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Operative pancreatic debridement: Contemporary outcomes in changing times☆

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ABSTRACT

Background/objectives: Operative pancreatic debridement (OPD) is the historic gold standard for treating necrotizing pancreatitis (NP). Recent success with minimally invasive NP treatment approaches have raised the question of which NP patients require OPD. We therefore sought to define contemporary outcomes of NP patients undergoing OPD.

Methods: A retrospective analysis was performed of 116 consecutive NP patients undergoing OPD using a prospectively maintained institutional NP database between 2006 and 2018.

Results: 86 (74%) patients underwent open pancreatic debridement (OD) and 30 (26%) underwent open transgastric debridement (TGD). Median follow-up was 16 months (interquartile range [IQR], 8–45 months). Median age was 51 years (IQR, 43–65 years); 73 (63%) were male. Pancreatitis etiology included biliary (53%), alcohol (22%), and idiopathic/other (25%). Median time from diagnosis to OPD was 64.5 days (IQR, 32–114.5 days). Mean APACHE-II score was: admission 8.5 (standard deviation [SD], 5.9); worst 12.6 (SD, 7.9); preoperatively 7.2 (SD, 4.6). 40 patients (34%) were initially managed with minimally invasive techniques (percutaneous drain only in 24, endoscopic only in 6, combination in 10). Median postoperative length of stay was 11 days (IQR, 7–19 days). 90-day morbidity and mortality were 70% and 2%, respectively.

Conclusions: NP patients who require OPD are critically and chronically ill. OPD is associated with substantial morbidity, but acceptable mortality in an experienced center with multidisciplinary support. This large contemporary series demonstrates that in properly selected patients, OPD remains an important treatment for NP.

Introduction

Acute pancreatitis (AP) is most often a relatively mild and self-limited disease that resolves with supportive management and causes minimal long-term sequelae [1]. However, necrotizing pancreatitis (NP) with variable amounts of parenchymal and/or peripancreatic necrosis develops in 10–20% of all patients with acute pancreatitis [2–4]. Patients with NP are plagued by prolonged illness associated with organ failure, malnutrition, infection, and hospital readmission [1,4,5]. Mortality in all patients with NP can reach 15%, and as high as 30% in those with infected pancreatic necrosis [4,6]. Patients with NP typically require intensive care and often multiple procedures before complete resolution of this disease process. Operative pancreatic debridement (OPD) is the historical gold standard treatment for NP patients requiring intervention. Initially, this procedure carried significant morbidity and mortality rates as high as 25–60% with early laparotomy and closed drainage[7–11]. Improved operative technique and surgeon experience significantly improved perioperative mortality rates in the modern era of treatment [12,13]. The publication of consensus guidelines for operative intervention and the regionalization of NP care at tertiary referral centers further improved operative mortality rates after OPD [12,14–16].

Over the past decade, endoscopic and percutaneous minimally invasive approaches have been applied to the treatment of NP patients. These minimally invasive necrosis interventions include percutaneous drainage, endoscopic drainage or debridement, video-assisted retroperitoneal debridement (VARD), and sinus tract necrosectomy (STN) [17–24]. Many patients require a combination

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of these techniques to achieve complete debridement. The modern algorithmic approach to the management of NP begins with supportive medical care and progresses as indicated to minimally invasive therapy [15]. As a result, in current treatment algorithms OPD is often reserved for the most severely ill NP patient refractory to less invasive means of treatment.

Within the context of the last decade's significant changes in management strategy, it is important to understand contemporary benchmark patient outcomes. As such, we queried the experience of our high-volume pancreatic referral center to evaluate outcomes of patients undergoing OPD as definitive therapy in the modern treatment algorithm. This cohort represents a subgroup of NP patients often refractory to minimally invasive treatment and typically the most chronically ill and challenging population. We therefore hypothesized that morbidity and mortality with operative pancreatic debridement may actually be higher in this group compared to historical trends.

Methods

Patient population and study definitions

The Indiana University NP database is a prospectively collected database including all NP patients admitted to Indiana University Health University Hospital (IU-UH), regardless of management strategy. All data are compiled and recorded in strict compliance with the protocols and guidelines set forth by the Indiana University's Institutional Review Board, which approved the conduct of this study. Informed consent is obtained in all patients prior to inclusion in the NP database. All consecutive NP patients undergoing operative pancreatic debridement (OPD) by a single surgeon (NJZ) with a practice focus on pancreatic surgery and extensive experience in pancreatitis management were included in this study. Operative pancreatic debridement included both traditional open pancreatic debridement (OD) and transgastric debridement (TGD) [21].

Acute pancreatitis, severe acute pancreatitis, and NP were defined according to the revised Atlanta classification published in 2012 [1]. Organ failure was defined according to the modified Marshall scoring system for organ dysfunction [1]. Necrotizing pancreatitis was defined as parenchymal and/or peripancreatic necrosis represented as lack of pancreatic parenchymal enhancement and/or findings of acute necrotic collection (ANC) or walled off necrosis (WON) on contrast-enhanced imaging [1]. Dedicated faculty pancreatic radiologists confirmed imaging features of necrosis.

Baseline patient characteristics were evaluated and recorded preoperatively. Each patient's individual clinical course was evaluated pre-, peri-, and postoperatively. Clinical information included age, sex, comorbidities, etiology of pancreatitis, Charlson comorbidity index, organ failure, intensive care admission, infectious complications, acute physiology and chronic health evaluation II (APACHE II) score, necrosis intervention, readmission, overall morbidity, and mortality. Extrapancreatic infectious complications included pneumonia, bacteremia, urinary tract infection, *C. difficile* colitis, and fungemia. Morbidity was recorded as any postoperative complication.

Operative pancreatic debridement was divided into one of three operative scenarios, as follows:

1. Elective: Patients with persistent pancreatic necrosis but without frequent hospitalization or prolonged hospital stays. Debridement was scheduled electively, and patients were admitted from home for OPD. Patients did not meet criteria of semi-elective or urgent/emergent OPD.
2. Semi-elective: Patients with symptomatic or infected pancreatic necrosis who required frequent hospitalization and/or prolonged hospital stays with short intervals between hospital admissions. In addition to symptomatic or infected necrosis, patients were commonly readmitted with extrapancreatic infection or failure to thrive. Patients were typically inpatient at the time of OPD. Patents did not meet criteria of urgent/emergent OPD.
3. Urgent/emergent OPD: Patients with symptomatic or infected pancreatic necrosis who required frequent hospitalization and/or prolonged hospital stays often complicated by organ failure, extrapancreatic infection, failure to thrive, malnutrition, and physical deconditioning. All patients were inpatient at the time of OPD and experienced clinical deterioration prompting OPD.

Approach to necrosis intervention

Our current treatment approach to NP mirrors the consensus guidelines set forth by the International Association of Pancreatology and the American Pancreatic Association [15]. This approach, as at nearly every major center treating pancreatitis patients, has evolved significantly over the past decade [25]. At the beginning of the study (2006), OPD was commonly first-line treatment for infected pancreatic necrosis. In 2006, percutaneous drainage (PD) was introduced to the treatment algorithm as a bridge to OPD. During the following three years, PD was applied selectively. Beginning in 2009, PD was more widely utilized as the first step in treatment of infected NP. This same year (2009), endoscopic debridement was introduced and applied selectively both as the first step in treatment as well as an adjunct to PD. Patients refractory to these minimally invasive debridement techniques were considered for OPD. Beginning in 2014, endoscopic debridement was applied more widely as a first intervention or as an adjunct to PD. With more widespread application of and experience with PD and endoscopic debridement, many fewer patients required OPD in the latter years of the study. Throughout the entire study period, patients with biliary pancreatitis requiring necrosis intervention are considered for an upfront surgical approach (often transgastric, as anatomy permits) to allow for cholecystectomy at the time of mechanical necrosis debridement. Patients with sudden clinical deterioration after relative clinical stability are considered for operative exploration to diagnose and treat other local complications, such as colonic or gallbladder ischemia or fulminant *C. difficile* colitis.

Statistical analysis

Categorical data are presented as number with percentage and continuous data are presented as mean values with standard deviation (SD) or as median values with interquartile range (IQR). Univariate analysis was performed using the chi-squared test, independent samples *t*-test, and analysis of variance (ANOVA). Multivariable regression analysis was performed using binary logistic regression and used variables with $P < 0.10$ on univariate analysis. Data were recorded using Microsoft® Excel® 2018 (Microsoft, Inc., Redmond, WA, USA) and analyzed with IBM® SPSS statistics 25.0 (IBM Corporation, Armonk, NY, USA). Statistical significance was defined as $P < 0.05$.

Results

Population characteristics

Between 2006 and 2018 a total of 681 NP patients were treated and 435 patients underwent OPD by nine surgeons. The breakdown

Table 1
Necrotizing pancreatitis patients between 2006 and 2018 (N = 681) and intervention by year.

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
NP Patients/Year, n	37	51	53	61	58	60	51	61	58	48	50	45	48
Any Intervention, n (%)	35 (95)	43 (84)	49 (92)	51 (84)	54 (93)	55 (92)	44 (86)	55 (90)	43 (74)	33 (69)	32 (64)	27 (60)	27 (56)
Any OPD, n (%)	30 (81)	39 (76)	39 (74)	44 (72)	41 (71)	46 (77)	40 (78)	49 (80)	36 (62)	22 (46)	17 (34)	18 (40)	14 (29)
Step-up, n (%)	6 (17)	8 (19)	15 (31)	18 (35)	9 (17)	15 (27)	14 (32)	27 (49)	24 (56)	22 (67)	25 (78)	18 (67)	16 (59)
Step-up to OPD, n (%)	3 (8)	4 (8)	8 (15)	12 (20)	5 (9)	9 (15)	10 (20)	12 (20)	13 (22)	4 (8)	7 (14)	7 (16)	4 (8)
No Intervention, n (%)	2 (5)	8 (16)	4 (8)	10 (16)	4 (7)	5 (8)	7 (14)	6 (10)	15 (26)	15 (31)	18 (36)	18 (40)	21 (44)

Abbreviations: NP – necrotizing pancreatitis; OPD – operative pancreatic debridement.

of NP patients and treatment strategy by year is shown in Table 1. During this time, a single surgeon (NJZ) performed 116 OPD, Fig. 1. Of these 116 patients analyzed, 86 (74%) underwent OD and 30 (26%) underwent TGD. Complete patient demographics are shown in Table 2. The median age was 51 years and the majority of patients were male. The most common etiology of pancreatitis was biliary (53%) or alcohol (22%).

Preoperative characteristics

Complete preoperative characteristics are included in Table 2. In summary, surgical ICU admission was required preoperatively in 47% of patients. Prior to OPD, organ failure occurred in 44% of patients; multiple system organ failure was present in 22% of patients. At least one extrapancreatic infectious complication developed preoperatively in 37% of patients. The mean APACHE II score was calculated at admission (8.5; SD, 5.9), at worst (12.6; SD, 7.9), and immediately preoperatively (7.2; SD, 4.6), Fig. 2. Overall, 34% of patients underwent a minimally invasive necrosis intervention preoperatively, Table 3. Infected necrosis was suspected preoperatively in 75 (67%) patients based on cross-sectional imaging or culture data from minimally invasive necrosis intervention and later confirmed by intraoperative cultures.

Operative details

The median time from NP onset to OPD was 64.5 days (IQR, 32–114.5 days). A concomitant procedure was performed in 89 (77%) patients. The most common additional procedures included gastrojejunostomy feeding tube placement in 62 (53%) patients and cholecystectomy in 47 (41%) patients. Other additional procedures included distal pancreatectomy (13 patients, 11%), colectomy (10 patients, 9%), small bowel resection (5 patients, 4%), common bile duct exploration (4 patients, 3%), splenectomy (3 patients, 3%), hepaticojejunostomy (2 patients, 2%), and oophorectomy (1 patient, 1%).

Postoperative outcomes

Complete postoperative outcomes are shown in Table 4. Postoperative admission to the surgical ICU was required in 56% of patients for a median of 5 days (IQR, 2–14 days). Postoperative organ failure was present in 40% of patients; multiple organ system failure was present in 17% of patients. Extrapancreatic infection developed postoperatively in 22% of patients. Six (5%) patients developed enterocutaneous fistulae postoperatively; three were managed with drains placed at the time of initial OPD and three were treated by repeat surgical intervention. The median postoperative length of stay was 11 days (IQR, 7–19 days). Repeat necrosis intervention was required in 35% of patients. Overall morbidity and mortality of OPD was 70% and 2%, respectively. The median postoperative follow-up period was 16 months (IQR, 8–45 months).

Patients undergoing a preoperative minimally invasive necrosis intervention (n = 40) were compared to patients undergoing OPD as their first necrosis intervention (n = 76). On univariate analysis,

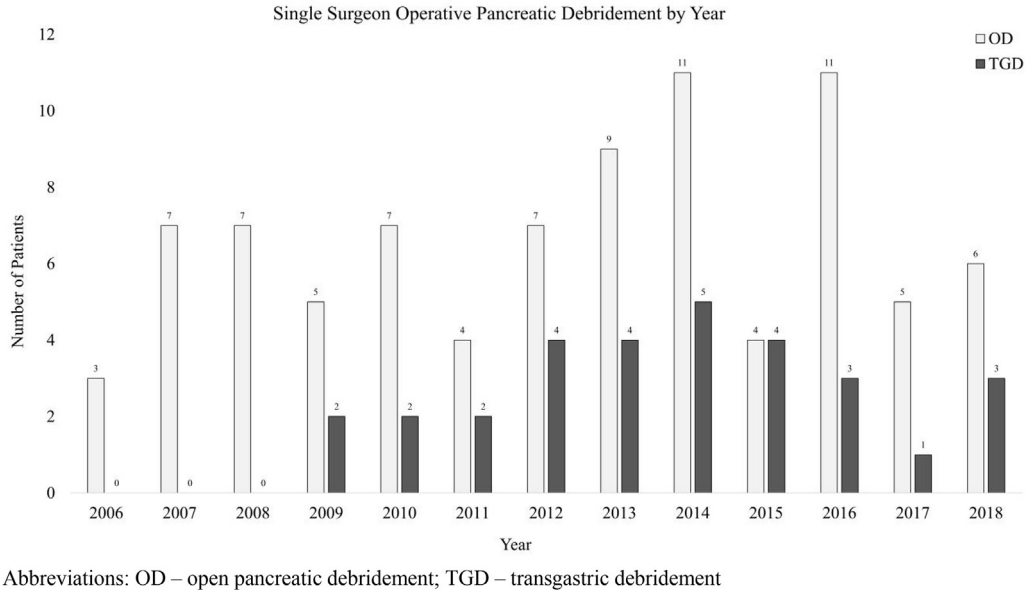
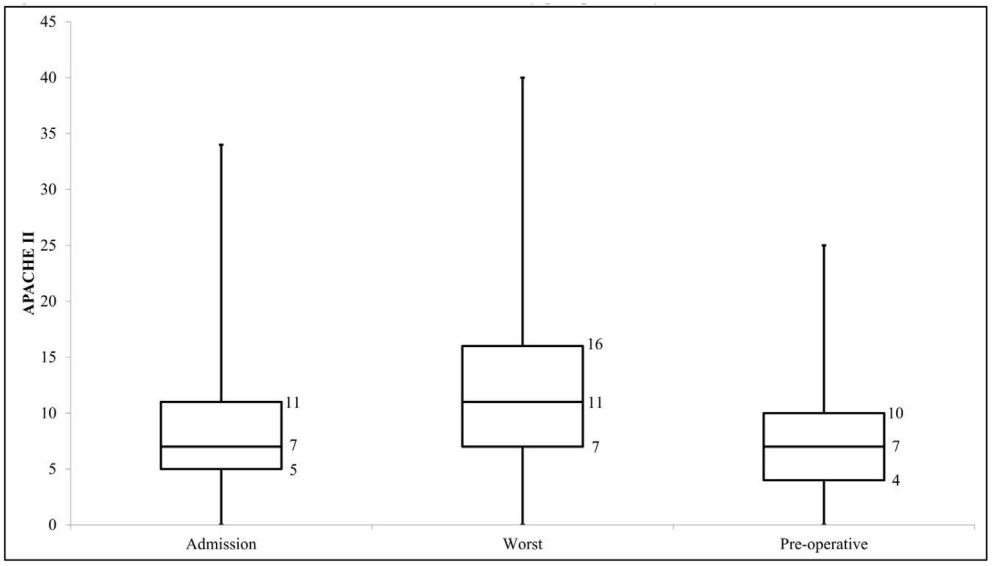


Fig. 1. Number and type of operative pancreatic debridement for necrotizing pancreatitis patients included in the analysis (n = 116) by year
Abbreviations: OD – open pancreatic debridement; TGD – transgastric debridement.



Abbreviations: APACHE II – acute physiology, age, and chronic health evaluation II

Fig. 2. APACHE II score at admission, worst, and immediately preoperatively
Abbreviations: APACHE II – acute physiology, age, and chronic health evaluation II.

compared to patients undergoing OPD upfront, patients undergoing a minimally invasive necrosis intervention had significantly increased rates of postoperative ICU admission, organ failure, infection, and overall morbidity (Table 5). However, using multivariable analysis to control for baseline differences in preoperative ICU admission, organ failure, infectious complications, and APACHE scores, preoperative minimally invasive necrosis intervention did not significantly impact these outcomes. Mortality was similar among groups on both univariate and multivariable analysis.

Patients were categorized according to one of three NP clinical courses. Operative pancreatic debridement was performed electively in 25 (22%) patients, semi-electively in 58 (50%) patients with a smoldering clinical course, and urgently/emergently in 33 (28%) patients with clinical deterioration. Transgastric debridement was performed in 13 of 25 (52%) patients undergoing elective OPD, in 15 of 58 (26%) patients undergoing semi-elective OPD, and in 2 of 33 (6%) patients undergoing urgent/emergent OPD. We evaluated time of worst APACHE score both from the time of NP onset as well as relative to time of debridement, Table 6. Not surprisingly, the worst APACHE was seen sooner in the overall NP course in those patients requiring urgent/emergent debridement. Similarly, the duration from worst APACHE to OPD was longer in patients undergoing elective debridement compared to those with either semi-elective or urgent/emergent debridement. No statistical analysis was conducted among these groups due to small sample size and distribution of values. The preoperative clinical course of each subgroup is shown in Fig. 3A. The indication for elective OPD was persistent symptomatic necrosis in 21 of 25 (84%) patients and infected necrosis refractory to minimally invasive approaches in the remaining four (16%) patients. Of note, four of 21 patients undergoing elective OPD for symptomatic necrosis were found to have occult necrosis infection based on intraoperative culture. As operative urgency increased from elective to semi-elective to urgent/emergent, a statistically significant increase in postoperative ICU admission, organ failure, multiple organ failure, extrapancreatic infection, repeat necrosis intervention, and morbidity were observed (Fig. 3B). Of the 33 patients requiring urgent/emergent OPD, a "damage control" staged debridement was performed in 13 (40%) patients. Mortality was highest among those patients requiring urgent/emergent OPD (6%) when compared to elective (0%) and semi-elective (0%); however, this difference did not reach statistical significance ($P = 0.08$).

Table 2
Patient demographics and preoperative characteristics.

Patient Characteristics (N = 116)	Number (%)
Demographics	
Age[a]	51 years (43–65)
Male Sex	73 (63)
Etiology	
Biliary	60 (53)
Alcohol	25 (22)
Post-ERCP	7 (6)
Triglyceride	5 (4)
Idiopathic/Other	19 (16)
Charlson Comorbidity Index[b]	1.7 (1.8)
Preoperative	
ICU Admission	54 (47)
Organ Failure	51 (44)
Respiratory	37 (32)
Renal	36 (31)
Cardiovascular	11 (9)
Multiple Organ Failure	25 (22)
Infected Necrosis	75 (65)
Extrapancreatic Infection	43 (37)
Pneumonia	20 (17)
Bacteremia	18 (16)
Urinary Tract Infection	14 (12)
C. difficile Colitis	6 (5)
Fungemia	4 (3)

Abbreviations: ERCP – endoscopic retrograde cholangiopancreatography; SEM – standard error of the mean; ICU – intensive care unit.
[a] Continuous variable reported as median value with interquartile range.
[b] Continuous variable reported as mean value with standard deviation.

Table 3
Minimally invasive intervention preoperatively.

Preoperative Intervention (N = 116)	Number (%)
Any	40 (34)
Percutaneous drain only	24 (21)
Endoscopic only	6 (5)
Combination	10 (9)

Table 4
Postoperative outcomes.

Postoperatively (N = 116)	Number (%)
ICU Admission	65 (56)
Organ Failure	46 (40)
Respiratory	41 (35)
Renal	14 (12)
Cardiovascular	16 (14)
Multiple Organ Failure	20 (17)
Extrapancreatic Infection	25 (22)
Pneumonia	15 (13)
Bacteremia	11 (9)
Urinary Tract Infection	6 (5)
C. difficile Colitis	6 (5)
Fungemia	1 (1)
Repeat Necrosis Intervention	41[a] (35)
Operative	23[b] (20)
Percutaneous Drain	21 (18)
Endoscopic	12 (10)
Length of Stay[c]	11 days (7–19)
Readmission	39 (34)
Morbidity	81 (70)
Mortality	2 (2)

Abbreviations: ICU – intensive care unit.
[a] 14 required a combination.
[b] 14/23 planned, staged debridement.
[c] Continuous variable reported as median value with interquartile range.

Discussion

This large contemporary series of NP patients undergoing OPD shows continued improvement in postoperative morbidity and a gratifyingly low mortality rate. Patients who required OPD were often critically ill and/or refractory to less invasive measures and represent the most challenging NP cases. Postoperatively these patients continue to be a challenge as their clinical course is further characterized by ongoing organ failure (40%), infection (22%), the need for repeat intervention (35%), and high rates of hospital readmission (34%). The overall morbidity after OPD was 70% and was directly associated with the acuity of the procedure. Morbidity was lowest in patients undergoing elective debridement (48%) and highest in patients undergoing urgent/emergent debridement (88%). Despite these challenges, mortality among all patients undergoing OPD was 2%, comparing favorable to modern series with mortality ranging from 4 to 18% [12,13,17,26,27].

Historically, OPD was applied widely in all NP patients and performed early in the disease course resulting in morbidity and mortality rates ranging from 60 to 90% and 25%–60%, respectively [7–11]. Postoperative complications in these patients were serious and included organ failure, hemorrhage, infection, enterocutaneous fistula, and pancreaticocutaneous fistula. Advances in critical care, improved technique of operative debridement, and a better understanding of the disease timeline significantly improved outcomes [12,13,16]. Over the last decade, minimally invasive techniques as a bridge to definitive therapy have been increasingly utilized, allowing for a period of recovery prior to definitive operative debridement [17,18,22,24]. These studies found that some NP patients undergoing minimally invasive necrosis intervention will recover without operative debridement. In the modern treatment algorithm, OPD commonly represents the final step of intervention in NP and the focus of this specific report was to evaluate outcomes after OPD; we have evaluated more specifically the efficacy of PD and predictors of success in a discrete report [23]. In the current series, OPD was performed safely in this setting as patients refractory to a minimally invasive necrosis intervention underwent OPD with acceptable morbidity (83%) and low mortality (5%).

Necrotizing pancreatitis represents an extremely heterogenous disease that mandates a treatment strategy individualized to the patient. This concept is particularly important given recent interest in minimally invasive necrosis intervention [4,15,23,25,28,29]. Studies evaluating minimally invasive techniques commonly enroll highly select NP patient populations. For example, in the landmark Dutch Pancreatitis Study Group “step-up approach” protocol 88 of 378 screened patients met enrollment criteria [17]. This point should not be taken as a criticism of these studies and in fact highlights the role for specific minimally invasive techniques in select NP patients. For example, necrosis tracking down the left or right paracolic gutter may be readily addressed with percutaneous drainage [22,30]. NP patients with necrosis isolated to the lesser sac can be approached with an endoscopic or surgical transgastric technique [20,21,24,31,32]. In patients undergoing endoscopic transgastric debridement with additional necrosis in either paracolic gutter, the transgastric technique may be combined

Table 5
Comparison of outcomes in patients without and with preoperative minimally invasive necrosis intervention.

	Upfront Operative Debridement (n = 76) Number (%)	Preoperative Minimally Invasive (n = 40) Number (%)	P Uni	P MVA
Clinical Course				
Worst APACHE[b]	11.4 (7.5)	14.7 (8.3)	0.04	
ICU Admission	28 (37)	26 (65)	0.004	
Organ Failure	30 (39)	21 (53)	0.2	
Respiratory	20 (26)	17 (43)	0.08	
Renal	24 (32)	12 (30)	0.9	
Cardiovascular	6 (8)	5 (13)	0.4	
Extrapancreatic Infection	22 (29)	21 (53)	29	
Days to Debridement[a]	52 days (27–106)	98.5 days (51.5–130)	0.007	
Postoperative				
ICU Admission	36 (47)	29 (73)	0.01	0.4
Organ Failure	23 (30)	23 (58)	0.004	0.4
Respiratory	20 (26)	21 (53)	0.005	0.6
Renal	9 (12)	5 (13)	0.9	–
Cardiovascular	4 (5)	12 (30)	0.0002	0.2
Infection	12 (16)	13 (33)	0.04	0.8
Morbidity	48 (63)	33 (83)	0.03	0.9
Mortality	0 (0)	2 (5)	0.1	0.7

Abbreviations: Uni – univariate analysis; MVA – multivariable analysis; ICU – intensive care unit; APACHE – acute physiology and chronic health evaluation; ICU – intensive care unit.
[a] Continuous variable reported as median value with interquartile range.
[b] Continuous variable reported as mean value with standard deviation.

Table 6
Timing of worst APACHE relative to necrotizing pancreatitis onset and operative pancreatic debridement among each acuity of debridement.

	Elective (n = 25) median (IQR)	Semi-Elective (n = 58) median (IQR)	Urgent/Emergent (n = 33) median (IQR)
Timing of Worst APACHE			
Days, NP Onset to Worst APACHE	41 (3–109)	25.5 (5–62)	15.5 (7–32)
Days, Worst APACHE to OPD	27.5 (1–84)	10 (1–42)	6 (1–23)

percutaneous drainage [19,33,34]. These studies share an important common theme: excellent success can be achieved by each of these techniques in experienced hands with proper patient selection.

Several questions remain unanswered with the modern treatment algorithm. Who will benefit from a surgery first approach? When is the appropriate time to "step-up" therapy and what treatment should be performed next? When is it time to abandon minimally invasive attempts and "step-up" to open surgery? In the current series, elective OPD was performed in 22% of patients with relatively low morbidity (48%) and no mortality. The majority of these patients had biliary etiology of pancreatitis and underwent transgastric debridement, allowing for a one-step operation addressing both the gallbladder and pancreatic necrosis. The safety

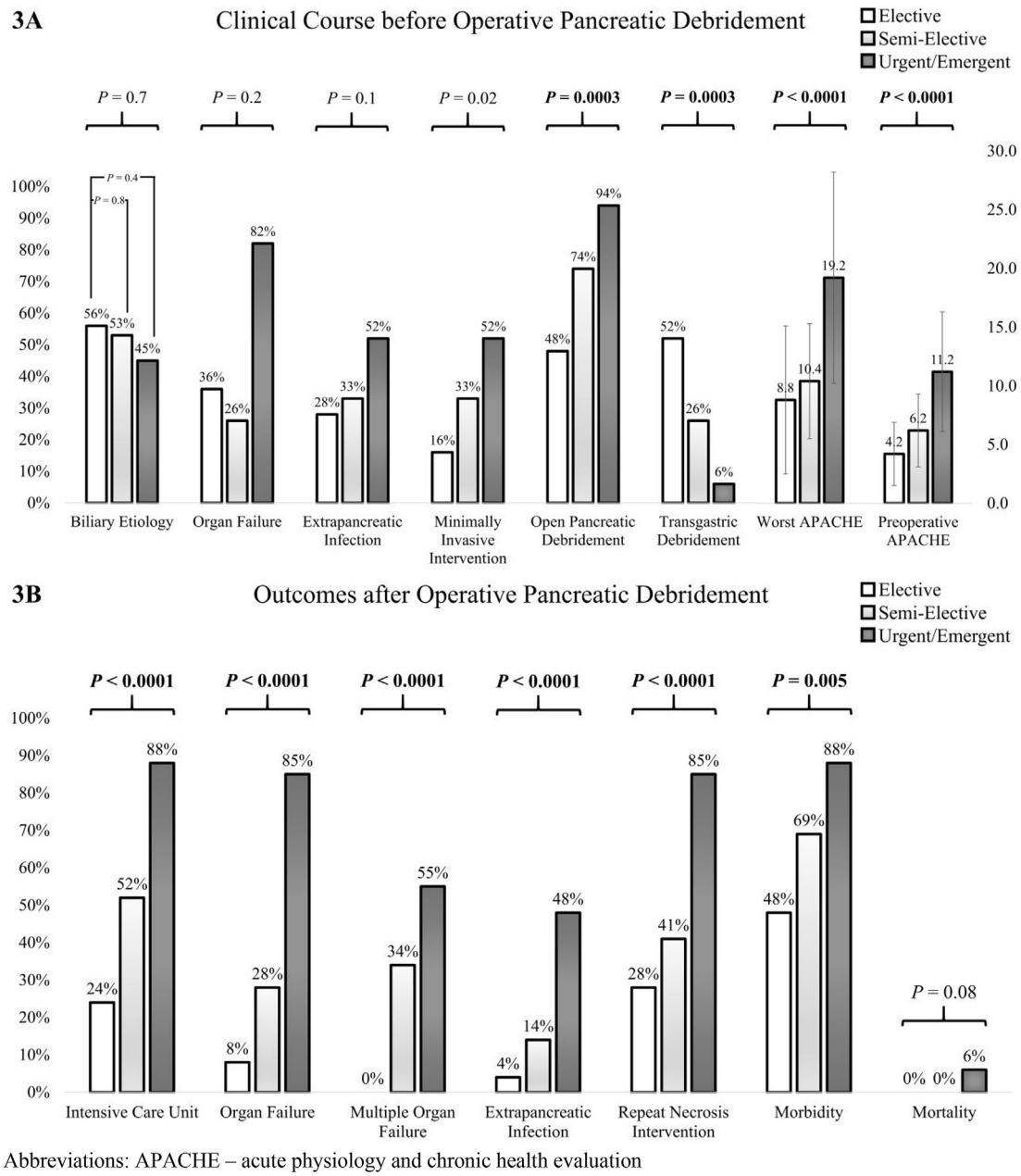


Fig. 3. Clinical course before operative pancreatic debridement (3A) and outcomes after operative pancreatic debridement (3B) among category of operative acuity. Abbreviations: APACHE – acute physiology and chronic health evaluation.

and efficacy of this procedure has been previously described in a multi-institutional experience [31]. In the current study, patients undergoing a minimally invasive procedure prior to OPD were more acutely ill and when "stepped-up" to OPD experienced significantly greater postoperative morbidity; however, mortality remained low (5%). In this complex patient population, multidisciplinary discussion is critical to discuss the timing to "step-up," balancing the morbidity of operating, chance of success or failure of additional minimally invasive intervention, and dynamics of the individual patient's physiologic condition. Currently, no objective metrics exist to guide the decision-making in regard to the timing of "step-up" to more invasive intervention. Finally, a subset of patients in this series required urgent/emergent OPD. Not surprisingly, postoperative morbidity in this setting was high (88%) Nevertheless, even in this "worst-case" scenario, OPD rescued the vast majority of these patients with a mortality rate of 6%. In the setting of emergent OPD and unfavorable physiology, a "damage control pancreatic debridement" with staged reoperation may be considered [35]. An important, unanswered question is whether a specific group of NP patients may benefit from operative debridement as a first-line approach. Specific examples may include those with multi-field necrosis, or a high-volume of solid necrosis, particularly those with biliary etiology. Unfortunately, answering this question with a prospective trial will be immensely challenging and likely impossible because of the relatively low volume of NP treated by most centers, as well as the broad heterogeneity of NP patients' necrosis volume, anatomic distribution, and general physiologic condition.

This study is limited by its retrospective nature and included patients treated during an evolution in NP therapy at our institution [25]. Early in the study period, the initial treatment approach was often OPD. This sequence evolved into minimally invasive techniques first, most often reserving operative intervention for surgical emergencies or patients refractory to less invasive techniques. The study includes patients undergoing operative debridement by a single, experienced pancreatic surgeon with long standing interest in pancreatitis. This analytic approach introduces the surgeon specific management strategy bias; however, (and importantly) minimized bias across individual patient decision-making. The intent was to produce a concise and concrete description of the necrosis treatment algorithm in all patients and timepoints during a decade in which treatment strategy evolved significantly. A significant strength of this study is the large number of patients undergoing OPD in the modern era of NP.

As the ideal treatment strategy for NP patients continues to evolve, identifying objective metrics to guide the selection of appropriate first line interventions for NP patients becomes increasingly important. Further, objective metrics to guide the timing of a "step-up" to additional or more invasive intervention are lacking and when identified will be of great benefit to clinicians treating NP. To date, treatment for NP patients is entirely reactive to disease complications and disease-modulating therapies are critically needed. One such disease-modulating therapy with potential demonstrated in preclinical studies is the use of stem cells to modulate the AP systemic inflammatory response [36]. Treatments impacting the pathophysiology of NP will inform further evolution in the management strategy of this disease.

Conclusion

Minimally invasive techniques play an increasingly important role in the treatment of necrotizing pancreatitis patients. These strategies provide definitive treatment in many; however, a select necrotizing pancreatitis patient population refractory to minimally invasive therapies benefit from operative intervention. A second discrete group of necrotizing pancreatitis patients are best approached by primary operative debridement. Operative pancreatic debridement can be performed safely and remains an important management strategy in the modern treatment algorithm in properly selected patients.

Author contribution

Acquisition, analysis, interpretation of data: TKM, KFF, AMR, NJZ.
Conception, drafting, and revision of work: TKM, KFF, AMR, NJZ.
Final approval of work: TKM, KFF, AMR, NJZ.

*All co-authors qualify for authorship according to the Uniform Requirements for Manuscripts as published in the guidelines of the International Committee of Medical Journal Editors in 1988.

References

[1] Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis–2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013;62(1):102–11.
[2] Fagenholz PJ, Fernandez-del Castillo C, Harris NS, Pelletier AJ, Camargo Jr CA. Direct medical costs of acute pancreatitis hospitalizations in the United States. Pancreas 2007;35(4):302–7.
[3] Banks PA. Freeman ML, practice parameters committee of the American college of gastroenterology. Practice guidelines in acute pancreatitis. Am J Gastroenterol 2006;101(10):2379–400.
[4] van Dijk SM, Hallensleben NDL, van Santvoort HC, Fockens P, van Goor H, Bruno MJ, et al. Acute pancreatitis: recent advances through randomised trials. Gut 2017;66(11):2024–32.
[5] Maatman TK, Mahajan S, Roch AM, Lewellen KA, Heimberger MA, Colgate CL, et al. High rates of readmission in necrotizing pancreatitis: natural history or opportunity for improvement? J Gastrointest Surg 2019;23(9):1834–9.
[6] Freeman M, Werner J, van Santvoort H, Baron T, Besselink M, Windsor J, et al. Interventions for necrotizing pancreatitis: summary of a multidisciplinary consensus conference. Pancreas 2012;41(8):1176–94.
[7] Rattner DW, Legermate DA, Lee MJ, Mueller PR, Warshaw AL. Early surgical debridement of symptomatic pancreatic necrosis is beneficial irrespective of infection. Am J Surg 1992;163(1):105–9. discussion 9-10.
[8] Mier J, Leon EL, Castillo A, Robledo F, Blanco R. Early versus late necrosectomy in severe necrotizing pancreatitis. Am J Surg 1997;173(2):71–5.
[9] Rau B, Bothe A, Beger HG. Surgical treatment of necrotizing pancreatitis by necrosectomy and closed lavage: changing patient characteristics and outcome in a 19-year, single-center series. Surgery 2005;138(1):28–39.
[10] Connor S, Alexakis N, Raraty MG, Ghaneh P, Evans J, Hughes M, et al. Early and late complications after pancreatic necrosectomy. Surgery 2005;137(5):499–505.
[11] Reddy M, Jindal R, Gupta R, Yadav TD, Wig JD. Outcome after pancreatic necrosectomy: trends over 12 years at an Indian centre. ANZ J Surg 2006;76(8):704–9.
[12] Howard TJ, Patel JB, Zyromski N, Sandrasegaran K, Yu J, Nakeeb A, et al. Declining morbidity and mortality rates in the surgical management of pancreatic necrosis. J Gastrointest Surg 2007;11(1):43–9.
[13] Parikh PY, Pitt HA, Kilbane M, Howard TJ, Nakeeb A, Schmidt CM, et al. Pancreatic necrosectomy: north American mortality is much lower than expected. J Am Coll Surg 2009;209(6):712–9.
[14] van Santvoort HC, Besselink MG, Bakker OJ, Hofker HS, Boermeester MA, Dejong CH, et al. A step-up approach or open necrosectomy for necrotizing pancreatitis. N Engl J Med 2010;362(16):1491–502.
[15] Working Group Iap/Apa Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology 2013;13(4 Suppl 2):e1–15.
[16] Ball CG, Hameed SM, Dixon E, Lillemoe KD. Severe acute pancreatitis for the acute care surgeon. J Trauma Acute Care Surg 2016;80(6):1015–22.
[17] Van Santvoort H, Besselink M, Bakker O, Hofker S, Boermeester M, Dejong C, et al. A step-up approach or open necrosectomy for necrotizing pancreatitis. N Engl J Med 2010;362:1491–502.
[18] van Santvoort HC, Bakker OJ, Bollen TL, Besselink MG, Ahmed Ali U, Schrijver AM, et al. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. Gastroenterology 2011;141(4):1254–63.
[19] Ross AS, Irani S, Gan SI, Rocha F, Siegal J, Fotoohi M, et al. Dual-modality drainage of infected and symptomatic walled-off pancreatic necrosis: long-term clinical outcomes. Gastrointest Endosc 2014;79(6):929–35.
[20] Gardner TB, Coelho-Prabhu N, Gordon SR, Gelrud A, Maple JT, Papachristou GI, et al. Direct endoscopic necrosectomy for the treatment of walled-off pancreatic necrosis: results from a multicenter U.S. series. Gastrointest Endosc 2011;73(4):718–26.
[21] Zyromski NJ, Nakeeb A, House MG, Jester AL. Transgastric pancreatic necrosectomy: how I do it. J Gastrointest Surg 2016;20(2):445–9.
[22] Horvath K, Freeny P, Escallon J, Heagerty P, Comstock B, Glickerman D, 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(9):814–25.
[23] Maatman TK, Mahajan S, Roch AM, Ceppa EP, House MG, Nakeeb A, et al. Disconnected pancreatic duct syndrome predicts failure of percutaneous therapy in necrotizing pancreatitis. Pancreatology 2020;20(3):362–8.
[24] Trikudanathan G, Tawfik P, Amateau SK, Munigala S, Arain M, Attam R, et al. Early (<4 Weeks) versus standard (>/= 4 Weeks) endoscopically centered step-up interventions for necrotizing pancreatitis. Am J Gastroenterol 2018;113(10):1550–8.
[25] Roch AM, Maatman T, Carr RA, Easler JJ, Schmidt CM, House MG, et al. Evolving treatment of necrotizing pancreatitis. Am J Surg 2018;215(3):526–9.
[26] van Brunschot S, Hollemans RA, Bakker OJ, Besselink MG, Baron TH, Beger HG, et al. Minimally invasive and endoscopic versus open necrosectomy for necrotising pancreatitis: a pooled analysis of individual data for 1980 patients. Gut 2018;67(4):697–706.
[27] Hollemans RA, Bakker OJ, Boermeester MA, Bollen TL, Bosscha K, Bruno MJ, et al. Superiority of step-up approach vs open necrosectomy in long-term follow-up of patients with necrotizing pancreatitis. Gastroenterology 2019;156(4):1016–26.
[28] Baron TH, DiMaio CJ, Wang AY, Morgan KA. American gastroenterological association clinical practice update: management of pancreatic necrosis. Gastroenterology 2020;158(1):67–75 e1.
[29] Garg PK, Zyromski NJ, Freeman ML. Infected necrotizing pancreatitis: evolving interventional strategies from minimally invasive surgery to endoscopic therapy-evidence mounts, but one size does not fit all. Gastroenterology 2019;156(4):867–71.
[30] van Grinsven J, Timmerman P, van Lienden KP, Haveman JW, Boerma D, van Eijck CH, et al. Proactive versus standard percutaneous catheter drainage for infected necrotizing pancreatitis. Pancreas 2017;46(4):518–23.
[31] Driedger M, Zyromski NJ, Visser BC, Jester A, Sutherland FR, Nakeeb A, et al. Surgical transgastric necrosectomy for necrotizing pancreatitis: a single-stage procedure for walled-off pancreatic necrosis. Ann Surg 2018;271(1):163–8.
[32] Maatman TK, Zyromski NJ. Transgastric pancreatic debridement: a step-by-step guide to a single-staged procedure for walled-off pancreatic necrosis (video). J Gastrointest Surg 2020. https://doi.org/10.1007/s11605-019-04375-x [Epub ahead of print].
[33] Gluck M, Ross A, Irani S, Lin O, Gan SI, Fotoohi M, et al. Dual modality drainage for symptomatic walled-off pancreatic necrosis reduces length of hospitalization, radiological procedures, and number of endoscopies compared to standard percutaneous drainage. J Gastrointest Surg 2012;16(2):248–56. discussion 56-7.
[34] Hyun JJ, Sahar N, Singla A, Ross AS, Irani SS, Gan SI, et al. Outcomes of infected versus symptomatic sterile walled-off pancreatic necrosis treated with a minimally invasive therapy. Gut Liver 2019;13(2):215–22.
[35] Maatman TK, Roch AM, Ceppa EP, House MG, Nakeeb A, Schmidt CM, et al. Damage control pancreatic débridement: salvaging the most severely ill. JOP 2019;20(1):37–43.
[36] Roch AM, Maatman TK, Cook TG, Wu HH, Merfeld-Clauss S, Traktuev DO, et al. Therapeutic use of adipose-derived stromal cells in a murine model of acute pancreatitis. J Gastrointest Surg 2020;24(1):67–75.