

EVOLVING TREATMENT OF NECROTIZING PANCREATITIS

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ABSTRACT

Background: Over the past decade, the treatment of necrotizing pancreatitis (NP) has incorporated greater use of minimally invasive techniques, including percutaneous drainage and endoscopic debridement. No study has yet compared outcomes of patients treated with all available techniques. We sought to evaluate the evolution of NP treatment at our high volume pancreas center. We hypothesized that minimally invasive techniques (medical only, percutaneous, and endoscopic) were used more frequently in later years.

Methods: Treatment strategy of NP patients at a single academic medical center between 2005-2014 was reviewed. Definitive management of pancreatic necrosis was categorized as: 1) medical treatment only; 2) surgical only; 3) percutaneous (interventional radiology – IR) only; 4) endoscopic only; and 5) combination (Surgery+/-IR+/-Endoscopy).

Results: 526 NP patients included biliary (45%), alcoholic (17%), and idiopathic (20%) etiology. Select patients were managed exclusively by medical, IR, or endoscopic treatment; use of these therapies remained relatively consistent over time. A combination of therapies was used in about 30% of patients. Over time, the percentage of NP patients managed without operation increased from 28% to 41%. 247 (47%) of patients had operation as the only NP treatment; an additional 143 (27%) required surgery as part of a multidisciplinary management.

Conclusion: Select NP patients may be managed exclusively by medical, IR, or endoscopic treatment. Combination treatment is necessary in many NP patients, and surgical treatment continues to play an important role in the definitive therapy of necrotizing pancreatitis patients.

INTRODUCTION

Acute pancreatitis is an inflammatory process of the pancreas with a wide range of clinical presentations and outcomes. Acute pancreatitis represents a major public health burden with over 300,000 hospitalizations/year in the United States, accounting for the second highest cost of hospital stays (2.5 billion dollars)¹. Most patients will have a mild self-limited course; however, up to 20% of patients with AP will ultimately develop necrotizing pancreatitis (NP) with an associated 20% mortality rate.

Major improvements have occurred in the care of NP over the past decades; nevertheless, optimal management of this complex heterogeneous disease process remains challenging^{2,3}. Patients with infected necrosis and those with symptomatic sterile necrosis require intervention of some sort. Traditionally, surgical necrosectomy has been the definitive management of NP, although operative debridement is accompanied by significant morbidity (34 to 95%) and perioperative mortality (11 to 39%).²⁻⁴ Recently, minimally invasive approaches to pancreatic debridement have gained popularity. These minimally invasive approaches include interventional radiology (IR)-guided percutaneous drainage and endoscopic drainage.⁵⁻⁷

Over the past several years, our experienced pancreatic multidisciplinary group has embraced minimally invasive approaches to NP treatment. Therefore, we sought to determine the evolution of treatment for NP at our high-volume pancreatic center. We hypothesized that minimally invasive approaches were used more commonly in recent years.

METHODS

Patients population

From 2005 to 2014, all consecutive patients with a diagnosis of NP admitted to Indiana University Hospital were included in this study, regardless of the type of treatment provided. Patients were identified from a prospectively collected NP database. Electronic medical records were queried, and the management strategy was retrospectively manually reviewed. Of the 553 NP patients treated during the study period, 27 (4.9%) had insufficient data for analysis and were excluded from the series. Data were compiled and reported in strict compliance with patient confidentiality protocols set forth by Indiana University School of Medicine's Institutional Review Board, which approved the conduct of this study.

Diagnosis of Necrotizing Pancreatitis (NP)

Acute pancreatitis was defined according to the 2012 revision of the Atlanta classification⁴ as an association of two of the three following features: typical abdominal pain (acute onset of a persistent, severe, epigastric pain often radiating to the back), serum lipase or amylase activity at least three times greater than the upper limit of normal, and characteristic findings of acute pancreatitis on abdominal cross-sectional imaging studies. Necrotizing pancreatitis was characterized by inflammation and associated pancreatic parenchymal necrosis and/or peripancreatic necrosis, as shown by a lack of pancreatic parenchymal enhancement and/or the presence of findings of acute necrotic collection and walled-off necrosis on contrast-enhanced computed tomography (CT).

Parameters assessed

Socio-demographic variables (gender, age at diagnosis) and clinical parameters (etiology, presence of infection) were recorded. Data regarding the episode of NP included the date of diagnosis (broken down by one-year period), and the type of treatment provided. We defined resolution of the NP disease process as the point where no further treatment was required.

Management options

Definitive management was divided into 6 categories. Patients were considered as “medical treatment only” if the only treatment provided was supportive measures (fluid resuscitation, intensive care, nutrition support) with or without administration of antibiotics. Patients were categorized as “surgical treatment only” if they underwent surgical debridement only, regardless of the approach. “Interventional radiology only” consisted of percutaneous drainage under CT guidance with placement of 12 to 30Fr catheters. The “endoscopic only” approach comprised transluminal endoscopic necrosectomy. The “combined” group included all patients who were treated with two or more approaches.

Statistical analysis

Data were recorded using Microsoft Excel® 2016 (Microsoft, Inc., Redmond, WA, USA) and analyzed with IBM SPSS statistics version 21.0® (Armonk, NY: IBM Corp). Descriptive statistics were applied to continuous data. Categorical data were expressed as numbers and percentages. Categorical data were compared with Fisher’s exact test. Statistical significance was defined at $p < 0.05$.

RESULTS

Population characteristics

From 2005 to 2014, 526 NP patients had complete data available for analysis. Mean age at diagnosis of NP was 53 years (range 13-96) with a gender ratio of 1.9 (341 men and 185 women). The leading etiologies for NP in this series were biliary (n=237, 45%) and alcohol (n=89, 17%). In 20% of this population, NP etiology was classified as idiopathic.

The 424 patients (79%) admitted at an outside institution and secondarily referred to our tertiary center were transferred within a median time of 17.2 days from onset of necrotizing pancreatitis (range 1 day to 54 days).

Evolving treatment strategy

Three hundred and ninety patients (74.1%) required surgical debridement over the course of their disease, 247 (46.9%) of them as the only treatment, and 143 (27.2%) as part of a combined treatment. Necrosectomy was performed via an open approach in 356 patients (91.3%), a laparoscopic approach in 25 patients (6.4%), and via a video-assisted retroperitoneal approach in 9 patients (2.5%). Overall 193 patients (36.7%) underwent non-surgical therapy with interventional radiology or endoscopic drainage. Fifty (9.5%) were treated with those minimally invasive approaches alone. Over the study period, 136 patients (25.9%) recuperated with supportive therapy, without need for intervention.

Over time, the percentage of NP patients managed without surgical intervention increased from 28% to 41%. Treatment strategies of NP patients are broken down by year in **Figure 1**.

Figure 2 shows overall treatment modality.

Of the 424 patients referred secondarily to our institution, only 19 (4.5%) had some

intervention at the outside institution, beside from medical/supportive management. Fifteen patients (3.5%) had surgery at the outside hospital, whereas the remaining 4 (1%) had percutaneous drainage with interventional radiology.

In-hospital mortality/year ranges from 8.1% in 2005 to 5.4% in 2014, which is consistent with data from the literature that describes an in-hospital mortality between 2 and 39%^{5,6}. When in-hospital mortality for the first 5 years (2005-2009) was compared to the one for the last five years (2010-2015), there was a statistically significant decrease from 6.4% to 4.1% ($p < 0.001$).

DISCUSSION

Necrotizing pancreatitis is a heterogeneous disease, and therapy of NP must be individualized to specific patient characteristics, including necrosis distribution. Our multidisciplinary group consists of expert endoscopists, interventional radiologists, and pancreatic surgeons. We utilized multiple approaches to NP treatment in this contemporary period, with multiple modality (combined) approaches were used more frequently in later years. Over this time, the number of NP patients treated without surgical debridement increased from 28% to 41%.

Necrosis of the pancreatic parenchyma or peripancreatic parenchyma may resolve on its own, or may persist without causing disability. Few data exist to document the incidence of necrosis resolution without treatment; in the current series, approximately 20% of patients recuperated without need for intervention, and this number remained relatively consistent over time.

Minimally invasive approaches to NP treatment were introduced nearly two decades ago; recently these techniques (IR directed treatment and endoscopic necrosectomy) have been applied with greater frequency.⁷⁻⁹ Over the time period of this study, we found more liberal use of percutaneous IR treatment (often as the first treatment in a step-up approach⁷) as well as the introduction of endoscopic necrosectomy. Endoscopic necrosectomy has been embraced, but applied sparingly in our institutional experience, likely reflecting highly select indications, as well as liberal use of surgical transgastric debridement.¹⁰ Nearly half of our NP patients have a biliary etiology; surgical transgastric necrosectomy in these patients permits definitive therapy of contained retrogastric necrosis as well as cholecystectomy (with cholangiography) in one procedure under one general anesthetic.

We have also utilized percutaneous drainage of NP more frequently over the past decade, often as a first step in patients who ultimately require multiple modality approach. While applied more commonly, IR drainage proved to be definitive treatment for a smaller percentage (approximately 10%) than has been reported elsewhere in the literature^{9,11,12}. This finding may reflect the complex nature of NP patients referred to our tertiary pancreas center.

Surgical debridement has long been the mainstay of treatment for NP.^{2,3,13} In our practice, operative surgical debridement continues to play an important treatment role for NP patients. We have applied minimally invasive surgical techniques to transgastric debridement, laparoscopic transabdominal debridement, and retroperitoneal debridement with increasing frequency. Importantly, these approaches are individualized based on specific patient characteristics including necrosis distribution, physiologic condition, and failure to progress after other treatment (most commonly percutaneous drainage).¹⁴ Over this time period we witnessed a significant increase in the number of NP patients successfully *without* surgery; the relatively high number that still require operative debridement (>50%) likely reflects the highly complex nature of patients referred to our tertiary center. These complex clinical scenarios include patients who have failed other therapies, as well as those with pancreatic head necrosis and necrosis tracking down paracolic gutters and the root of the small bowel mesentery.

This single institution retrospective series may reflect some selection bias, as patients treated with any intervention are easier to track than patients treated by supportive care alone. Nevertheless, our prospectively collected NP database is robust, and does include these medically treated patients. The purpose of this report was simply to evaluate trends in treatment over a time period where minimally invasive treatments have been applied more commonly, and we specifically did not focus on patient outcomes. Two studies are currently under way at our institution, analyzing specific morphology of necrosis and subsequent management, and specifically focusing on long-term outcomes of patients with necrotizing pancreatitis. Those studies will help further understand the natural history and long-term outcomes of this multi-faceted disease.

In conclusion, necrotizing pancreatitis is a complex and heterogeneous disease. Treatment must be individualized to specific patients based on their disease process and anatomic distribution of necrosis. Select patients will recuperate with supportive care alone, percutaneous drainage alone, or endoscopic debridement. Many patients will require more than one modality to effect disease resolution, and

operative debridement continues to play an important role in management of these patients. Evaluation by a multidisciplinary treatment team composed of experienced gastroenterologists, surgeons, and interventional radiologists is crucial for treatment planning and to achieve optimal patient outcomes.

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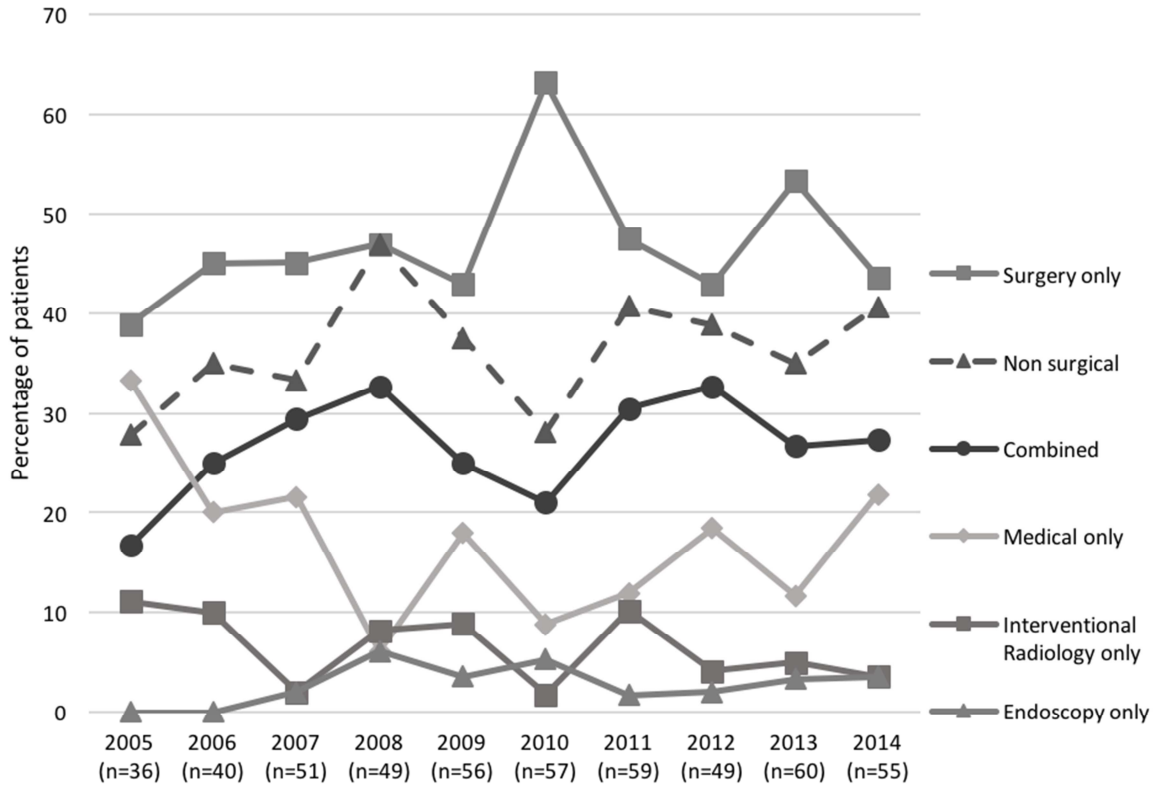
Figure 1. Evolution of management strategy for necrotizing pancreatitis

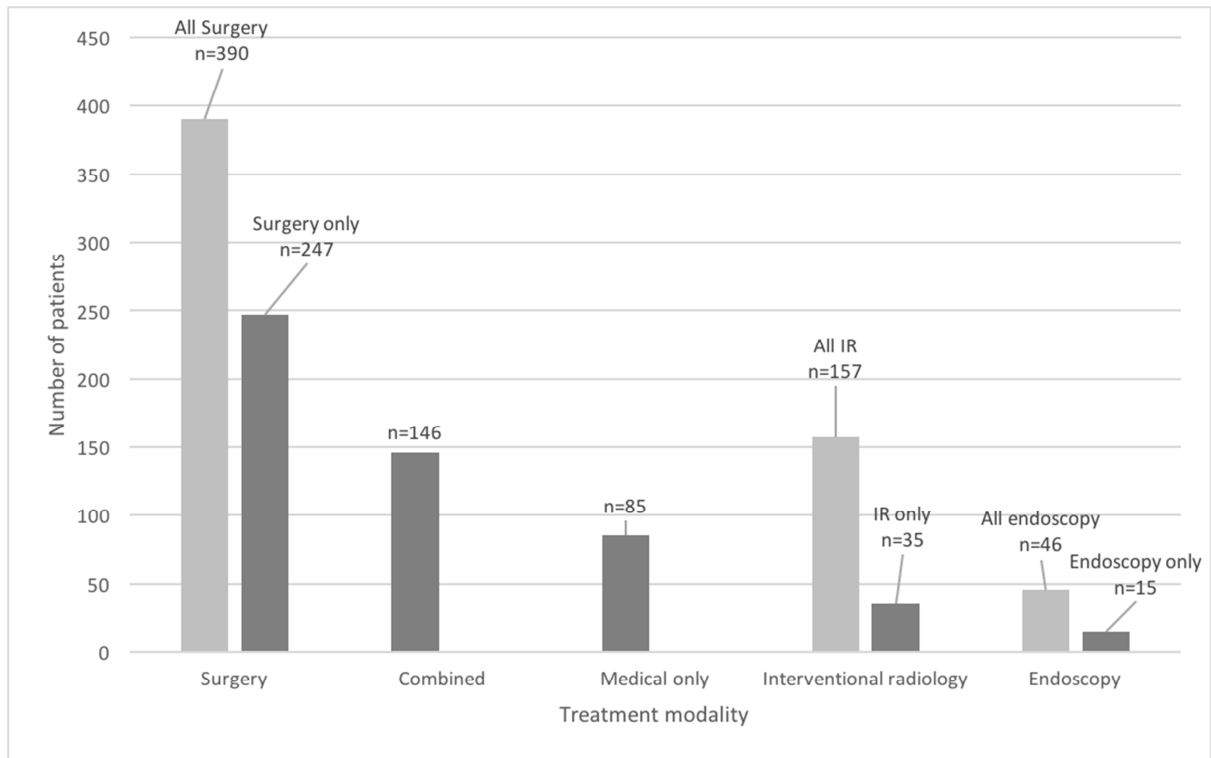
Figure 2. Overall treatment modality over the entire study period

Footnote:

IR: Interventional radiology

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Research highlights

- Optimal management of necrotizing pancreatitis (NP) remains unclear
- Over the past decades, management of NP has become multidisciplinary
- Select NP patients may be managed exclusively by medical, IR, or endoscopic treatment.
- Combination treatment is necessary in many NP patients
- Surgical treatment continues to play an important role in the definitive therapy of necrotizing pancreatitis patients.