

Necrotizing Pancreatitis 2010

An Unfinished Odyssey

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In comparison to its higher profile cousin pancreatic cancer, acute pancreatitis (AP) often seems to get shortchanged. Perhaps this is due to the (still) poorly understood pathophysiology, lack of specific medical therapy, long-term challenge of treating patients with severe AP, or relative paucity of dedicated treatment units (after all, what rational surgeon wants to hang out their shingle as a pancreatitis doctor?). Nevertheless, the fact remains that compared with pancreatic cancer, each year more than 6 times as many Americans—240,000 in all—are affected by AP.^{1,2} AP is clearly a substantial clinical problem.

Approximately 15% to 20% of patients with AP will develop a severe disease course, with variable necrosis of the pancreatic parenchyma and peripancreatic soft tissue. Despite advances in critical care therapy and improved understanding of managing patients with AP, the mortality of patients with necrotizing pancreatitis (NP) reported in many contemporary series continues to hover around 20%. NP is not a “benign” disease.

Many patients who succumb to AP do so within the first 2 weeks of disease onset, typically from overwhelming multiorgan failure.³ Patients who survive the initial insult of AP present a formidable clinical challenge; current management of just these patients is the focus of reports in this issue of the *Annals* from 2 established pancreatic units in the United Kingdom.

Babu et al from Manchester present a 7½-year experience, published in this issue of *Annals of Surgery*, of 28 patients treated exclusively by open necrosectomy.⁴ In contrast, Raraty et al from Liverpool, also published in this issue of *Annals*, document an 11-year experience treating 189 NP patients.⁵ The Liverpool group have been committed leaders in minimally invasive necrosectomy, as is evidenced by the fact that 137 (72%) of these patients were approached with a minimally invasive technique—minimal access retroperitoneal pancreatic necrosectomy (MARPN).

In addition to the intriguing aspect of minimally invasive necrosectomy, data from both of these studies inform other contemporary topics of discussion in pancreatitis. The overall mortality in both of these studies (22% and 24%) is in line with other recent reports, and emphasizes the severity of this disease process. Late mortality observed in both series highlights the need for long-term follow-up of these patients to provide accurate, clinically important measures of mortality.

The presence of infection in (peri) pancreatic collections was the predominant indication for operation in both series (Liverpool 69%, Manchester 82%), although the fact that 71% of patients in the Manchester series underwent preoperative percutaneous drain placement (and not simply fine needle aspiration) surely effected their findings. Both groups follow the currently accepted practice of allowing time for maturation of necrosis. This is evidenced by the time between disease onset and operation of 34 and 32 days.

The routine use of prophylactic antibiotics in patients with pancreatic necrosis remains controversial despite the conduct of 7 prospective, randomized controlled trials. Many groups (including the Liverpool unit and our own group at Indiana University) have moved away from routine prophylactic antibiotic administration. Others, including the Manchester group, continue this practice. At referral centers, most patients with NP are received in transfer after some period of treatment (generally including antibiotic administration) at local hospitals. This finding is true in both of these series (Manchester 86%, Liverpool 69%), and highlights the challenge in assessing antibiotic treatment effect outside the aegis of controlled clinical trials.

In 2010, open pancreatic necrosectomy remains a viable option (and indeed, first line treatment) for many pancreatic surgeons. Patients in Manchester undergoing open pancreatic necrosectomy had excellent outcomes. The authors of this report must also be commended for providing the denominator of all patients with AP treated during the time of this analysis, a number frequently missing in other reports. In line with other recent series, 10% of all patients with AP were treated in the Manchester ICU (ICU treatment presumably being used a surrogate to define those

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patients with severe NP). Surprisingly few of these ICU patients, however, (19%) required definitive intervention in the form of operation. This raises several questions about the remainder of this cohort. What percentage of patients resolved their illness without intervention? Did a percentage of patients respond to percutaneous drainage alone? Were a percentage of patients judged “too sick” to survive operation, and died without intervention? Although difficult to track retrospectively, these data are necessary to provide a more complete understanding of the complete spectrum of disease biology.

In 2010, minimally invasive pancreatic necrosectomy is also a viable treatment option for pancreatic surgeons (and indeed, in Liverpool, this approach represents the current first line of treatment for most patients). Comparing patients with MARPN and those undergoing open necrosectomy, the Liverpool group highlight decreased postoperative acute physiology and chronic health evaluation (APACHE) II scores (8 vs. 11), reduced need for postoperative ICU stay (43% vs. 77%), decreased postoperative morbidity (55% vs. 83%), and significantly decreased mortality (19% vs. 38%) in the MARPN group. These findings must be taken on balance: the MARPN group also had lower preoperative APACHE II scores and a lower incidence of preoperative organ failure. Patients undergoing MARPN also required more procedures and had a longer overall hospital and postoperative length of stay.

The tantalizing conclusion that MARPN “may offer significant benefits for the patient when compared with a traditional open necrosectomy” must be interpreted cautiously. At their base, these 2 groups of patients are different, as evidenced by the fact that patients treated with open necrosectomy not only had severe preoperative illness severity, but also were those with pancreatic head and neck necrosis (and thus not amenable, even in the later years of the study, to MARPN). The authors acknowledge this limitation of their analysis, and must be commended for equalizing these differences as fairly as possible with intention-to-treat analysis, and by forcing imbalanced criteria into their multifactorial statistical analysis.

Nevertheless, proof of the concept that minimally invasive necrosectomy offers clinical benefits relative to open necrosectomy will require direct, prospective comparison of these 2 modalities in a balanced patient population. To this end, the multicenter, prospective Dutch PANTER trial evaluates precisely this question; results from this trial are eagerly anticipated.⁶

It must be noted that the report from Liverpool represents the largest series of minimally invasive pancreatic necrosectomy currently available, and provides a great deal of important information. Their experience makes clear that the minimally invasive technique is applicable to a large portion of patients with NP. Although a

learning curve with this operation exists, these experienced pancreatic surgeons were able to ascend it quickly both from a technical standpoint (fewer “conversions” in the later time period) and with regard to patient selection (recognizing that patients with head/neck necrosis are not good candidates for the minimally invasive approach). Finally, the importance of a decreased physiologic insult must not be minimized. It is quite conceivable that increasing comfort with minimally invasive necrosectomy will be mirrored by shorter length of stay.

This report also raises several important questions about minimally invasive necrosectomy. First, of course, is the question of whether this technique will provide short- and long-term advantages in patient outcomes and cost compared with open necrosectomy. Second, which patients will benefit?—perhaps not those with necrosis of the pancreatic head. And finally, since this is a highly specialized technique with a discrete learning curve and performed in a complex population of patients, which surgeons exactly should attempt minimally invasive necrosectomy?

So what is the take home message? In 2010, open pancreatic necrosectomy remains a viable option to treat patients with NP. Minimally invasive necrosectomy (and MARPN in particular) is safe and applicable to a large proportion of patients with NP. The questions of whether minimally invasive necrosectomy offers advantages over the open technique, which patients may benefit from minimally invasive necrosectomy, and which surgeons should perform this operation remain open.

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