HHS Public Access
Author manuscript
Ann Surg. Author manuscript; available in PMC 2022 April 29.

Published in final edited form as:
Ann Surg. 2021 September 01; 274(3): 516–523. doi:10.1097/SLA.0000000000004997.

Outcomes in Endoscopic and Operative Transgastric Pancreatic Debridement

Thomas K. Maatman, MD, **Sean P. McGuire, MD**, **Katelyn F. Flick, MD**, **Mackenzie K. Madison, MS**, **Mohammad A. Al-Haddad, MD**, **Benjamin L. Bick, MD**, **Eugene P. Ceppa, MD**, **John M. DeWitt, MD**, **Jeffrey J. Easler, MD**, **Evan L. Fogel, MD**, **Mark A. Gromski, MD**, **Michael G. House, MD**, **Glen A. Lehman, MD**, **Attila Nakeeb, MD**, **C. Max Schmidt, MD**, **Stuart Sherman, MD**, **James L. Watkins, MD**, **Nicholas J. Zyromski, MD**✉
Departments of Surgery and Division of Gastroenterology, Indiana University School of Medicine and Indiana University Health, Indianapolis, IN.

Abstract

Objectives: Select patients with anatomically favorable walled off pancreatic necrosis may be treated by endoscopic (Endo-TGD) or operative (OR-TGD) transgastric debridement (TGD). We compared our experience with these 2 approaches.

Summary Background Data: Select necrotizing pancreatitis (NP) patients are suitable for TGD which may be accomplished endoscopically or surgically. Limited experience exists contrasting these techniques exists.

Methods: Patients undergoing Endo-TGD and OR-TGD at a single, high-volume pancreatic center between 2008 and 2019 were identified from a prospective database. Patient characteristics, procedural details, and outcomes of these 2 groups were compared.

Results: Among 498 NP patients undergoing necrosis intervention, 160 (32%) had TGD: 59 Endo-TGD and 101 OR-TGD. The groups were statistically similar in age, comorbidity, pancreatitis etiology, necrosis anatomy, pancreatitis severity, and timing of TGD from pancreatitis insult. OR-TGD required 1.1 ± 0.5 and Endo-TGD 3.0 ± 2.0 debridements/patient. Fewer hospital readmissions and repeat necrosis interventions, and shorter total inpatient length of stay were observed in OR-TGD patients. New-onset organ failure [Endo-TGD (13%); OR-TGD (13%); $P = 1.0$] was similar between groups. Hospital length of stay after TGD was significantly longer in patients undergoing Endo-TGD (13.8 ± 20.8 days) compared to OR-TGD (9.4 ± 6.1 days; $P = 0.047$). Mortality was 7% in Endo-TGD and 1% in OR-TGD ($P = 0.04$).

Conclusions: Operative and endoscopic transgastric debridement achieve necrosis resolution with different temporal and procedural profiles. Clear multidisciplinary communication is essential to determine appropriate approach to individual necrotizing pancreatitis patients.

✉ nzyromsk@iupui.edu.
T.K.M. and S.P.M. contributed equally to this work and serve as co-first authors.
The authors report no conflicts of interests.

Keywords

endoscopic transgastric debridement; necrotizing pancreatitis; pancreatitis; surgical transgastric debridement; transgastric debridement

Among the 300,000 American patients hospitalized annually with acute pancreatitis, 10% to 15% will develop variable necrosis of the pancreatic parenchyma and peripancreatic soft tissue.[1,2] Necrotizing pancreatitis (NP) represents the most severe manifestation of the disease, with multiple organ dysfunction, extended disease course, and even in contemporary times substantial (15%–20%) mortality.[2] Intervention is indicated in NP patients who develop infection or symptoms such as pain and feeding intolerance.[1,3] Interventional management of NP has evolved dramatically over the past 15 years; since publication of the seminal Dutch PANTER trial, minimally invasive interventions have become standard practice in most major pancreatic centers.[4–6] Minimally invasive therapies include surgical, percutaneous, and transluminal endoscopic approaches.

Transgastric pancreatic necrosectomy was first reported in 1996, and the first surgical reports of transgastric necrosectomy shortly thereafter.[7,8] Transgastric debridement (TGD) was initially implemented solely at high volume experienced pancreas centers, but is presently gaining broader traction, in part due to advances in endoscopic equipment and technique. Natural history studies suggest that 20% to 30% of all NP patients have necrosis isolated to the lesser sac; this necrosis morphology is suitable for transgastric evacuation of pancreatic necrosis, which may be accomplished either by endoscopic techniques or operatively.[9]

Several reports in the literature have compared endoscopic transgastric and surgical “minimally invasive” debridement, including three prospective randomized trials.[10–12] The generally small sample size of highly select patients and other methodologic considerations hamper the ability to definitively compare endoscopic and surgical transgastric techniques; the optimal approach to pancreatic debridement should still remain individualized to the specific patient’s clinical condition. Nevertheless, both endoscopic and surgical transgastric debridement are practiced with increasing frequency, and therefore the goal of this report was to review carefully our large volume institutional experience with transgastric necrosectomy approached endoscopically and surgically. Indiana University is an established pancreatic center treating one of the largest cohorts of NP patients in North America. The IU faculty include both a highly respected advanced endoscopy group as well as an experienced surgical group with longstanding interest in necrotizing pancreatitis treatment. We hypothesized that endoscopic and surgical debridement both would accomplish necrosis evacuation, albeit with different temporal and procedural profiles.

METHODS

Study Population

Between 2008 and 2019, 643 consecutive NP patients were treated at Indiana University Health University Hospital (IU-UH) and catalogued into the institution’s prospective NP database. Informed consent was obtained from all patients; data were stored in a manner

compliant with the Health Insurance Portability and Accountability Act (HIPAA). This database includes patients' age 18 years or older with acute NP from any etiology, regardless of treatment strategy. The Indiana University Institutional Review Board approved the study protocol.

Definitions

Acute pancreatitis was defined as 2 of the following three features: acute onset, severe, epigastric abdominal pain (often radiating to the back); serum amylase or lipase at least 3 times the upper limit of laboratory normal; and characteristic findings of acute pancreatitis on abdominal cross-sectional imaging.[3] Necrotizing pancreatitis was defined as a lack of pancreatic parenchymal enhancement and/or findings of peripancreatic necrosis such as acute necrotic collection (ANC) or walled off necrosis (WON) on contrast-enhanced cross-sectional imaging.[13] Organ failure was defined according to the modified Marshall scoring system for organ dysfunction.[13] Infected necrosis was suspected by the presence of gas within an ANC or WON on cross-sectional imaging and confirmed with cultures of pancreatic necrosis obtained during intervention on pancreatic necrosis.[1] Disconnected pancreatic duct syndrome (DPDS) was diagnosed when pancreatic necrosis involved at least 2 cm of parenchyma leaving a viable upstream (left-sided) pancreatic tail and pancreatography demonstrated extravasation of contrast or total cutoff of the main pancreatic duct.[14,15] A computed tomography severity index (CTSI) was calculated according to the definitions outlined in the 2004 modification of CTSI.[16,17] Disease resolution was defined as clinical and radiographical resolution of necrosis without further necrosis intervention during follow-up.

Intervention Strategy in Necrotizing Pancreatitis

Institutional NP treatment strategy reflected the expert consensus, evidenced-based guidelines for intervention in NP.[1,2] Initial treatment consists of best supportive medical care. Necrosis intervention is avoided when possible and if indicated is delayed at least 4 to 6 weeks after NP onset. Indications for mechanical necrosis intervention include infected necrosis refractory to antibiotic therapy and symptomatic necrosis with persistent unwellness >8 weeks after NP onset. Transgastric debridement is favored in patients with necrosis predominantly isolated to the lesser sac. The decision to perform endoscopic or operative TGD is made in the multidisciplinary setting and considers the individual patient's medical history, NP etiology, and NP clinical course. A flowsheet of patients included in the study and in each group is outlined in Figure 1.

Parameters Assessed

Demographic variables (sex, age), comorbidities, body mass index, and pancreatitis etiology were recorded at the onset of pancreatitis. Clinical parameters recorded throughout the duration of acute NP included: date of pancreatitis onset, CTSI, organ failure, infected necrosis, DPDS, splanchnic vein thrombosis, necrosis intervention, hospital length of stay (LOS), readmission, indication for readmission, NP disease duration, and mortality. Pertinent variables recorded at the time of transgastric debridement included Acute Physiology, Age, and Chronic Health Evaluation II (APACHE II) score, largest dimension of retrogastric WON, the presence of organ failure, and inpatient status. After initial

TGD, outcomes evaluated included hospital LOS, infected necrosis, new-onset organ failure (within 48 hours of procedure), readmission, readmission indication, readmission length of stay, repeat necrosis intervention, total hospital length of stay, disease duration, and mortality. Long-term follow-up evaluated the incidence, presentation of, and intervention for DPDS.

Statistical Analysis

Data were recorded using Microsoft Excel 2007–2015 (Microsoft, Inc., Redmond, WA) and analyzed with IBM SPSS statistics version 25.0 (IBM Corp, Armonk, NY). Descriptive statistics for continuous data included median (with range or interquartile range, IQR), mean (with standard deviation, SD). Categorical data were expressed as numbers and percentages. Independent groups *t* tests were used to compare means of parametric continuous data. Chi-squared test or 1-way analysis of variance on ranks tests were used to compare categorical data. $P < 0.05$ was accepted as statistically significant.

RESULTS

Baseline Demographics

TGD of pancreatic necrosis was performed in 160 patients; endoscopic TGD (Endo-TGD) was performed in 59 patients (37%) and operative TGD (OR-TGD) was performed in 101 patients (63%). Baseline demographic information and comorbidities were similar between groups. Pancreatitis etiology was more commonly from alcohol in the Endo-TGD group and gallstones in the OR-TGD group (Table 1).

Pancreatitis Features

The mean CTSI was similar between Endo-TGD (6.7 ± 2.0) and OR-TGD (7.0 ± 1.7), $P = 0.3$. The degree of pancreatic gland necrosis and location of pancreatic gland necrosis were similar between groups (Figure 2). No significant differences were observed between groups in the clinical course of NP before TGD. Rates of organ failure at any time before TGD were similar between Endo-TGD patients (any, 32%; respiratory, 30%; renal, 19%; cardiovascular, 14%) and OR-TGD patients (any, 25%; respiratory, 23%; renal, 14%; cardiovascular, 5%), $P = 0.3$.

Clinical Status at Transgastric Debridement

At the time of TGD, the 2 groups were similar in clinical features including indication for intervention, presence of DPDS, presence of sinistral portal hypertension, organ failure, and previous percutaneous drainage (Fig. 3). The mean APACHE II score on the day of TGD was similar between Endo-TGD (6.1 ± 3.7) and OR-TGD (6.0 ± 3.1) groups, $P = 0.8$. The mean largest dimension of the ANC/WON was similar between groups (Endo-TGD, 11.8 ± 5.3 cm; OR-TGD, 12.9 ±4.4 cm; $P = 0.14$). No endoscopic or operative TGD was performed in an emergent setting. Transgastric debridement was performed 78.9 ± 14.0 days after NP onset in the Endo-TGD group and 83.1 ± 7.1 (SEM) days after NP onset in the OR-TGD group ($P = 0.8$).

Comparative Outcomes

Outcomes after Endo-TGD and OR-TGD are shown in Table 2. The incidence of new onset organ failure was similar between Endo-TGD (12%) and OR-TGD (13%) groups ($P = 0.9$). Rates of new-onset respiratory, renal, and cardiovascular organ failure were similar between groups. The overall cohort underwent a mean of 2.2 ± 2.3 interventions. The Endo-TGD group required more interventions (3.8 interventions/patient) compared to patients in the OR-TGD group (1.2 interventions/patient). Repeat intervention was performed in 34% of the overall cohort (55 patients). In the Endo-TGD group repeat intervention was performed in 81% of patients and included repeat endoscopic debridement (42 patients, 71% of Endo-TGD), operative debridement (14 patients, 24%), and percutaneous drainage (10 patients, 17%). Repeat intervention was performed in 7% of the OR-TGD group and included endoscopic debridement (2 patients, 2% of OR-TGD), repeat operative debridement (2 patients, 2%), and percutaneous drainage (3 patients, 3%). These differences in the number of interventions, repeat intervention, and types of repeat intervention were statistically significant. Three patients undergoing endoscopic TGD required emergent operation for gastric perforation with peritonitis (2 patients) and hemorrhagic shock (1 patient); no OR-TGD patient had emergent reoperation. In the OR-TGD group, 2 (2%) patients developed incisional surgical site infection and two (2%) patients developed grade B postoperative pancreatic fistula.

In the entire cohort, postoperative LOS following initial TGD was 11.0 ± 13.7 days. Postoperative LOS was longer in the Endo-TGD group (13.8 ± 20.8 days) compared to the OR-TGD group (9.4 ± 6.1 days) ($P = 0.047$). Overall readmission rates were higher in the Endo-TGD group (67%) compared to the OR-TGD group (20%), ($P < 0.001$). Four patients in the Endo-TGD group were readmitted for planned repeat endoscopic debridement; the remaining 33 patients were unplanned readmission. All readmissions (20 patients) in the OR-TGD group were unplanned. The mean total number of inpatient hospital days following debridement was longer in the Endo-TGD group (22.7 ± 24.8 days) compared to the OR-TGD group (11.9 ± 10.7 days) ($P < 0.001$).

Rates of infected necrosis were similar between groups: 36/59 (61%) in the Endo-TGD group and 58/101 (57%) in the OR-TGD group ($P = 0.7$). In the overall cohort, 117 patients underwent TGD with presumed sterile necrosis; among these patients, 51 (44%) patients were diagnosed with infected necrosis based on cultures obtained at the time of TGD. Rates of occult-infected necrosis were similar in the Endo-TGD group (44%, 18/41 patients) and OR-TGD group (43%, 33/76 patients).

Follow-up of the overall cohort was a median of 17 months (interquartile range, 8–56 months). No difference in NP disease duration was observed between patients undergoing endoscopic TGD (6.2 ± 4.0 months) and patients undergoing operative TGD (5.4 ± 3.6 months), $P = 0.2$.

During long-term follow-up of 88 patients with DPDS, 16 patients (18%) underwent late operation to address symptoms of DPDS at a median of 11 months (range, 3–80 months) after TGD. The most common presentation of DPDS was recurrent pancreatitis (n = 10) and recurrent pseudocyst (n = 6). More patients with DPDS undergoing endoscopic TGD

(8/26, 31%) underwent late operation when compared to operative TGD (8/62, 15%), $P = 0.047$. Fourteen patients underwent distal pancreatectomy and 2 patients underwent internal drainage of the disconnected pancreatic tail via pancreaticojejunostomy.

Mortality before disease resolution was 7% in the Endo-TGD group and 1% in the OR-TGD ($P = 0.04$).

DISCUSSION

This large contemporary series of necrotizing pancreatitis patients undergoing endoscopic and operative TGD highlights clinical outcomes achieved at a high-volume pancreatic center with experienced surgical and advanced endoscopy teams and a longstanding interest in treating this difficult disease. Patients in both endoscopic and operative groups had similar comorbid medical profiles, pancreatic parenchymal involvement, and pancreatitis severity. Not surprisingly, the endoscopic approach required more discrete sessions to achieve complete necrosis evacuation, with associated longer overall hospital times. A higher incidence of unplanned readmission in the endoscopic group contributed to the increased overall hospital length of stay as well. Patients approached initially with operative transgastric debridement more often achieved durable and complete debridement in 1 setting. However, some operatively treated patients underwent subsequent endoscopic and percutaneous treatment, and some patients treated initially by endoscopy had subsequent operative and/or percutaneous intervention highlighting the importance of multidisciplinary collaboration to effectively treat this challenging disease.

Three prospective randomized trials (PRTs) have compared endoscopic transgastric pancreatic debridement to “minimally invasive surgery” approaches.[10–12] It is worth noting that none of these trials evaluated exclusively surgical endoscopic debridement; many or most patients in the surgical arms of all three trials had videoscopic assisted retroperitoneal debridement (VARD). This point is relevant as all three prospective trials were designed with composite endpoints that included major morbidity, mortality, and also importantly enterocutaneous fistula/ pancreatic fistula (which does not occur with pure transgastric approach, either endoscopic or surgical). The first published PRT—the Penguin trial—is a small (n = 20), well-designed trial from 4 Dutch hospitals published in JAMA in 2012.[10] The trial showed that endoscopic transgastric necrosectomy reduced systemic inflammatory response as measured by interleukin-6 and decreased the composite endpoint predominantly because of decreased enterocutaneous fistula in the endoscopic group. The MISER trial from a single center in Florida randomized 66 patients to total endoscopic versus minimally invasive surgical treatment (14/32 patients in the surgical arm underwent VARD or percutaneous drainage).[11] Major morbidity, new-onset organ failure, and mortality were similar between groups, but the composite endpoint in this trial favored endoscopy because of decreased enterocutaneous fistula/pancreatic fistula. The largest PRT comparing endoscopic and minimally invasive surgical debridement was designed as a superiority trial and conducted in 19 Dutch hospitals.[12] This trial randomized 98 of 418 screened patients to either endoscopy or surgical step-up approaches. The endoscopic approach was not found to be superior in reducing the incidence of major complications or death; however, the rate of pancreatic fistula and length of hospital stay were lower in the endoscopy group.

The endoscopic approach to pancreatic transgastric debridement dates back to the initial report from the Mayo Clinic in 1996.[7] Advances in endoluminal therapeutic equipment and techniques—particularly the introduction of lumen apposing metal stents—have facilitated the endoscopic approach; however, endoscopic debridement largely remains confined to tertiary centers with experienced advanced endoscopists.[18] Bleeding must be considered especially in the common situation of splenic vein thrombosis with left sided portal hypertension.[19] As observed in this report, the risk of hollow viscus perforation may be increased in the setting of aberrant anatomy with disorienting necrosis and fluid collections. A major limitation of the endoscopic approach is the relatively small size of both cyst enterostomy as well as grasping/debriding instruments that must fit through the endoscope's working channels. Multiple sessions are required even in the most experienced hands to achieve complete necrosis resolution.[6,11] A major advantage of endoscopic therapy, obviously, is avoiding laparotomy and the potential for hernia in the long term; this advantage must be balanced with the need for general anesthetic required for most, if not all of the multiple endoscopic procedures required to achieve necrosis resolution. Outstanding overall outcomes achieved in centers with dedicated physician investment such as the Minnesota advanced endoscopy group highlight the critical importance of mature judgement and close follow up by the treating team during the active phase of NP.[20,21]

Our group's introduction to the concept of surgical transgastric debridement came from the Freiberg group, who used a combination of endoscopy and laparoscopy for debridement.[22] Surgical groups in Glasgow and Calgary were also early proponents of operative transgastric debridement, demonstrating effective necrosis clearance in a subset of appropriately selected patients.[23,24] One clear advantage of the surgical approach to transgastric necrosectomy is the ability to create a large cystogastrostomy permitting single session debridement of all solid necrosis. It is possible that this larger cystogastrostomy promotes more durable drainage in the long term; however, it is clear that long term follow-up is needed in all patients treated with the transgastric approach as 20% to 25% will develop recurrent retroperitoneal pseudocyst and/or left sided pancreatitis.[25] Surgical transgastric necrosectomy is the preferred approach for patients with biliary necrotizing pancreatitis and appropriate necrosis anatomy, as cholecystectomy with intraoperative cholangiogram is accomplished at the same single session as complete debridement. Early experience has shown the importance of necrosis anatomy in selecting patients appropriate for the transgastric approach. Necrosis confined to the lesser sac, either with or without disconnected pancreatic duct is attractive, while necrosis extending down the paracolic gutters and/or the small bowel mesentery root is less than ideal anatomic morphology—the dependent portions of this cavity are at high risk for reaccumulating fluid, abscess, and recurrent necrosis over time.

Hospital readmission is common in NP patients and has been a focus of prior investigation by our group.[26,27] A review of 601 NP patients treated in our hospital between 2005 and 2017 identified 72% incidence of unplanned readmission,[26] significantly higher than the 19% to 34% unplanned readmission rate published in pancreatitis patients with less severe disease.[28,29] Addition of a dedicated pancreatitis nurse coordinator into our practice significantly improved outpatient communication, coordination of care, and decreased the number of unplanned readmissions in NP patients.[27] Our nurse coordinator functions

as a central communication point both for the patient and among different treating physician teams, and proactively identified and treated predictable disease complications such as symptomatic necrosis, failure to thrive, infectious processes (including non-necrosis infections), and drain/feeding tube dysfunction. This study's finding of different unplanned readmission rates between endoscopically treated and surgically treated groups deserves further in-depth analysis. It is quite possible that disciplinary practice patterns influence this finding; in addition, our RN coordinator was initially brought in by the surgical group, and more recently has expanded her duty to include covering NP patients managed primarily by hospitalist, endoscopy, and pulmonary critical care teams. It is clear that no matter the primary modality of treatment utilized in NP (ie, surgical, endoscopic, percutaneous) ideal outcomes are achieved when 1 physician takes ownership for the duration of the patient's illness, including communication among different treating teams.

Our present institutional approach highlights the importance of clear communication among treating physicians including gastroenterology, surgery, interventional radiology, hospitalists, and pulmonary/critical care physicians. Multidisciplinary discussion informs choice and timing of therapeutic interventions. A single treating physician (or often co-management by a surgeon and endoscopist) is identified to follow the course is that patient's disease. Necrosis morphology factors heavily into the choice of initial interventional approach. The presence of disconnected pancreatic duct syndrome is often diagnosed or at least suspected pre-intervention. Experience has shown that early intervention is hazardous and at the least limits technical ability to achieve complete debridement.[30] Thus, intervention is delayed until at least 4 weeks and ideally longer if possible. Early infection should be treated as needed including systemic antibiotic administration, percutaneous drainage, and occasionally early transgastric drainage. In the present experience, most patients were presumed to have sterile necrosis as they came to elective transgastric debridement. However, nearly half of these patients were diagnosed with occult infection, highlighting the importance of a high degree of suspicion and the need to obtain intraoperative cultures at the time of procedure. It is also important to note that percutaneous drainage does not preclude subsequent transgastric intervention by either endoscopic or surgical approaches. Once intervention has been initiated, expedient progression toward complete evacuation of solid necrosis is critical as infected necrosis is highly catabolic to the patient's physiology. During this active phase of treatment, close follow-up by dedicated physician teams is crucial as patient physiology and necrosis morphology are dynamic. Though not the specific focus of the present study, long-term follow-up is important as a significant percentage of these patients will have subsequent difficulty due to the disease process.[25,31]

The retrospective nature of this review limits our ability to comment with specificity on clinical decision making, especially during the active treatment phase of these complex patients. This limitation becomes clear particularly in trying to better understand mortality. Over the decade of review, endoscopic equipment and techniques advanced rapidly, and the learning curve (arguably more challenging in the endoscopic arena) was considerable. Cost analysis is critically important; however, it requires in-depth evaluation and was not a specific focus of this analysis. It is clear that long-term follow up of all NP patients is important, as long-term disease complications are remarkably frequent.[31] As time passes and data from transgastric approach mature, long-term follow up of this cohort will

likewise provide important future information. Critically important future work will focus on identifying objective metrics of time of intervention and time to step up once intervention is initiated.[32] The largest deficit presently in acute pancreatitis is complete lack of therapy for this disease.

This large series provides a contemporary benchmark view of endoscopic and operative transgastric pancreatic debridement outcomes from a high-volume pancreatic center with experienced advanced endoscopists and pancreatic surgeons. Endoscopic and surgical approaches both effectively achieved transgastric pancreatic debridement, although both have discrete intervention and outcome profiles. Surgical transgastric debridement should be the first choice for patients with biliary necrotizing pancreatitis and suitable anatomy.

REFERENCES

1. Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology. 2013;13:e1–e15. [PubMed: 24054878]
2. Baron TH, DiMaio CJ, Wang AY, et al. American Gastroenterological Association Clinical Practice Update: management of pancreatic necrosis. Gastroenterology. 2020;158. 67–75.e1. [PubMed: 31479658]
3. Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62:102–111. [PubMed: 23100216]
4. van Santvoort HC, Besselink MG, Bakker OJ, et al. A step-up approach or open necrosectomy for necrotizing pancreatitis. N Engl J Med. 2010;362:1491–1502. [PubMed: 20410514]
5. Horvath K, Freeny P, Escallon J, et al. Safety and efficacy of video-assisted retroperitoneal debridement for infected pancreatic collections: a multicenter, prospective, single-arm phase 2 study. Arch Surg. 2010;145:817–825. [PubMed: 20855750]
6. Gardner TB, Chahal P, Papaehristou GI, et al. A comparison of direct endoscopic necrosectomy with transmural endoscopic drainage for the treatment of walled-off pancreatic necrosis. Gastrointest Endosc. 2009;69:1085–1094. [PubMed: 19243764]
7. Baron TH, Thaggard WG, Morgan DE, et al. Endoscopic therapy for organized pancreatic necrosis. Gastroenterology. 1996;111:755–764. [PubMed: 8780582]
8. Ammori BJ. Laparoscopic transgastric pancreatic necrosectomy for infected pancreatic necrosis. Surg Endosc. 2002;16:1362.
9. Maatman TK, Roch AM, Lewellen KA, et al. Disconnected pancreatic duct syndrome: spectrum of operative management. J Surg Res. 2020;247:297–303. [PubMed: 31685250]
10. Bakker OJ, van Santvoort HC, van Brunschot S, et al. Endoscopic transgastric vs surgical necrosectomy for infected necrotizing pancreatitis: a randomized trial. JAMA. 2012;307:1053–1061. [PubMed: 22416101]
11. Bang JY, Arnoletti JP, Holt BA, et al. An endoscopic transluminal approach, compared with minimally invasive surgery, reduces complications and costs for patients with necrotizing pancreatitis. Gastroenterology. 2019;156. 1027–40.e3. [PubMed: 30452918]
12. van Brunschot S, van Grinsven J, van Santvoort HC, et al. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial. Lancet. 2018;391:51–58. [PubMed: 29108721]
13. Marshall JC, Cook DJ, Christou NV, et al. Multiple organ dysfunction score: a reliable descriptor of a complex clinical outcome. Crit Care Med. 1995;23:1638–1652. [PubMed: 7587228]
14. Kozarek RA, Traverso LW. Pancreatic fistulas: etiology, consequences, and treatment. Gastroenterologist. 1996;4:238–244. [PubMed: 8957097]
15. Sandrasegaran K, Tann M, Jennings SG, et al. Disconnection of the pancreatic duct: an important but overlooked complication of severe acute pancreatitis. Radiographics. 2007;27:1389–1400. [PubMed: 17848698]

16. Balthazar EJ, Robinson DL, Megibow AJ, et al. Acute pancreatitis: value of CT in establishing prognosis. Radiology. 1990;174:331–336. [PubMed: 2296641]
17. Mortele KJ, Wiesner W, Intriere L, et al. A modified CT severity index for evaluating acute pancreatitis: improved correlation with patient outcome. AJR Am J Roentgenol. 2004;183:1261–1265. [PubMed: 15505289]
18. DeWitt JM, Arain M, Chang KJ, et al. Interventional endoscopic ultrasound: current status and future directions. Clin Gastroenterol Hepatol. 2021;19:24–40. [PubMed: 32950747]
19. Butler JR, Eckert GJ, Zyromski NJ, et al. Natural history of pancreatitis-induced splenic vein thrombosis: a systematic review and meta-analysis of its incidence and rate of gastrointestinal bleeding. HPB (Oxford). 2011;13:839–845. [PubMed: 22081918]
20. Freeman ML, Werner J, van Santvoort HC, et al. Interventions for necrotizing pancreatitis: summary of a multidisciplinary consensus conference. Pancreas. 2012;41:1176–1194. [PubMed: 23086243]
21. Trikudanathan G, Tawfik P, Amateau SK, et al. Early (<4 weeks) versus standard (≥4 weeks) endoscopically centered step-up interventions for necrotizing pancreatitis. Am J Gastroenterol. 2018;113:1550–1558. [PubMed: 30279466]
22. Fischer A, Schrag HJ, Keck T, et al. Debridement and drainage of walled-off pancreatic necrosis by a novel laparoendoscopic rendezvous maneuver: experience with 6 cases. Gastrointest Endosc. 2008;67:871–878. [PubMed: 18367186]
23. Munene G, Dixon E, Sutherland F. Open transgastric debridement and internal drainage of symptomatic non-infected walled-off pancreatic necrosis. HPB (Oxford). 2011;13:234–239. [PubMed: 21418128]
24. Gibson SC, Robertson BF, Dickson EJ, et al. 'Step-port' laparoscopic cystgastrostomy for the management of organized solid predominant post-acute fluid collections after severe acute pancreatitis. HPB (Oxford). 2014;16:170–176. [PubMed: 23551864]
25. Driedger M, Zyromski NJ, Visser BC, et al. Surgical transgastric necrosectomy for necrotizing pancreatitis: a single-stage procedure for walled-off pancreatic necrosis. Ann Surg. 2020;271:163–168. [PubMed: 30216220]
26. Maatman TK, Mahajan S, Roch AM, et al. High rates of readmission in necrotizing pancreatitis: natural history or opportunity for improvement? J Gastrointest Surg. 2019;23:1834–1839. [PubMed: 30706374]
27. Maatman TK, McGreevy KA, Sood AJ, et al. Improved outpatient communication decreases unplanned readmission in necrotizing pancreatitis. J Surg Res. 2020;253:139–146. [PubMed: 32353639]
28. Vipperla K, Papachristou GI, Easler J, et al. Risk of and factors associated with readmission after a sentinel attack of acute pancreatitis. Clin Gastroenterol Hepatol. 2014;12:1911–1919. [PubMed: 24815327]
29. Whitlock TL, Repas K, Tignor A, et al. Early readmission in acute pancreatitis: incidence and risk factors. Am J Gastroenterol. 2010;105:2492–2497. [PubMed: 20531398]
30. Mier J, León EL, Castillo A, et al. Early versus late necrosectomy in severe necrotizing pancreatitis. Am J Surg. 1997;173:71–75. [PubMed: 9074366]
31. Maatman TK, Roch AM, Ceppa EP, et al. The continuum of complications in survivors of necrotizing pancreatitis. Surgery. 2020;168:1032–1040. [PubMed: 32843212]
32. Yee EJ, Maatman TK, Sood AJ, et al. Dynamic frailty: objective physiological assessment to guide management in necrotizing pancreatitis. Surgery. 2020;169: 1078–1085. [PubMed: 33339652]

DISCUSSANT

Dr. Elijah Dixon

My name is Elijah Dixon, I am from the University of Calgary.

It is my honor and privilege to be the discussant on this outstanding study and presentation by Professor Nic Zyromski, I want to thank the ASA for the invitation. I would like to thank Professor Zyromski for sending me a copy of the manuscript in advance.

We have made huge improvements in the care of patients with necrotizing pancreatitis in the past 20–25 years; we have gone from a disease with a mortality approximating 50% with survivors being subjected to multiple laparotomies and often ending up with huge ventral hernias (not infrequently with skin grafts on the luminal gastrointestinal tract). Now most patients survive and often with just one definitive intervention. Centers like Indiana University and Professor Zyromski's group have led the charge in improving outcomes in this difficult disease (along with improvements in critical care).

I have four questions for Nic.

1. Can you tell me how you get these patients out to the ideal 4–6 week mark before performing a definitive intervention? We often struggle with this, as the intensive care unit is often pushing for earlier intervention in these patients who are often VERY ill for weeks before the 4 week mark is reached.
2. Can you tell us more about your interventional gastroenterology colleagues that perform the endoscopic debridement? This is a rare skill set and it is very difficult to get a lot of experience in these procedures (high volume centers would see 1–3 patients with necrotizing pancreatitis a month, and many go to surgery as opposed to endoscopic intervention). How many people are in this group? Do they do the procedures together?
3. Your data shows that operative transgastric debridement has lower mortality rates, lower length of stay, and lower rates of reintervention/reoperation. Despite these better outcomes a significant percentage of your patients under endoscopic debridement first. Can you comment on the multidisciplinary team that makes these decisions? What factors go into the decision of operative versus endoscopic debridement? Specifically, can you discuss what role BMI and obesity have in the decision making process. In addition, please discuss the anatomy of the necrosum (single central necrosum versus more complex central with extension in the retroperitoneum down the paracolic gutters on both sides) and the effect this has on the approach taken. Please comment on any other important factors that are taken into consideration when deciding the timing and interventional approach.
4. Can you comment on where we go from here in terms of treating this disease? Prevention? Other improvements to the care of these patients.

Again, thank you for the opportunity to discuss this paper Professor Zyromski, very nice job by a truly expert center.

Response Dr. Nicholas J. Zyromski

Thank you Dr.Dixon for these insightful questions. Dr. Dixon's Calgary group embraced the transgastric approach early, publishing their institutional experience in HPB in 2011, and combining their experience with our IU experience and Brendan Visser's Stanford group for a 2020 Annals multi-institutional experience.

1. Regarding timing of intervention – we know from hard experience that early necrosectomy is not only significantly more morbid, but also leads to incomplete evacuation of immature necrosis. In the less common case of early infection with clinical deterioration through antibiotic therapy, percutaneous drainage or in very select cases early transgastric debridement is appropriate. Mature clinical judgement from experienced clinicians is important and highlights the need for a single patient advocate (whether surgeon, gastroenterologist or other). We definitely focus on communication and education with our medical colleagues regarding the timing and approach of mechanical intervention, need to progress expediently once intervention has been initiated, and timing of "step-up."

2. I am extremely fortunate to have worked for many years with a world class group of interventional endoscopists at IU. Among this group of 10 physicians, 6 have done endoscopic TGD, and I would qualify 4 as relatively enthusiastic about this patient population. Importantly, we all (surgeons and endoscopists) work in the same hospital area, which greatly facilitates communication. I will note that surgeons historically have managed NP at IU; our endoscopy group got a relatively later start with TGD – which is reflected in the data we present today.

3. Three very important points are raised in this question: first, communication is really paramount among all the treating physicians who need to be involved in the care of every NP patient. Biliary NP patients should generally be approached with surgery, as cholecystectomy can be performed at the same setting as debridement – this is a major take-home message from the current analysis. However, sometimes a biliary NP patient will come to us having already undergone cholecystectomy early in the disease course, before maturation of their necrosis. In these cases, endoscopic TGD may be the best choice. Similarly, patients with non-biliary NP etiology such as alcohol, HTG, or PEP and suitable anatomy may be best approached with endoscopic TGD as opposed to surgery. Your point about necrosis morphology in my opinion is also one of the most important considerations in determining treatment strategy. This group as in all reports of technical approach (including the PRT – PANTER, MISER, the Dutch Lancet study) is a highly select group. Perhaps 25% of all NP patients have necrosis morphology suitable for TG approach. Necrosis tracking down the paracolic gutters or small bowel mesenteric root creates cavities that are dependent

and hard to drain effectively with a pure transgastric approach. In these situations, combination therapy with endoscopy and percutaneous approaches as advocated by the Virginia Mason endoscopy group may be most effective. In some patients with multi-field necrosis, an “old fashioned” open operative debridement will be most effective at expediently clearing all the necrosis. Again, this point reiterates the crucial importance of clear communication among treating physician groups, and the need for a single physician to take ownership of a patient over the 5–6 month period of active disease. Finally, you asked about influence of obesity on pancreatitis. Work from our group and others has shown that obesity is associated with a higher incidence of AP in the general population, as well as more severe disease. One of our excellent IU GNS residents and co-first author of this ASA paper Sean McGuire will be presenting data next month at the SSAT meeting showing that NP patients with BMI > 30 have increased organ failure and disease duration compared to those with BMI < 30. Mortality in this cohort of 536 NP patients (57% of whom had BMI > 30) increased with increasing BMI; the inflection point was seen at BMI of 30-

4. Your final question relates to future direction. NP is a complex and extremely heterogeneous disease – one size treatment does not fit every patient, and in fact, many patients will benefit from multiple approaches (i.e. percutaneous, endoscopic, surgical). I feel strongly that we need to get beyond an “us versus them” mentality – i.e. surgery versus GI; endoscopic versus percutaneous, etc. and focus on important questions such as identifying more objective metrics with which to determine the most appropriate technique and timing of intervention, as well as time to “step-up” during the active, dynamic disease phase. You mention prevention, which is indeed a very challenging idea. Perhaps most importantly, we have no specific disease therapy for this very common inflammatory disease that affects 300,000 Americans each year – currant therapy is purely supportive and directed towards disease complications. We and others are working actively on approaches to treating the disease process of AP once it has started – that is to say abrogating the inflammatory response and promoting tissue repair and renewal.

Thank you again for these astute questions.

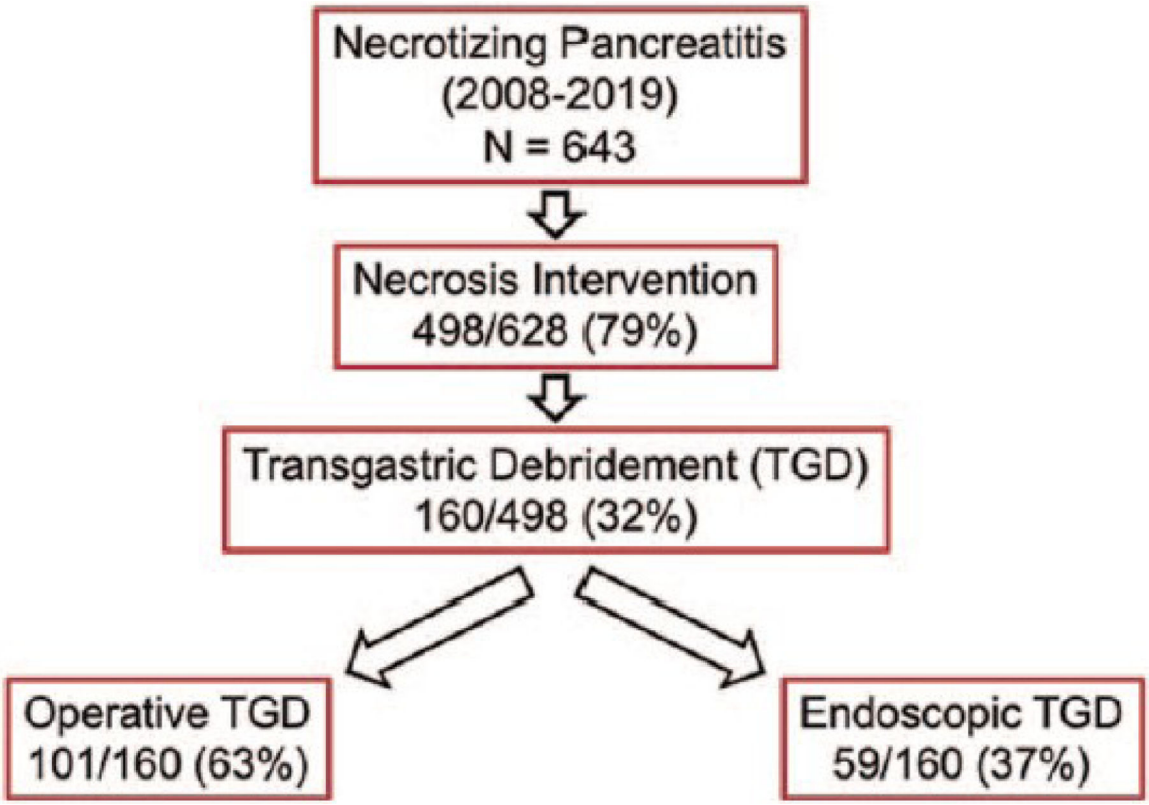

FIGURE 1.
Flow sheet of study patients.

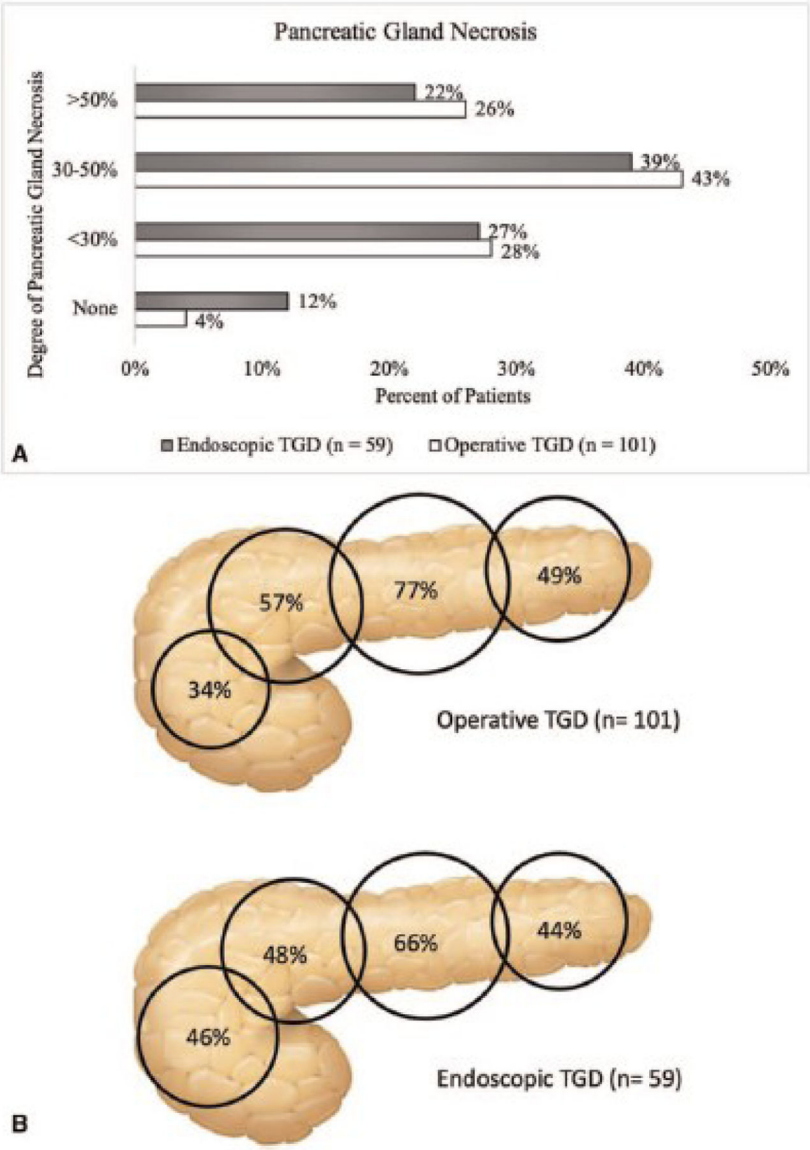

FIGURE 2.

Degree (A) and distribution (B) of pancreatic gland necrosis in necrotizing pancreatitis patients undergoing endoscopic and operative transgastric debridement. No difference was observed between groups (*P* = NS). Note: Cumulative percentage in Figure 1B is greater than 100% due to overlapping necrosis fields.

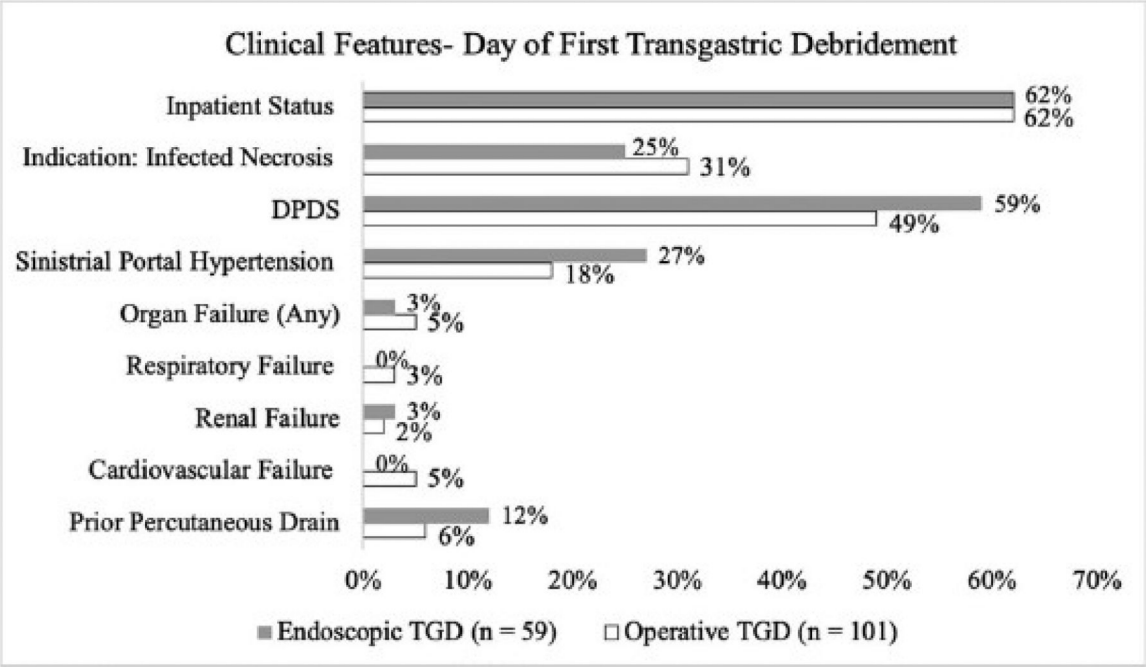

FIGURE 3.

Clinical features on the day of transgastric debridement in necrotizing pancreatitis patients undergoing endoscopic and operative transgastric debridement.

TABLE 1.

Baseline Demographics in Patients Undergoing Operative and Endoscopic Transgastric Debridement

Demographics	Endoscopic TGD (n = 59) n (%)	Operative TGD (n = 101) n (%)	*P*
Age, y*	50.2 (16.3)	55.0 (14.1)	0.051
Etiology of pancreatitis			
Biliary	23 (39%)	62 (61%)	0.006
Alcohol	18 (31%)	14 (14%)	0.01
Post-ERCP	3 (5%)	4 (4%)	0.9
Hypertriglyceridemia	4 (7%)	2 (2%)	0.1
Idiopathic/other	11 (19%)	19 (19%)	0.98
Male	42 (71%)	64 (63%)	0.3
Hypertension	38 (64%)	65 (64%)	0.995
Obesity (BMI >30)	29 (49%)	43 (43%)	0.4
Tobacco use	24 (41%)	37 (37%)	0.6
Hyperlipidemia	19 (32%)	32 (32%)	0.9
Diabetes mellitus	14 (24%)	22 (22%)	0.8
Coronary artery disease	2 (3%)	13 (13%)	0.047
Chronic obstructive pulmonary disease	5 (9%)	10 (10%)	0.8
Atrial fibrillation	1 (2%)	7 (7%)	0.1
Congestive heart failure	0 (0%)	7 (7%)	0.04
Cerebrovascular accident	1 (2%)	5 (5%)	0.3

*Mean value (with, standard deviation).

BMI indicates index body mass index; ERCP, endoscopic retrograde cholangiopancreatography.

TABLE 2.

Outcomes in Necrotizing Pancreatitis Patients Undergoing Operative and Endoscopic Transgastric Debridement

Outcomes	Endoscopic TGD (n = 59) n (%)	Operative TGD (n = 101) n (%)	*P*
New-onset organ failure	7 (12%)	13 (13%)	0.9
New-onset respiratory failure	4 (7%)	5 (5%)	0.6
New-onset renal failure	1 (2%)	0 (0%)	0.2
New-onset cardiovascular failure	1 (2%)	1 (1%)	0.7
Necrosis interventions/patient*	3.8 (2.9)	1.2 (0.8)	<0.00001
Subsequent necrosis intervention			
Endoscopic debridement	42 (71%)	2 (2%)	<0.00001
Operative debridement	14 (24%)	2 (2%)	<0.00001
Percutaneous drain	10 (17%)	3 (3%)	0.002
Length of stay after TGD, days*	13.8 (20.8)	9.4 (6.1)	0.047
Unplanned readmission	33 (56%)	20 (20%)	<0.00001
Total inpatient LOS, days*	23.7 (25.1)	11.9 (10.7)	<0.00001
Infected necrosis	36 (61%)	58 (57%)	0.7
Disease duration, mo	6.2 (4.0)	5.4 (3.6)	0.2
Mortality	4 (7%)	1 (1%)	0.04

*Mean value (with, standard deviation).