0·36–4·77)	0·74
Operating time (min)	60 (44–78)	58 (44–70)		0·47
Total length of stay after randomisation (days)	3 (2–5)	3 (2–4)		0·94
Need for intensive care unit admission	1 (1%)	1 (1%)		1·00

- Prophylactic ES should be considered in patients who are **unfit for surgery** due to comorbidities
- In patients with severe biliary pancreatitis, cholecystectomy should be delayed until **resolution of pancreatic collections** or formation of a **walled-off necrosis**

4. Early endoscopic / surgical intervention in necrotizing pancreatitis

- interventions should be delayed to **at least 4 weeks** after the onset of acute pancreatitis

Indications for interventions

- proof that there is a necrotic collection on imaging that shows features of **infection**
- high suspicion for infection with persistent signs of sepsis
- being persistently unwell
- disconnected duct syndrome
- gastric outlet obstruction
- pancreatic fistulas

a step-up approach

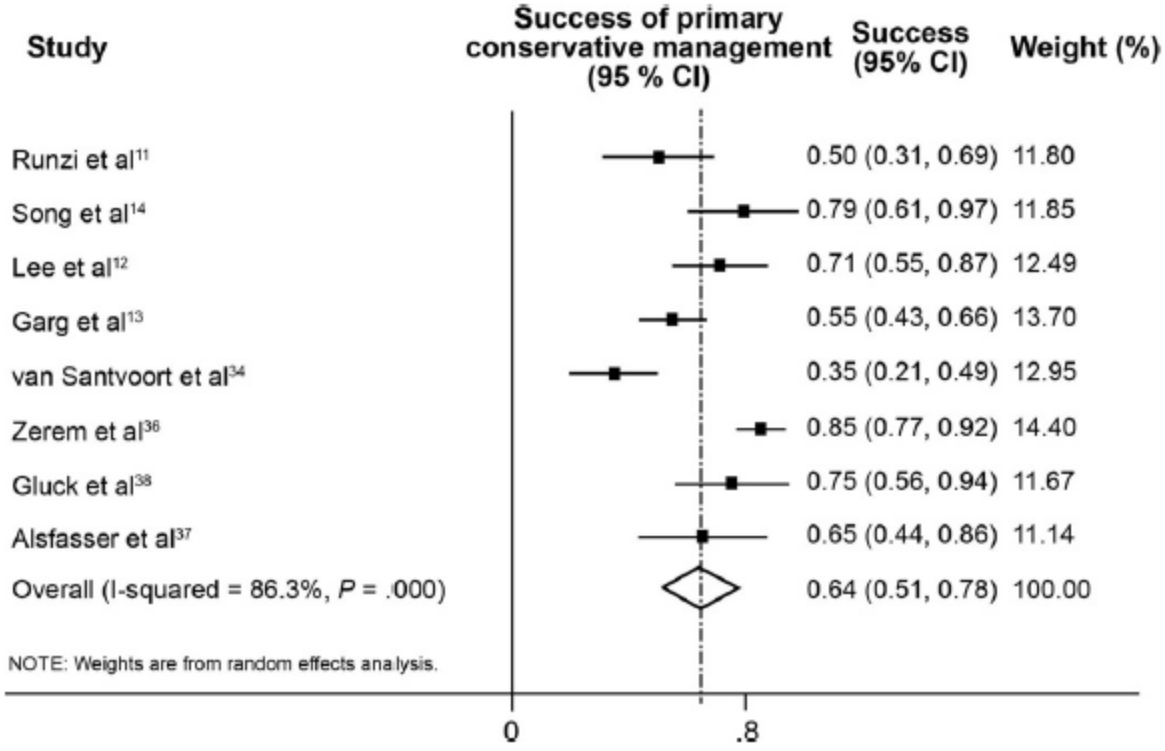
- start with endoscopic or minimal invasive percutaneous **drainage** procedures
- endoscopic stent placement (double pigtail stents or self-expanding wall stents)
- percutaneous retroperitoneal tubes (with **irrigation**)

- If drainage and irrigation does not lead to improvement, then **minimal invasive necrosectomy** (either endoscopically or via the percutaneous access)
- **Open surgery** in patients in whom the previously mentioned methods have failed to improve the situation

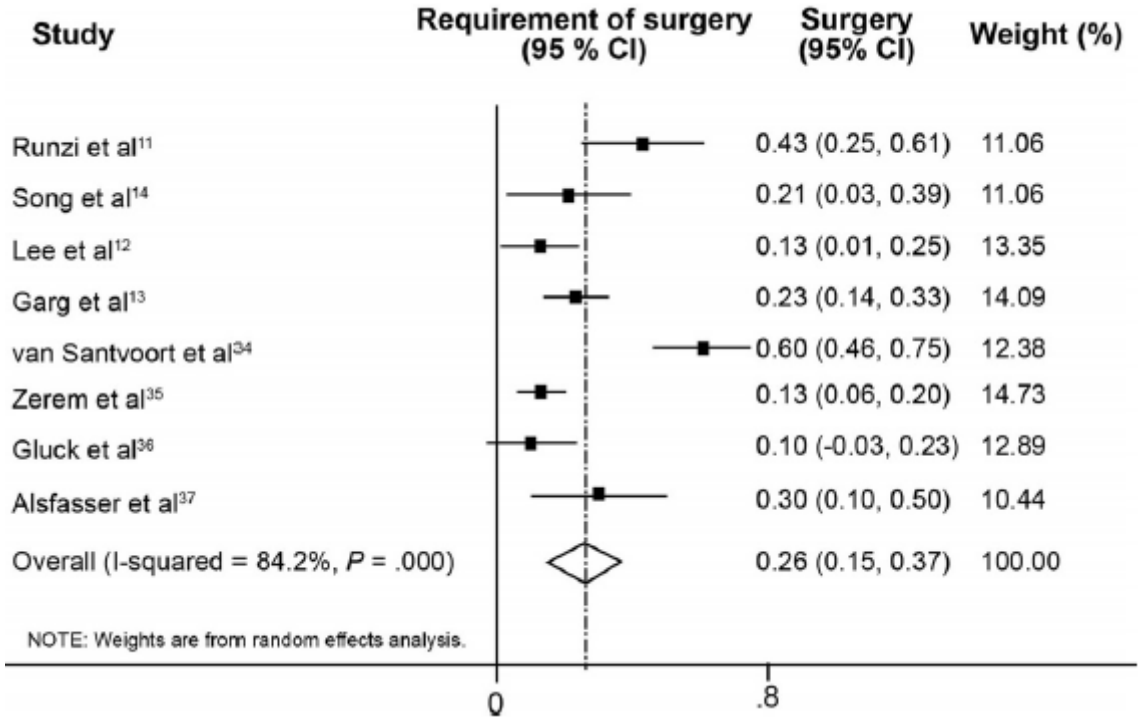
Conservative management

- in some patients even infected necrotic collections can be managed conservatively (IV antibiotics and supportive therapy)

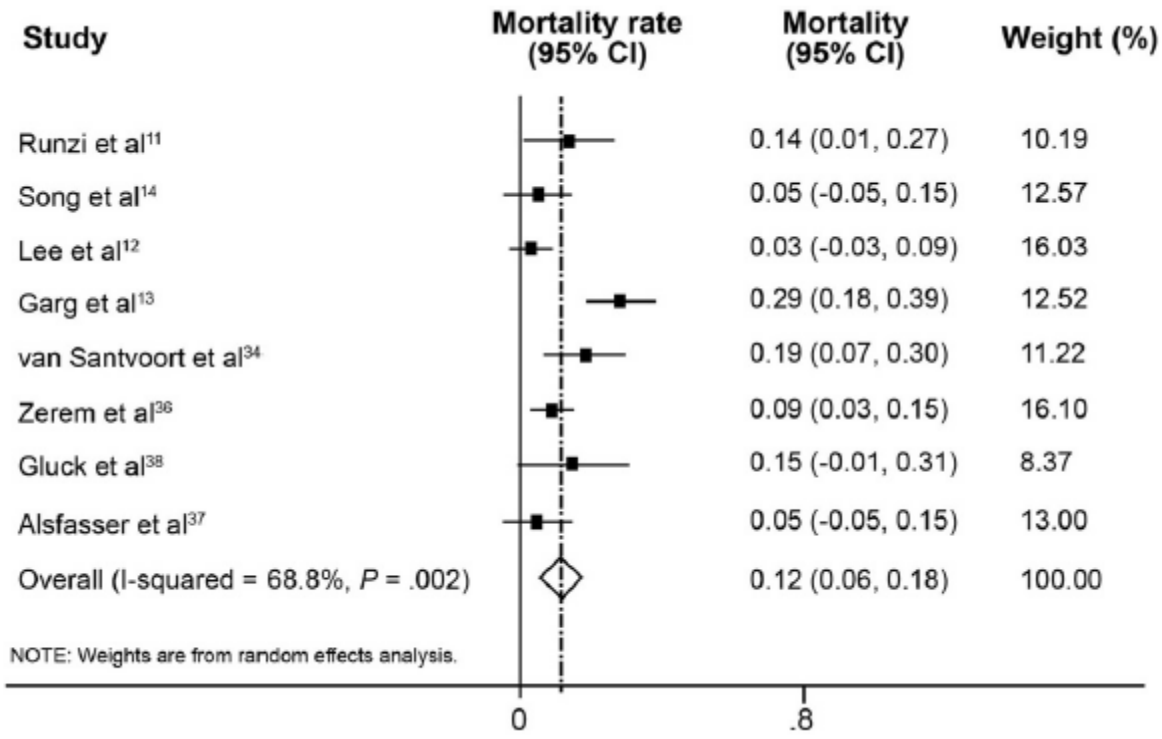
conservative management in IPN: success 64%



need for necrosectomy or additional surgery: 26%



Mortality: 12%



5. Administering prophylactic antibiotics

- AGA, IAP/APA- 2013
- **prophylactic** ABS in severe AP **not recommended**
- use of ABS **in sterile** necrosis **not** recommended
- systemic antibiotics be started **only if an infection, pancreatic or not, is proven** or very likely

Japanese guidelines 2015

- early (48–72hrs) **prophylactic** administration of antibiotics in patients with **severe necrotizing pancreatitis** might reduce mortality and the rate of infected necrosis

6. Unnecessary bowel rest

- enteral feeding prevents mucosal atrophy of the gut and thus **prevents bacterial translocation** and intra-abdominal infection

- in mild AP nutrition can be started immediately with solid low-fat diet
- in severe AP **enteral nutrition** is recommended to avoid infectious compls
- TPN should be avoided

- In patients with severe disease nutritional support is often needed, but the optimal time point for initiation of feeding is still unknown

patients with severe disease did not benefit from early (24h) feeding

Table 2. Primary and Secondary End Points, According to the Intention-to-Treat Analysis.*

Outcome	Early Tube Feeding (N=101)	On-Demand Tube Feeding (N=104)	Risk Ratio (95% CI)	P Value
Primary composite end point: infection or death — no. (%)	30 (30)	28 (27)	1.07 (0.79–1.44)	0.76
Secondary end points				
Infection — no. (%)†	25 (25)	27 (26)	0.97 (0.70–1.34)	0.87
Infected pancreatic necrosis	9 (9)	15 (14)	0.74 (0.43–1.26)	0.28
Bacteremia	17 (17)	18 (17)	0.98 (0.68–1.43)	1.00
Pneumonia	12 (12)	13 (12)	0.97 (0.63–1.50)	1.00
Death — no. (%)	11 (11)	7 (7)	1.27 (0.85–1.89)	0.33
Necrotizing pancreatitis — no. (%)‡	64 (63)	65 (62)	1.06 (0.77–1.47)	0.76
CT severity index§	4±2	4±3	—	0.29
ICU admission after randomization — no. (%)	18 (18)	20 (19)	0.95 (0.66–1.38)	0.86
Mechanical ventilation — no. (%)	12 (12)	14 (13)	0.93 (0.60–1.44)	0.84
New-onset organ failure — no./total no. at risk (%)¶				
Single organ failure	26/67 (39)	31/73 (42)	0.92 (0.65–1.32)	0.73
Persistent single organ failure	10/67 (15)	10/73 (14)	1.05 (0.65–1.70)	1.00
Multiple organ failure	7/67 (10)	6/73 (8)	1.14 (0.67–1.95)	0.77
Persistent multiple organ failure	4/67 (6)	4/73 (5)	1.05 (0.51–2.14)	1.00

7. Perform routine CT imaging on admission

- current guidelines do **not** recommend routinely performing a CT scan i**n the first two to three days** after the onset of symptoms
- The extent of the disease, especially necrosis, might not be fully visible before several days into the disease course

- cases of diagnostic uncertainty,
- suspicion for abdominal compartment syndrome
- vascular complications including hemorrhage or bowel ischemia