

Severe Acute, Necrotizing Pancreatitis: Optimal Treatment

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M E D I C I N E

Nothing to disclose

Objectives

- Review evidence-based guidelines and new studies in the treatment of necrotizing pancreatitis.
- Discuss percutaneous, endoscopic and surgical techniques use in the management of necrotizing pancreatitis.
- Review optimal algorithms for diagnosis and management of necrotizing pancreatitis.

Working Group IAP/APA Acute Pancreatitis Guidelines. “IAP/APA evidence-based guidelines for the management of acute pancreatitis.” *Pancreatology*. 2013;13: e1-e15.

IAP/APA evidence-based guidelines for the management of acute pancreatitis[☆]

Working Group IAP/APA Acute Pancreatitis Guidelines^{a,b,*,1}

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^b American Pancreatic Association, PO Box 14906, Minneapolis, MN 55414, USA

Working Group IAP/APA Acute Pancreatitis Guidelines / Pancreatology 13 (2013) e1–e15

Severe Pancreatitis

- Severe pancreatitis can be accompanied by profound SIRS and MOF
- Identical to sepsis
- Approx 10% of cases results in pancreatic necrosis

Diagnosis?

- CT scan: contrast enhanced
 - Arterial phase
 - Venous phase
- MRI
 - Gadolinium

Indications for imaging?

Working Group IAP/APA Acute Pancreatitis Guidelines. *Pancreatology*. 2013;13: e1-e15.

- 1) Diagnostic uncertainty
 - 2) Confirmation of severity
 - 3) Failure to respond to conservative treatment
- *Ideal timing: 72-96 hours after onset of symptoms*

(LOE Grade 1C, strong agreement)

Necrosis is Bad

Buchler MW, et al. Acute Necrotizing Pancreatitis: Treatment Strategy According to the Status of Infection. Ann Surg. 2000;232:619-626.

	Edematous pancreatitis N=118	Necrotic Pancreatitis N = 86	P
Pts MOF	0	30 (35%)	< 0.0001
Pulm insuff	4 (3%)	54 (63%)	< 0.0001
AKI	1 (1%)	11 (13%)	< 0.0017
Pressors	3 (3%)	20 (26%)	< 0.0001
Sepsis	0	9 (10%)	< 0.006

Necrosis as a Predictor?

- Severe pancreatitis can be accompanied by profound SIRS and MOF
- Identical to sepsis
- While there is an association between necrosis and MOF, it is not causal and cannot be used to guide management alone

Mole, DJ, et al. Discrepancy Between the Extent of Pancreatic Necrosis and Multiple Organ Failure Score in Severe Acute Pancreatitis. World J Surg 2009; 33:2427-2432.

Reality

- Sterile necrosis can be managed non-operatively - *well*

Table 4. CHARACTERISTICS OF PATIENTS WITH STERILE AND INFECTED NECROSIS

	SPN (n = 57)	IPN (n = 29)	P
Female	20	11	
Male	37	18	
Mean age (range)	56.1 (28–87)	57.6 (29–75)	
Biliary cause	22 (39%)	16 (55%)	NS
Alcohol	23	9	
Other or undefined cause	12	4	
Mean serum c-reactive protein in mg/L (range)*	222 (112–343)	231 (101–456)	NS
Mean Ranson score (range)	3.8 (0–8)	4.2 (0–7)	NS
Mean APACHE II score (range)*	12.2 (5–28)	13.2 (6–22)	NS
Mean hospital stay in days (range)	23.5 (11–85)	84.8 (22–209)	<.001
Surgical treatment (%)	1 (2%)	27 (93%)	<.0001
Hospital deaths	2 (3.5%)	7 (24%)	<.01

IPN, infected pancreatic necrosis; SPN, sterile pancreatic necrosis.

* Peak value in the first week of disease.

Buchler MW, et al. Ann Surg. 2000;232:619-626.

Truth: Infected Necrosis is Worse

- Infected necrosis carries a high morbidity

	Sterile Pancreatic Necrosis N=57	Infected Pancreatic Necrosis N = 86	P
Pts MOF	10 (18%)	20 (69%)	< 0.0001
Pulm insuff	27 (47%)	27 (93%)	< 0.0001
AKI	3 (5%)	8 (28%)	< 0.01
Pressors	5 (9%)	15 (52%)	< 0.0001
Sepsis	1 (2%)	8 (28%)	< 0.01

Buchler MW, et al. Ann Surg. 2000;232:619-626.

Truth: Infected Necrosis is Worse

- **Infected necrosis carries a high mortality**
 - **80% of patients who died associated with infected necrosis**

Factors associated with mortality:

% necrosis:

30% <10 % mortality

50% 25% mortality

Near total >50%

Extrapancreatic necrosis: 34 % (vs. 16%)

Pancreatic ascites: 37 % (vs. 9%)

Bacteria infection: 32 % (vs. 10%)

Beger HG, et al. Natural course of acute pancreatitis.

***World J Surg* 1997; 21: 130–135.**

Thus: Aggressive Management?

- **Intervention / necrosectomy for infected pancreatic necrosis in critically ill patients.**
 - **Aimed at source control**

Indications for interventions

Working Group IAP/APA Acute Pancreatitis Guidelines. *Pancreatology*. 2013;13: e1-e15.

- 1) Clinical suspicion of or documented infection with clinical deterioration (preferably after several weeks).
- 2) In the absence of documented infection, ongoing organ failure several weeks after onset of symptoms.

(LOE Grade 1C, strong agreement)

To aspirate or not to aspirate, that is the question....

Working Group IAP/APA Acute Pancreatitis Guidelines. *Pancreatology*. 2013;13: e1-e15.

- 1) Infection can be confirmed by FNA; there is a risk of false negative.
- 2) Routine aspiration is not indicated (clinical and imaging signs are often enough).

(LOE Grade 1C, strong agreement)

Identification of Infected Necrosis

- Clinical signs
 - Persistent fever
 - Inflammatory markers
- Imaging signs
 - Gas in peri-pancreatic tissue

Is Culture Sampling Reliable?

- Yes
- **Buchler M, et al. Ann Surg, 2000.**
 - **27 of 28 patients correctly diagnosed with pre-op FNA sampling**

Number Aspirations	Sterile necrosis 15 patients	Infected necrosis 28 patients
1	12	16
2	3	6
3	0	5
> 3	0	1

In whom does culture not inform?

- **Patients with necrosis and intraperitoneal air on CT → necrosectomy**
 - Not amenable to percutaneous drainage
- **Hemodynamically stable (afebrile, chronically unwell) patients with CT finding of necrosis → expectant management**

What about sterile pancreatic necrosis?

Aggressive Management?

- **Invasive intervention for pancreatic necrosis in:**
- **Critically ill patients?**
 - **Aimed at inflammation control**
- **Chronically ill patients?**
 - **More anatomic considerations**

Intervention in Sterile Pancreatic Necrosis

Working Group IAP/APA Acute Pancreatitis Guidelines. *Pancreatology*. 2013;13: e1-e15.

- 1) Obstruction (gastric outlet, intestinal, biliary) due to mass effect.
 - 2) Persistent symptoms (pain, “unwellness”).
 - 3) Disconnected duct syndrome.
- For all recommended timing markedly later (>8 weeks).

(LOE Grade 2C, strong agreement)

Declining Morbidity and Mortality Rates in the Surgical Management of Pancreatic Necrosis

Thomas J. Howard • Jay B. Patel • Nicholas Zyromski •
Kumar Sandrasegaran • Jian Yu • Atilla Nakeeb •
Henry A. Pitt • Keith D. Lillemoe

J Gastrointest Surg (2007) 11:43–49

Table 3 Indications for Debridement, Time to Debridement, Reoperation Rate, Morbidity, Mortality, and ICU and Hospital Length of Stays

	Group I 1993–2001 (N=59)	Group II 2002–2005 (N=43)	<i>p</i> Value
Indications for debridement			0.79
Infected necrosis (%)	42 (76)	34 (72)	
Symptomatic sterile necrosis (%)	11 (20)	12 (26)	
Progressive organ failure (%)	2 (4)	1 (2)	
Time to initial debridement (days±SD)	46±46	44±40	0.82
Reoperation rate (%)	37 (67)	32 (68)	0.93
Morbidity rate (%)	49 (89)	34 (72)	0.03
Pancreatic fistula rate (%)	27 (49)	28 (60)	0.29
Intensive care unit length of stay (days±SD)	13±25	9±13	0.33
Hospital length of stay (days±SD)	38±33	26±23	0.04
Mortality rate (%)	10 (18)	2 (4)	0.03

Improvement!

- **Necrosectomy is best delayed until 4 weeks to allow delineation of and detachment of necrotic tissues**
- **Howard TJ, et al. Declining morbidity and mortality rates in the surgical management of pancreatic necrosis. *J Gastrointest Surg* 2007;11:43-9. Mortality 18% → 4%**
- **Rodriguez JR, et al. Debridement and closed packing for sterile or infected necrotizing pancreatitis: insights into indications and outcomes in 167 patients. *Ann Surg* 2008;247:294-9. Mortality 23% → 5%**
- **Besselink MGH, et al. Timing of surgical intervention in necrotizing pancreatitis. *Arch Surg* 2007;142:1194-201. Mortality 75% → 45% → 8%**

Timing of Intervention

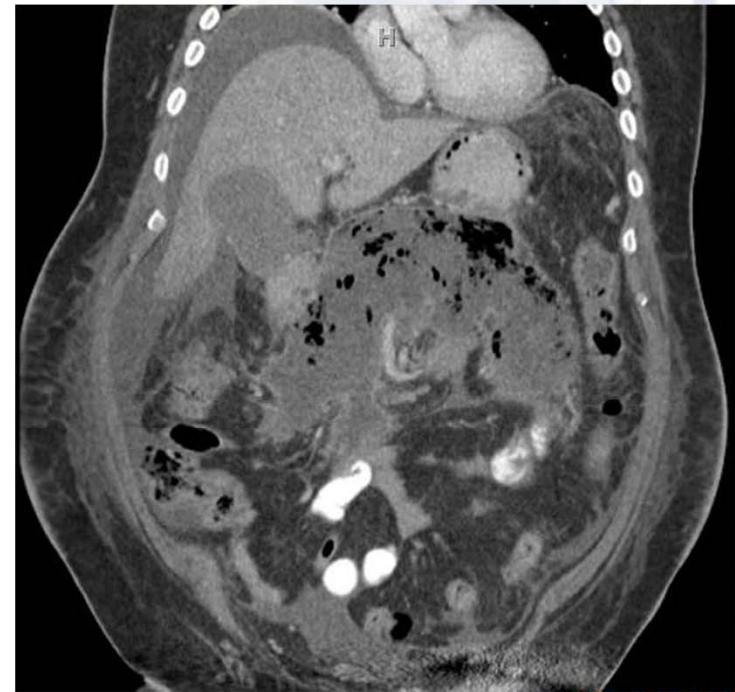
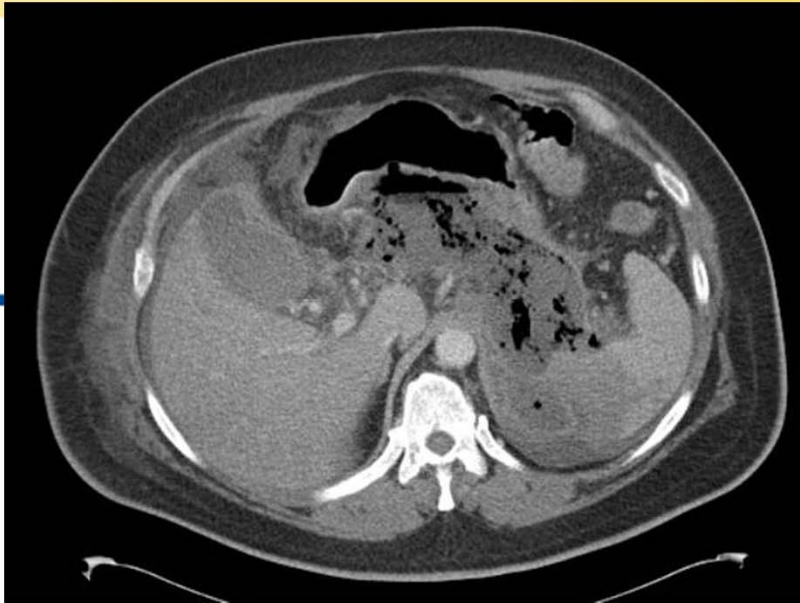
Working Group IAP/APA Acute Pancreatitis Guidelines. *Pancreatology*. 2013;13: e1-e15.

- 1) Surgical necrosectomy (any method):
after 4 weeks (if possible).
 - 2) Endoscopic or radiologic intervention
(any method): after 4 weeks (if
possible).
- ***“Walled off”: euphemism for
liquefied or actually debridable!***

(LOE Grade 1C, strong agreement)

Typical presentation...

- 55 yo man presents to the ED with abdominal pain, nausea, weight loss
- Multiple recent hospitalizations at OSH over past 6 weeks for acute pancreatitis
- “No one wants to do anything!”
- PSHx: L Hip replacement, appy
- PMHx (chronic): HTN, IDDM, HLD, cholelithiasis
- PMHx (acute): DVT, recent AKI requiring short course of HD, ARDS with 3 day vent course



Open necrosectomy

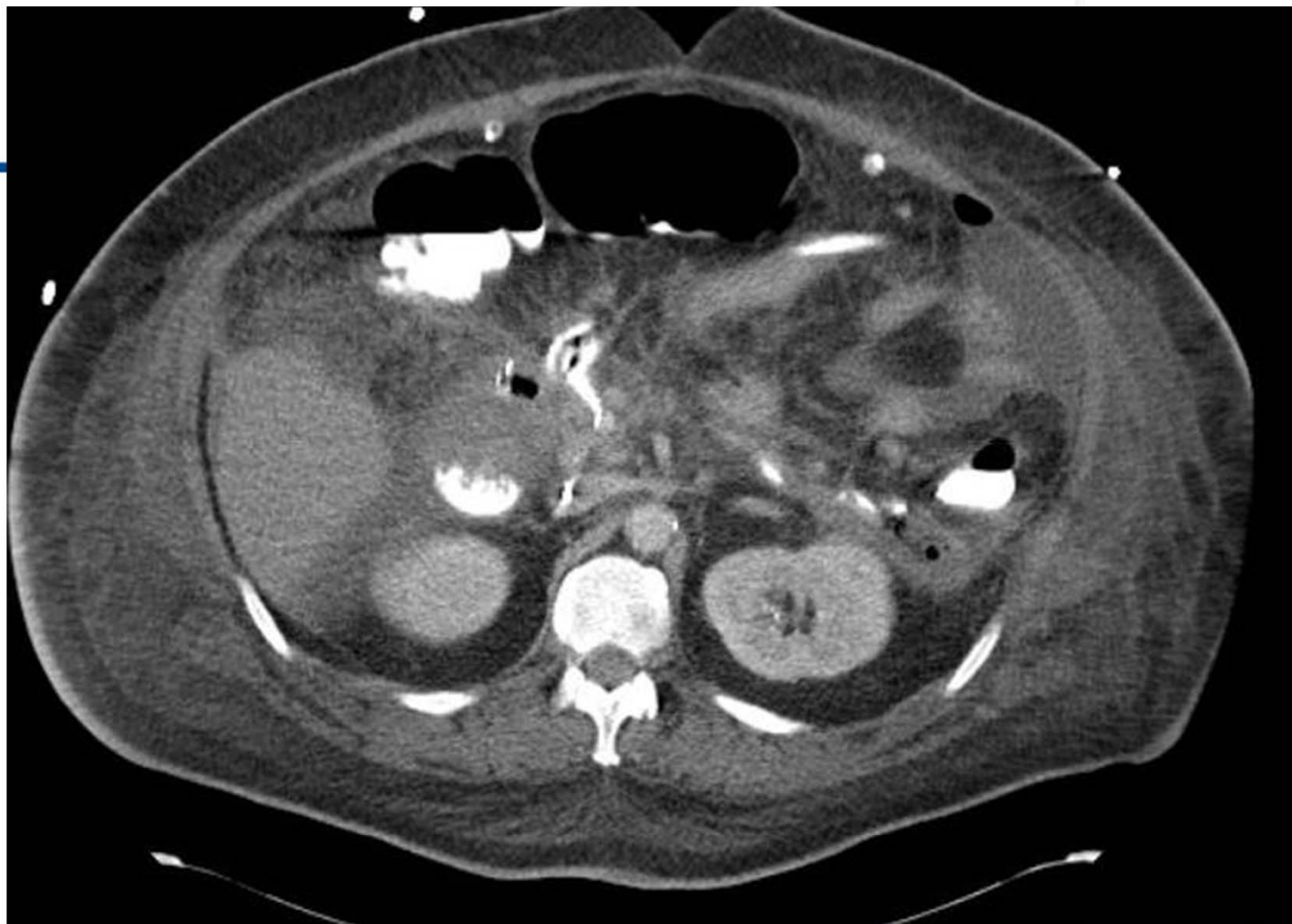
- To OR
- Open debridement pancreatic bed, washout and wide drainage.
- Upper abdomen frozen (initial approach to lesser sac via the transverse mesocolon, then gastro-colic window)
- Gall bladder left in place (unapproachable)
- G-tube not possible (stomach would not come up)
- Closure over 4 large drains throughout retroperitoneum

Infected necrosis

- Fluid
- HEAVY CITROBACTER YOUNGAE
- HEAVY KLEBSIELLA PNEUMONIAE
- HEAVY STAPHYLOCOCCUS SPECIES, COAGULASE NEGATIVE
- HEAVY LACTOBACILLUS SPECIES
- Tissue
- HEAVY KLEBSIELLA PNEUMONIAE
- HEAVY ENTEROCOCCUS FAECALIS
- HEAVY STAPHYLOCOCCUS LUGDUNENSIS
- HEAVY PREVOTELLA SPECIES BETA LACTAMASE PRODUCING
- HEAVY BACTEROIDES FRAGILIS GROUP BETA LACTAMASE PRODUCING

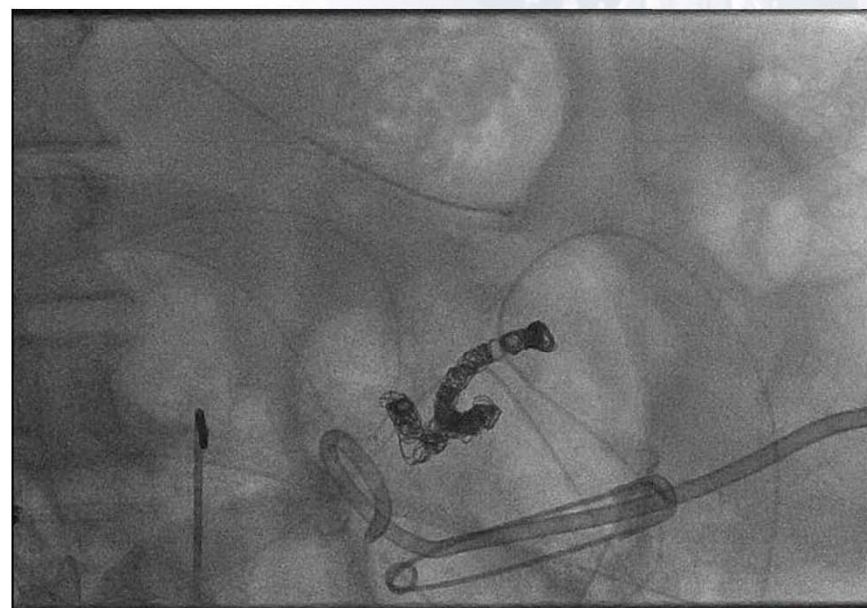
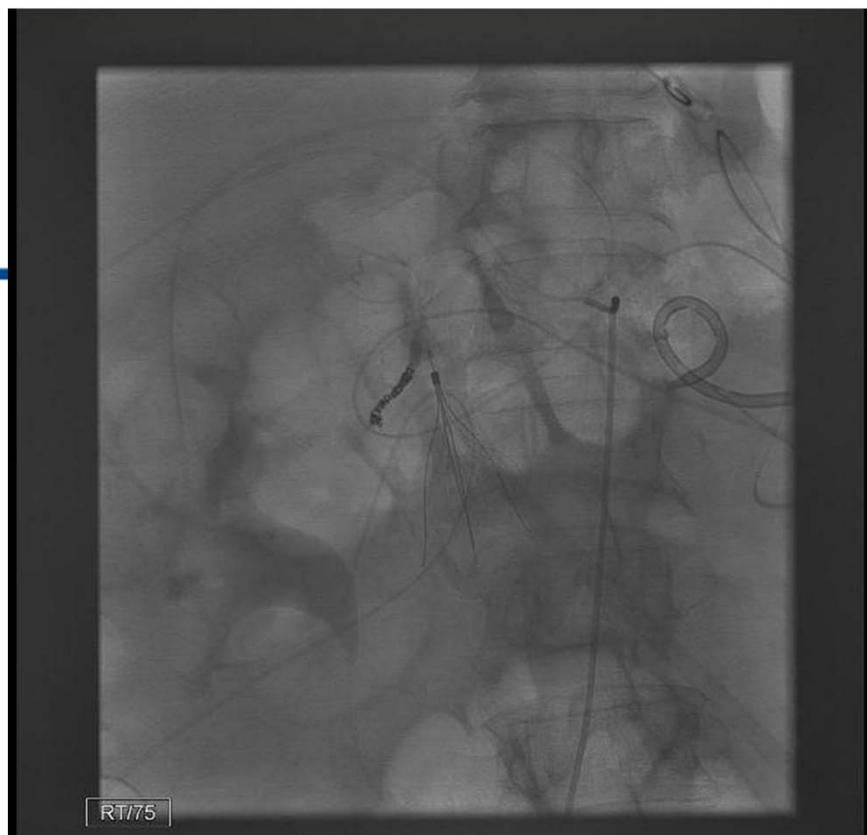
Post-op....

- Early ICU course: SIRS
- Weaned from vent by POD 4
- Early parenteral nutrition
- POD7: Bilious fluid in drains, Non-contrast CT shows no collections and excellent drainage
- POD10: persistent low volume bilious drainage, PO contrast CT



Post-op....

- UGI confirm small leak from medial c-loop of duodenum
- Improving, moving bowels, low output from drains
- POD 34 : hypotension, BRB from drains
- To SICU, stabilized, CT showed no blush
- Sentinel bleed: to angiography
- Severe irregularity of both GDA and splenic arteries
- Both embolized



Post-op....

- Persistent low volume bilious drainage
- PEG on POD 61
- Exchanged to PEG-J for feeding 13 days later
- Tolerating feeds no change in drainage
- POD 81: severe abdominal pain, WBC to the 40's, CT showing cecal pneumatosis

Post-op....

- To the OR emergently
- Upper abdomen still frozen
- No ischemia found
- Clearly septic
- Damage control, open abdomen, bowel edema from resuscitation
- ? Re-feeding cholecystitis, sepsis:
Cholecystostomy

Post-op...

- Small bowel fistula (open abdomen complication)
- Several months: duodenal fistula closed, drains out, on TPN but taking PO
- Abdominal wound contraction
- 10/2012 ready for EC fistula takedown, abdominal wall reconstruction and CCY

Resolution...

- Returned to normal diet, activity
- Off TPN
- Significant DM
- Doing well

Complications...

- Mortality? NO
- Arterial pseudoaneurysm and bleed
- Enteric fistula
 - Duodenal (early)
 - Small bowel (late)
- Abdominal wall reconstruction

A Step-up Approach or Open Necrosectomy for Necrotizing Pancreatitis

N Engl J Med 2010;362: 1491-1502.

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

Current Best Practice for Intervention

Working Group IAP/APA Acute Pancreatitis Guidelines. *Pancreatology*. 2013;13: e1-e15.

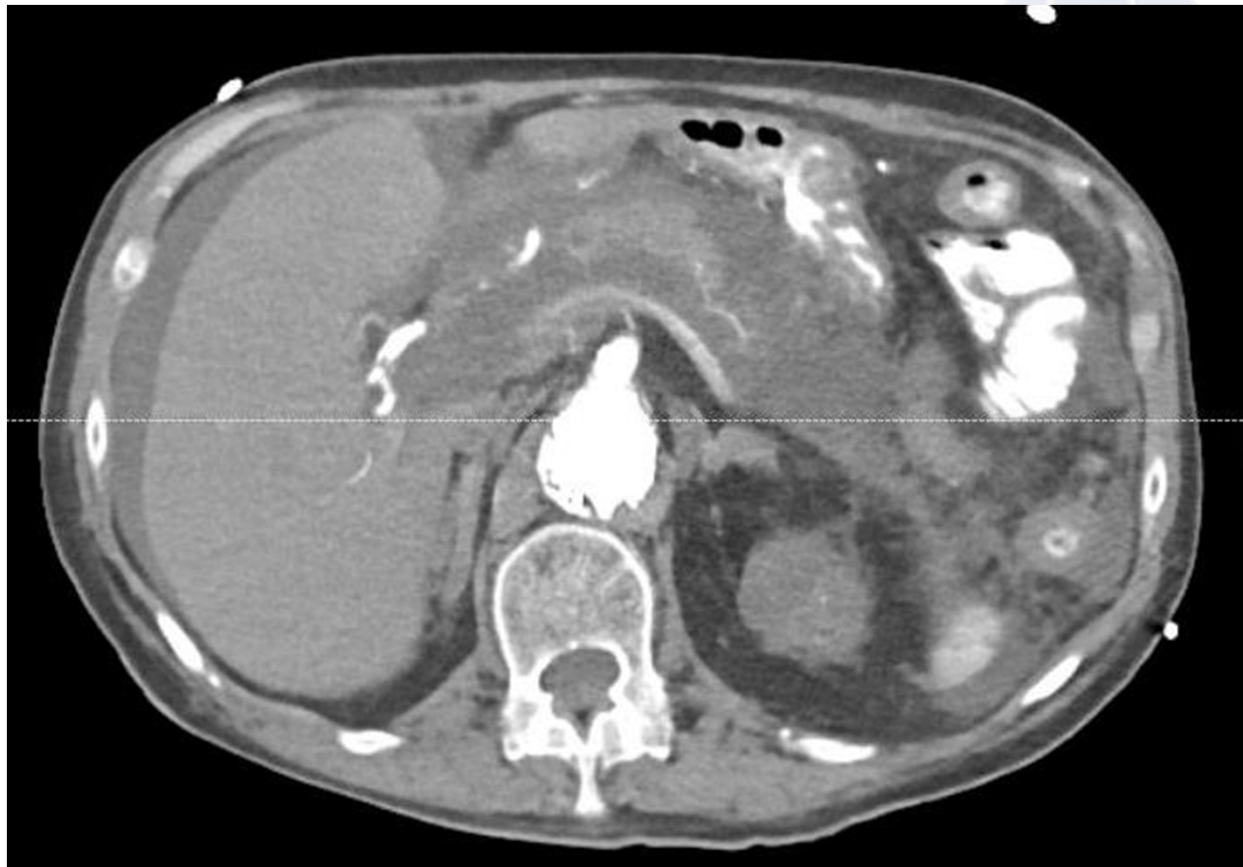
- 1) Percutaneous or endoscopic drainage should be the first step.
- 2) This then is followed by step up to interventional necrosectomy if necessary (endoscopic or surgical).

(LOE Grade 1A, strong agreement)

Drain only

- 66 yo male vasculopath
- CAD, ESRD on peritoneal dialysis
- s/p EVAR
- Complicated by severe pancreatitis
- Early sepsis, MOF

Drain only



Drain only



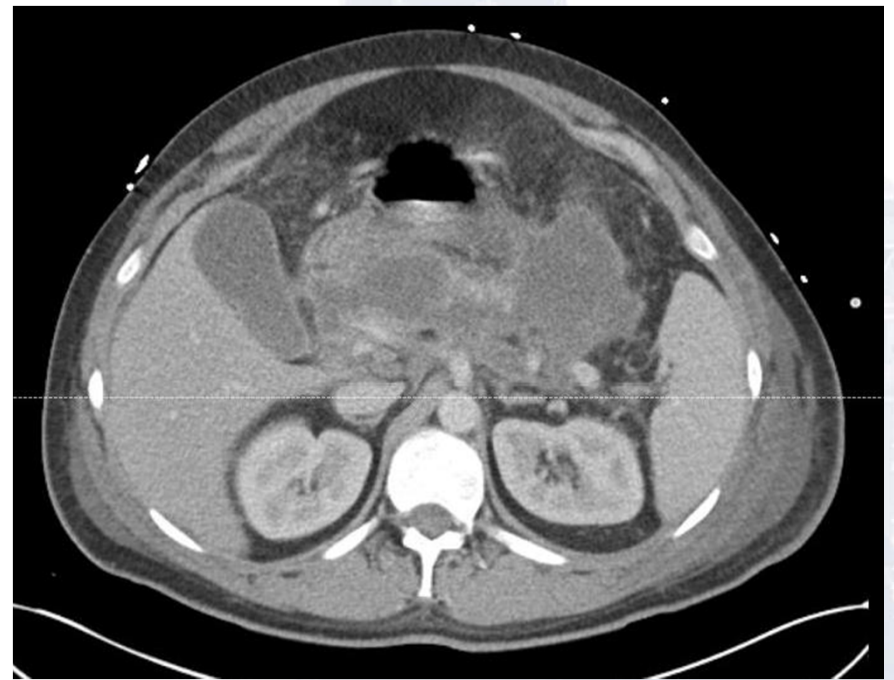
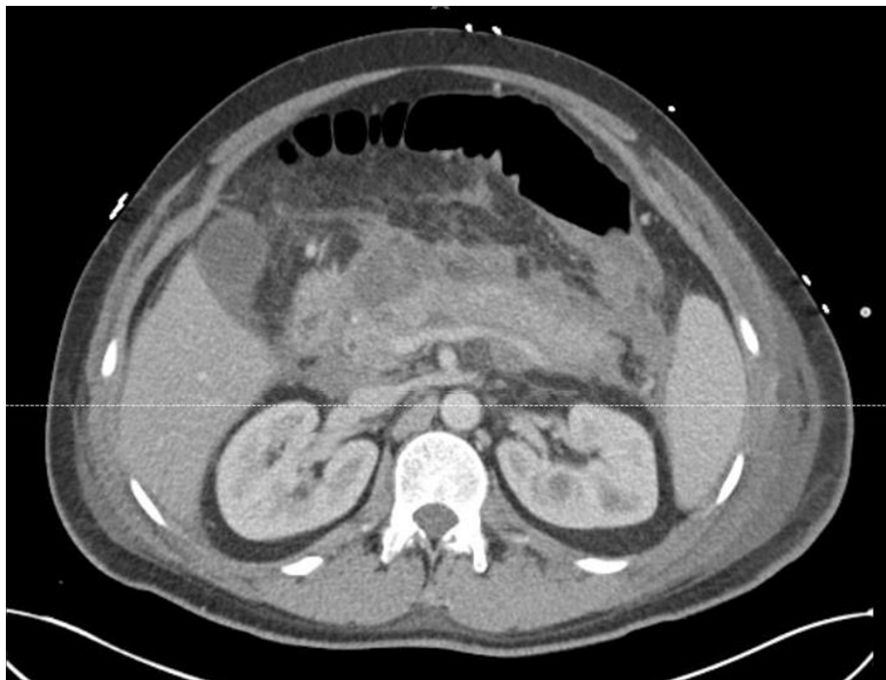
Drain only

- Persistent moderate volume pancreatic rich fluid (200 cc/day) over approximately 8 weeks
- Converted to serous fluid
- Cavity self-sclerosed
- Drain ultimately removed

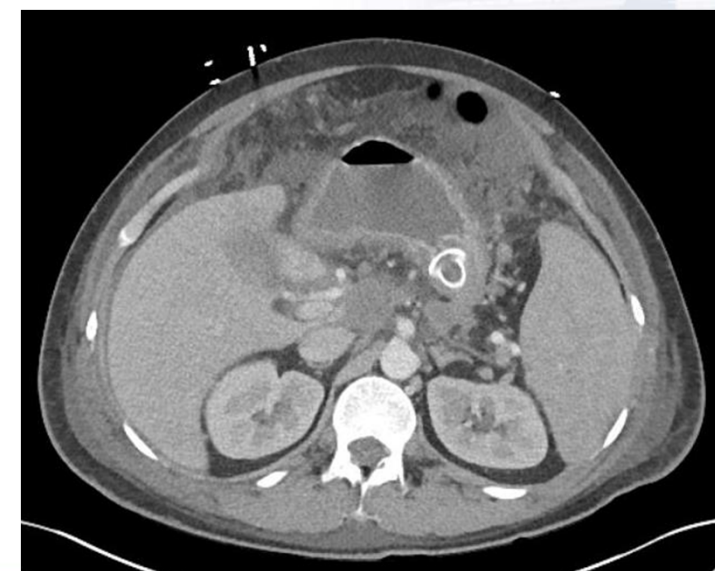
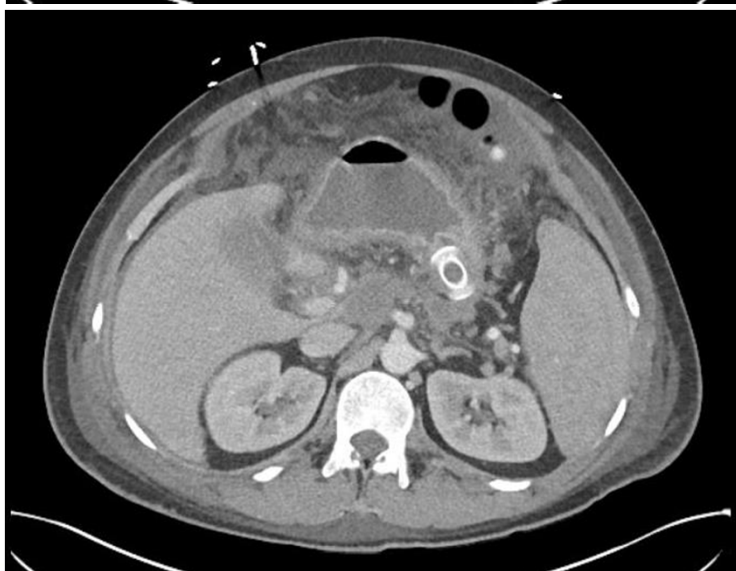
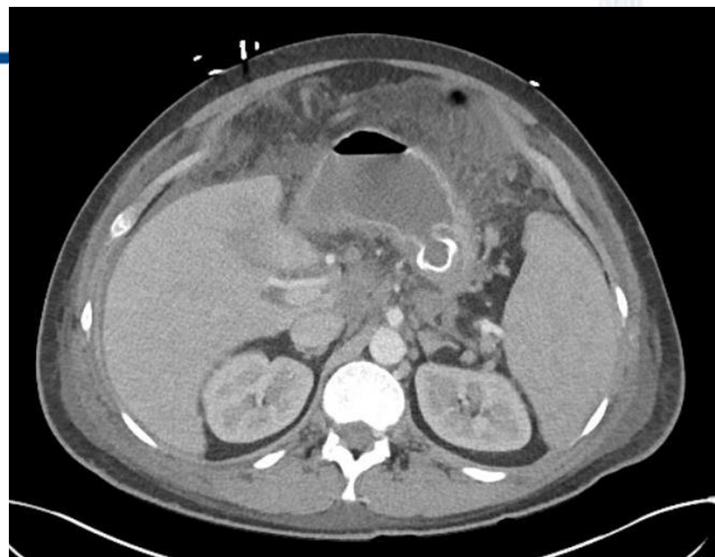
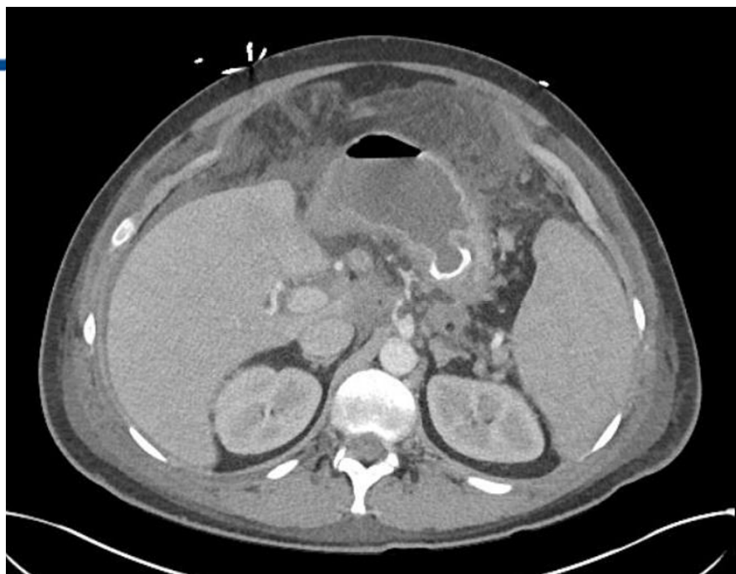
Endoscopic drainage

- 24 yo male with minimal history
- Presents with severe alcohol associated pancreatitis
- Chronically unwell
- Symptoms of poor gastric outlet

Endoscopic drainage



Endoscopic drainage

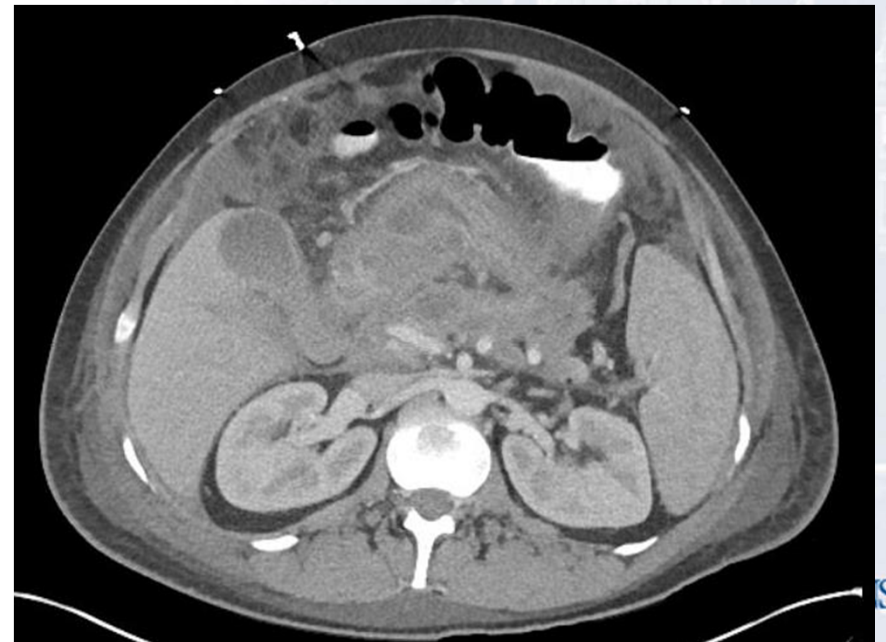


Endoscopic drainage



Pre

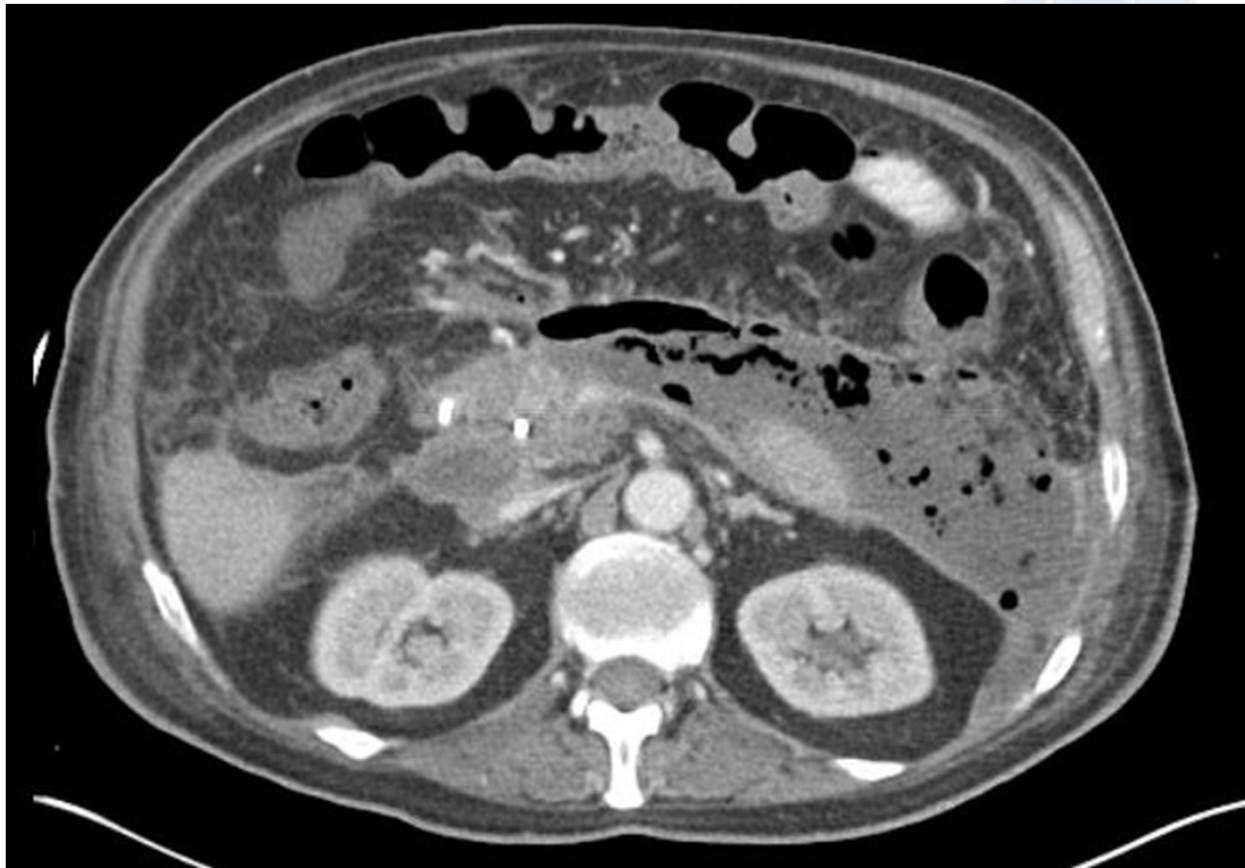
Post



Video Assisted Retroperitoneal Debridement (VARDs)

- 61 yo male
- Hx of prior cholecystectomy
- s/p ERCP with perforation
- Further complicated by severe acute necrotizing pancreatitis.

Video Assisted Retroperitoneal Debridement (VARDs)



Video Assisted Retroperitoneal Debridement (VARDs)



Getting the Dead Out: Modern Treatment Strategies for Necrotizing Pancreatitis

Monica M. Dua • David J. Worhunsky •
Sabina Amin • John D. Louie • Walter G. Park •
George Triadafilopoulos • Brendan C. Visser

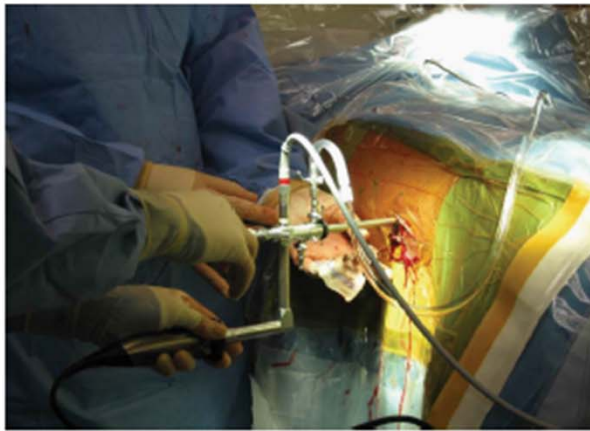


Fig. 6 Intraoperative pancreatic necrosectomy with a nephroscope aiming at creating adequate space within the necrotic cavity

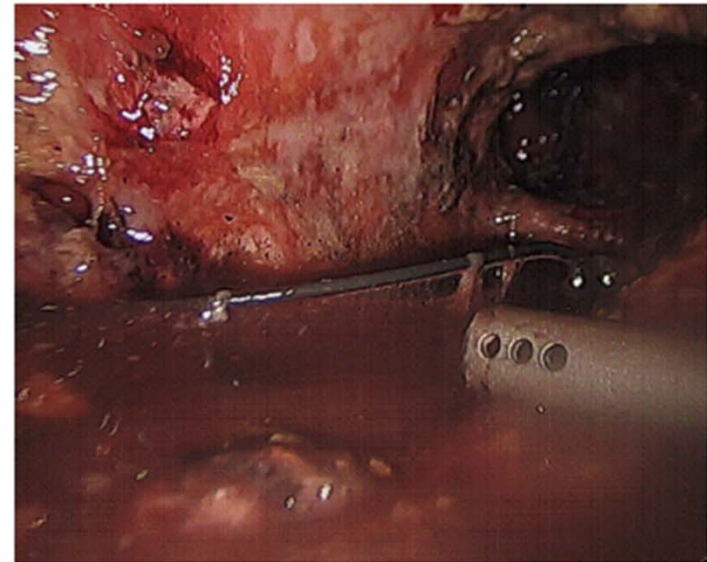


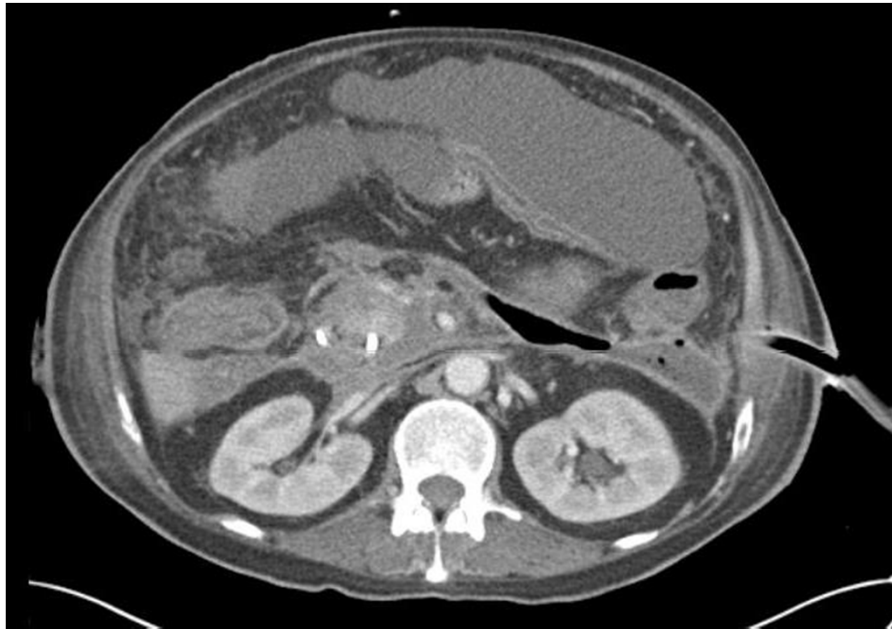
Fig. 7 Intraoperative view of the necrotic cavity during MIRP debridement and lavage. After nephroscopic debridement, the nephroscopic sheaths are exchanged for laparoscopic ports to introduce working instruments for debridement under direct visual guidance

Dig Dis Sci 2014 Apr; [epub]

VARDs: Personal preferences

- Percutaneous drains placed
- Upsize to 20 french
- Cystoscopic set
- Urologic drapes, decubitus or semi-decubitus positions
- Ring clamps, Bowel clamp (“linen-shod”), Aortic cross-clamp (curved)

Video Assisted Retroperitoneal Debridement (VARDs)



Video Assisted Retroperitoneal Debridement (VARDs)

- Persistent pancreatic fistula
- Finally closed at 4 months
- Multiple bouts of sepsis
- Drain out, regular diet

Transluminal endoscopic step-up approach versus minimally invasive surgical step-up approach in patients with infected necrotising pancreatitis (TENSION trial): design and rationale of a randomised controlled multicenter trial [ISRCTN09186711]

Sandra van Brunschot^{1,2*}, Janneke van Grinsven^{1,2}, Rogier P Voermans¹, Olaf J Bakker³, Marc GH Besselink⁴, Marja A Boermeester⁴, Thomas L Bollen⁵, Koop Bosscha⁶, Stefan A Bouwense^{2,7}, Marco J Bruno⁸, Vincent C Cappendijk⁹, Esther C Consten¹⁰, Cornelis H Dejong¹¹, Marcel GW Dijkgraaf¹², Casper H van Eijck¹³, G Willemien Erkelens¹⁴, Harry van Goor⁷, Mohammed Hadithi¹⁵, Jan-Willem Haveman¹⁶, Sijbrand H Hofker¹⁶, Jeroen JM Jansen¹⁷, Johan S Laméris¹⁸, Krijn P van Lienden¹⁸, Eric R Manusama¹⁹, Maarten A Meijssen²⁰, Chris J Mulder²¹, Vincent B Nieuwenhuis²², Jan-Werner Poley⁸, Rogier J de Ridder²³, Camiel Rosman²⁴, Alexander F Schaapherder²⁵, Joris J Scheepers²⁶, Erik J Schoon²⁷, Tom Seerden²⁸, BW Marcel Spanier²⁹, Jan Willem A Straathof³⁰, Robin Timmer³¹, Niels G Venneman³², Frank P Vleggaar³³, Ben J Witteman³⁴, Hein G Gooszen², Hjalmar C van Santvoort³, and Paul Fockens¹ for the Dutch Pancreatitis Study Group

Algorithm

- **Pancreatic necrosis on CT?**
 - **Signs of infection? No**
 - expectant management (with repeat imaging for evolution of clinical picture)
 - **Signs of infection? Yes,**
 - **Is it <4 weeks? Yes**
 - Consider course of abx
 - **Is it <4 weeks? No**
 - Endoscopic or perc drainage with abx

Algorithm

- **Pancreatic necrosis on CT?**
 - **Signs of infection? No**
 - expectant management (with repeat imaging for evolution of clinical picture)
 - **Persistent unwellness, obstruction? Yes**
 - **Is it <8 weeks? Yes**
 - Continue supportive care
 - **Is it <8 weeks? No**
 - Endoscopic or perc drainage with abx

Algorithm

- **Endoscopic or perc drainage**
 - **Resolution of symptoms? Yes**
 - Supportive care (i.e. drain / fistula management)
 - **Resolution of symptoms? No**
 - Consider further endoscopy / drainage or upsize
 - Consider necrosectomy (endo, VARDS, open)

Conclusion

- Principles for management of necrotizing pancreatitis are largely unchanged...
 - Supportive care
 - Sterile versus infected necrosis
 - Debridement and source control
- The approach continues to evolve...
 - Avoidance of massive insult
 - Source control with measured intervention