Minimal Access Retroperitoneal Pancreatic Necrosectomy

Improvement in Morbidity and Mortality With a Less Invasive Approach

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Objective: Comparison of minimal access retroperitoneal pancreatic necrosectomy (MARPN) versus open necrosectomy in the treatment of infected or nonresolving pancreatic necrosis.

Summary of Background Data: Infected pancreatic necrosis may lead to progressive organ failure and death. Minimal access techniques have been developed in an attempt to reduce the high mortality of open necrosectomy.

Methods: This was a retrospective analysis on a prospective data base comprising 189 consecutive patients undergoing MARPN or open necrosectomy (August 1997 to September 2008). Outcome measures included total and postoperative ICU and hospital stays, organ dysfunction, complications and mortality using an intention to treat analysis.

Results: Overall 137 patients underwent MARPN versus open necrosectomy in 52. Median (range) age of the patients was 57.5 (18–85) years; 118 (62%) were male. A total of 131 (69%) patients were tertiary referrals, with a median time to transfer from index hospital of 19 (2–76) days. Etiology was gallstones or alcohol in 129 cases (68%); 98 of 168 (58%) patients had a positive culture at the first procedure. Of the 137 patients, 34 (31%) had postoperative organ failure in the MARPN group, and 39 of 52 (56%) in the open group ($P < 0.0001$); 59/137 (43%) versus 40/52 (77%), respectively, required postoperative ICU support ($P < 0.0001$). Of the 137 patients 75 (55%) had complications in the MARPN group and 42 of 52 (81%) in the open group ($P = 0.001$). There were 26 (19%) deaths in the MARPN group and 20 (38%) following open procedure ($P = 0.009$). Age ($P < 0.0001$), preoperative multiorgan failure ($P < 0.0001$), and surgical procedure (MARPN, $P = 0.016$) were independent predictors of mortality.

Conclusion: This study has shown significant benefits for a minimal access approach including fewer complications and deaths compared with open necrosectomy.

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Acute pancreatitis is a common condition with the potential to cause significant morbidity and mortality. Incidence rates vary widely between studies because of differences in geographical and etiological factors but have tended to increase over time,[1] and rates of more than 70 cases per 100,000 population per year have been reported from some studies.[2,3] United Kingdom studies tend to report a lower overall incidence,[1] because of a lower level of alcohol consumption, but the trend of increasing incidence with time is still apparent.[4,5]

Most patients with acute pancreatitis suffer only a mild attack, without local or systemic complications as defined by the Atlanta criteria.[6] Approximately 20% of patients, however, will suffer a severe attack with associated morbidity and a mortality rate between 17% and 39%.[7–10] The predominant feature of the patients who have severe acute pancreatitis is the development of pancreatic necrosis,[11,12] which tends to peak between weeks 2 and 4.[13] In 40% to 70% of these patients, the pancreatic necrosis will become infected[14] and unlike sterile necrosis, which can be treated conservatively in the majority of cases,[15] it requires adequate debridement and drainage via surgical or radiologic means.[16–18] Failure to adequately control infected pancreatic necrosis results in an almost 100% mortality because of overwhelming organ failure.[19,20] Of 340 patients in the study by Götzinger et al,[19] there were 94 patients in whom surgery failed to clear the necrosis, and in this group the mortality rate was 100% (almost exclusively because of multiorgan failure), yet in the 246 patients in whom successful debridement was achieved the mortality rate was only 19%. Similarly, the introduction of surgery for infected pancreatic necrosis at the Mayo clinic resulted in a fall in mortality from 70% to 20%.[21]

It is generally considered that delayed rather than early intervention is preferable in those with pancreatic necrosis.[22–24] It is also widely accepted that sterile necrosis in the absence of significant symptoms does not require routine debridement,[16,18] but most authorities still recommend urgent debridement for infected necrosis.[18,25,26] Infected necrosis develops over time, peaking at approximately 3 weeks after disease onset.[13] Patients with infected necrosis tend to have more necrosis and worse organ failure than those with sterile necrosis and hence an increased mortality.[20,27] Because increasing severity of illness at the time of intervention is directly associated with an increasing mortality it is now common practice to monitor patients with significant pancreatic necrosis for signs of infection and intervene urgently if and when such infection becomes apparent.[9,19,26]

The techniques for necrosectomy include open necrosectomy, laparostomy and closed packing with or without lavage,[23,28–31] and minimal access techniques via laparoscopy[32–34] or endoscopy.[35–37] Published mortality rates for open necrosectomy range from 6%[23] to 47%,[24] but it is difficult to compare studies directly because of differences in patient populations, entry criteria, and surgical techniques. Half of the reported series are of less than 50 patients each, whereas only 11 series have reported on 100 patients or more with a median (IQR) reported mortality of 19% (13.5%–26.35%), see Table 1.[19,27,38-48]

The Liverpool Pancreas Centre adopted a minimal access retroperitoneal technique for pancreatic necrosectomy in 1998,[8,9,49] and we now present a retrospective investigation on our experience

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TABLE 1. Large Published Series of Open Pancreatic Necrosectomy

Author	Year	No. Patients	No. Deaths	Mortality (%)
Borie et al[38]	1994	157	28	17.8
Armbruster et al[39]	1998	108	30	27.8
Bradley[40]	1999	176	23	13.1
Kriwanek et al[41]	1999	100	19	19.0
Gotzinger et al[19]	2002	340	133	39.1
Rau et al[27]	2005	285	71	24.9
Farkas et al[42–45]	2006	281	39	13.9
Olakowski et al[45]	2006	126	26	20.6
Reddy et al[46]	2006	118	45	38.1
Howard et al[47]	2007	102	12	11.8
Rodriguez et al[48]	2008	167	19	11.4

this technique over an 11-year period using a prospective data base with an intention to treat analysis.

PATIENTS AND METHODS

Details of all patients undergoing pancreatic necrosectomy have been kept in a prospectively maintained database at the Regional Pancreas Centre, Department of Surgery, University of Liverpool and Royal Liverpool University Hospital since August 1997.

Patients with predicted or actual severe acute pancreatitis (as defined by the Atlanta criteria[6]) were managed according to the United Kingdom and International Association of Pancreatology guidelines[16,18] with the exception of prophylactic antibiotics, which are not used routinely in our institution. Antibiotics were only employed as treatment of proven infection and prophylactic antibiotics started at another unit were discontinued on transfer of the patient, in line with recent findings on the lack of benefit for antibiotic prophylaxis.[50,51] Endoscopic sphincterotomy was performed in all patients with severe disease of biliary etiology (presence of gallstones, dilated bile ducts, high bilirubin, or an elevated alanine transaminase of $\geq$60 IU/L within 48 hours of admission).[52]

Contrast enhanced computed tomography (CE-CT) was performed 3 to 5 days after onset of symptoms or soon after transfer for tertiary referrals, to identify the extent of pancreatic or peripancreatic necrosis. The Balthazar radiologic severity score[53] was calculated and the highest scores recorded. CT-guided fine needle aspiration for bacteriology (CT-FNAB) was performed in patients with more than 30% necrosis in the second week after the onset of symptoms and thereafter at weekly intervals depending on clinical status and serum CRP levels. The aspirates were sent for Gram staining, bacteriology, and fungal culture. Positive FNAB stain or culture or extraintestinal gas on CE-CT were taken as indications for urgent necrosectomy. In addition, patients with sterile necrosis but persisting systemic or local symptoms despite 3 to 4 weeks of maximal conservative treatment were also offered surgery.

Preoperative data recorded included demographic data, the maximal extent of pancreatic necrosis as defined by CE-CT, the degree of physiological disturbance on hospital admission and immediately preoperatively as measured by the Acute Physiology and Chronic Health Evaluation (APACHE) II score,[54] organ dysfunction score,[55] and serum C-reactive protein (CRP).[56] Physiological and organ dysfunction scores were also repeated 24 hours postoperatively. Outcome measures recorded were total and postoperative hospital and ICU stays, postoperative organ dysfunction, complications, and mortality. Routine care included enteral feeding in preference to parenteral nutrition where feasible, and antibiotics to treat identified infections.

Surgical Techniques

The surgical technique employed for MARPN has been previously described in detail.[49,57] Briefly, access to the necrotic cavity is obtained via the left flank and a 12F pigtail catheter inserted under CT-guidance. The patient is transferred to the operating theater and placed in a supine position on the operating table, but with a sandbag under the left side to elevate the access track to a roughly horizontal position. Under x-ray screening and general anesthesia, the catheter is exchanged over a guide wire for serial renal dilators and the track dilated to 30F. An operating nephroscope with a wide-bore operating channel (initially Wolf, later Storz) is then used to access the necrosis and this is removed piecemeal with forceps. Samples of the removed necrosis are sent for microbiological examination. Following initial debridement, an irrigating drain, consisting of a 28F chest drain and 10F nasogastric tube sutured together, is inserted into the cavity and 0.9% saline solution used to irrigate the cavity continuously at a rate of 125 mL/h. The patients are carefully monitored postoperatively, using serial CE-CT scans and CRP measurements to follow disease progress. Repeated debridements are performed at 7- to 10-day intervals until the necrosis cavity is seen to be clear and lined by healthy granulation tissue. As a general rule, the initial procedure involving dilatation of the track is performed under general anesthetic with subsequent procedures performed using local anesthetic with or without light sedation (patient preference). In patients with severe comorbidity such as aortic stenosis local anesthetic can be used from the outset. In some patients, more than one access track is created to gain access to all the necrosis—access from the right side or anteriorly is technically more challenging but feasible as long as the distance between the abdominal wall and necrosis is not too great. Once the necrosis has been cleared, the irrigation is stopped and the patient discharged home with a simple tube drain left in situ. This is later removed during regular outpatient follow-up.

The technique used for open necrosectomy is that described by Beger et al.[28] The lesser sac is entered via either the gastro-colic omentum or the transverse mesocolon and blunt, finger dissection used to remove the necrotic pancreatic tissue. Irrigating drains similar to those described for MARPN are inserted into the cavity and follow-up follows a similar pattern to that described above.

After discharge, all patients were followed up at the Regional Pancreas Clinic monthly for the first 3 months, 3 monthly up to 1 year and annually thereafter. Pancreatic fistula during follow-up was defined as a persistent discharge of amylase rich fluid for more than 2 weeks once all of the drains were removed. Pancreatic endocrine insufficiency was diagnosed on the basis of an abnormal oral glucose tolerance test (once the patient had recovered from their acute illness). Pancreatic exocrine insufficiency was diagnosed on the basis of clinical symptoms of steatorrhoea and fecal elastase-1 estimation.

Having learnt the technique of MARPN in 1998, we have tried to apply it in all cases unless there was felt to be no safe percutaneous route into the necrosis or there was some other indication for open surgery.

Statistical Analysis

Comparisons between MARPN and open necrosectomy were performed on an intention to treat basis. Median and range are used to describe continuous data, and categorical data are summarized with frequency counts and percentages. The χ^2 test and the Fisher exact test probability test were used for categorical data analysis and the 2-tailed Mann-Whitney U test was used for continuous data analysis. Multivariable logistic regression was used to assess which preoperative risk factors (age, gender, tertiary referral, pancreatic infection, $>$50% necrosis, preoperative ICU admission, preoperative

multiorgan failure, and type of surgery) were significant in predicting mortality when taken in combination. Any variables that were significantly associated with survival at the univariable level ($P < 0.1$) were selected for potential entry into the multivariable model. A backwards stepwise selection procedure was used to determine the final model (criteria for entry $P < 0.05$ and for removal $P > 0.05$), with forced entry of any factors that were considered to be clinically and/or statistically significantly imbalanced between the 2 groups at baseline. We used Stata version 8.2, Statsdirect version 2.6.2 and SPSS version 15.0 software for this analysis.

RESULTS

Between August 1997 and September 2008, a total of 189 patients underwent pancreatic necrosectomy at the Royal Liverpool University Hospital (Fig. 1). Initially, these were all performed as open procedures, but since 1998 increasing numbers of minimal access procedures were performed as experience was gained. A total of 137 patients had an attempted MARPN and 52 had a primary open necrosectomy (Table 2). There were no statistically significant differences in demographics between those patients undergoing MARPN or open surgery (Table 2). In general, this was the case for all preoperative findings between the 2 groups although those patients undergoing MARPN had a lower preoperative APACHE II score than those undergoing open surgery, (8 vs. 10, $P = 0.038$), and a trend toward a lower incidence of preoperative multiorgan failure (26% vs. 38%, $P = 0.144$). It was, however, noted that there was no difference between admission APACHE II score or need for preoperative ICU care (Table 3). The overall median (range) age of the patients was 57.5 (18–85) years; 118 (62%) were male. Overall 131 (69%) patients were tertiary referrals, with a median time to transfer from index hospital of 19 (2–76) days. Etiology was gallstones or alcohol in 129 cases (68%).

Of 166 patients, 115 (69.3%) were operated on for suspected or proven infected necrosis (positive FNA in 43; clinical/radiologic suspicion of infection in 72). The remainder were operated on for persistent SIRS/failure to improve with optimal ICU care. Overall 107 of 166 (64.5%) patients had proven infection at the time of first operation either on preoperative FNA or on operative specimens taken at the time of surgery. Only 44 were sterile at the time of first surgery (26.5%) (15 inadequate data). About 18 (10.7%) had fungal infection; 111 (58.7%) of the patients had received prophylactic antibiotics (Table 3). Invariably all patients had positive cultures postoperatively. One hundred and ten patients (58%) had >50% necrosis at the time of surgery with a median (range) Balthazar severity score of 9 (3–10). Fifty-six patients (29.6%) had multiorgan failure preoperatively and 75 (39.7%) required ICU admission. Median (range) APACHE II score on admission was 10 (1–31) and median (range) admission CRP was 260 (5–577) mg/L. Immediately prior to surgery these values were 9 (1–29) and 186 (5–526) mg/L, respectively. The median (range) time to surgery from index admission was 32 (1–181) days.

Of the 137 patients in whom MARPN was attempted, 19 (13.9%) required conversion to an open procedure or an additional open procedure; 6 because of an inability to place the initial guide-wire or to dilate the track (all of these were in the early years of our experience), 4 because of bleeding, 4 because of the presence of remote or inaccessible collections not amenable to percutaneous drainage, 2 for secondary colonic necrosis, 2 because of ischemic colitis requiring resection, and 1 with a colonic fistula requiring defunctioning ileostomy. For the purposes of statistical analysis,

TABLE 2. Demographic Data

	MARPN	Open	*P*
No. patients	137	52	
Median (range) age, yr	56 (18–83)	59 (19–85)	0.696
Male:female	82:55	36:16	0.312
Tertiary referral (%)	99 (72.8)	32 (61.5)	0.157
Median (range) time to transfer, d	17 (2–73)	24.5 (2–76)	0.157
Etiology			0.186
Alcohol	38 (27.7%)	17 (32.7%)	
Stones	54 (39.4%)	20 (38.5%)	
ERCP	4 (2.9%)	6 (11.5%)	
Idiopathic	15 (10.9%)	9 (17.3%)	
Other	4 (2.9%)	0	
Unknown	22 (16.1%)	0	

TABLE 3. Preoperative Data

	MARPN n = 137	Open n = 52	*P*
Culture-proven pancreatic infection at first operation	74/116 (64%)	33/46 (72%)	0.336
Fungal infection	14/121 (12%)	4/45 (9%)	0.337
Prophylactic antibiotics	75 (55%)	36 (69%)	0.101
Median (range) maximum CT score	9 (4–10)	9 (3–10)	0.199
>50% necrosis	79 (58%)	31 (60%)	0.938
ICU preoperatively	53 (39%)	22 (42%)	0.773
Median (range) initial APACHE II score	10 (2–31)	9 (1–17)	0.341
Median (range) preoperative APACHE II score	8 (1–29)	10 (2–20)	0.038
Preoperative MOF present	36 (26%)	20 (38%)	0.144
Median (range) initial CRP, mg/L	268 (31–577)	234 (17–508)	0.152
Median (range) preoperative CRP, mg/L	162 (5–490)	216 (5–526)	0.682
Median (range) time to surgery, d	32 (1–181)	34 (1–95)	0.745

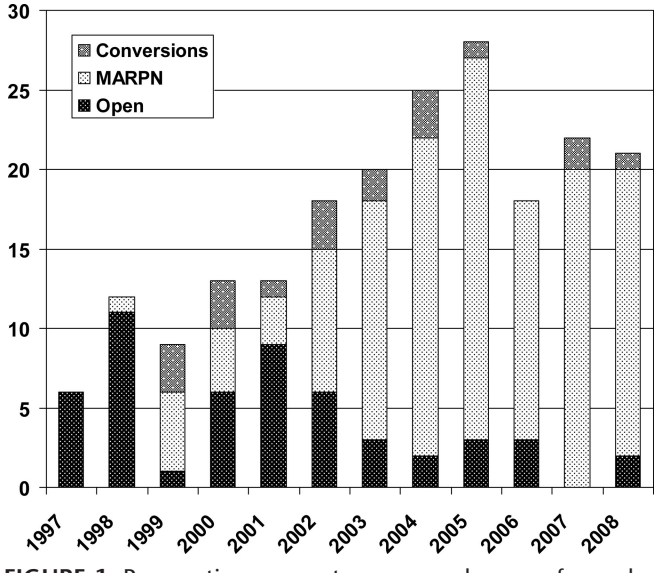

FIGURE 1. Pancreatic necrosectomy procedures performed and conversion rate over a 10-year period in one institution..

TABLE 4. Postoperative Findings

	MARPN n = 137	Open n = 52	*P*
Postoperative MOF present	34 (31%)	39 (56%)	<0.0001
Median (range) postoperative APACHE II score	8 (1–22)	11 (2–24)	0.0006
Median (range) postoperative CRP, mg/L	173 (8–443)	216 (33–378)	0.142
Number of patients with one or more complications	75 (54.7%)	42 (80.8%)	0.001
Mortality	26 (19%)	20 (38%)	0.009
Median (range) time to death, d	77 (16–252)	47.5 (13–222)	0.099
Median (range) time to death postsurgery, d	51 (5–220)	16 (1–164)	0.091
Median (range) time to discharge, d	96 (29–300)	89 (8–180)	0.139
Median (range) time to discharge postsurgery, d	64 (15–272)	43 (5–158)	0.004
Median (range) length of stay—all patients, d	94.5 (16–300)	85 (8–222)	0.011
Median (range) stay postsurgery—all patients, d	60 (5–272)	36 (1–164)	0.0002
Number of patients needing ICU postoperatively	59 (43%)	40 (77%)	<0.0001
Median (range) ICU stay for those needing ICU only	15 (1–118)	10 (1–82)	0.299
Median (range) no. procedures	3 (1–9)	1 (1–9)	<0.0001

TABLE 5. Complications

	MARPN n = 137	Open n = 52	*P*
Myocardial infarct	4 (2.9%)	5 (9.6%)	0.122
Cerebrovascular event	2 (1.5%)	2 (3.8%)	0.652
Pseudocyst	3 (2.2%)	5 (9.6%)	0.063
Bleeding	16 (11.7%)	9 (17.3%)	0.436
Biliary stricture	3 (2.2%)	5 (9.6%)	0.253
Pancreatic fistula	5 (3.6%)	4 (7.7%)	0.434
Enteric fistula	10 (7.3%)	5 (9.6%)	0.865
Pulmonary embolus	1 (0.7%)	1 (1.9%)	0.621
Colonic necrosis	4 (2.9%)	3 (5.8%)	0.621
Hepatic portal/superior mesenteric/splenic vein thrombosis	7 (5.1%)	4 (7.7%)	0.741
Clostridium difficile infection	4 (2.9%)	1 (1.9%)	0.893
Miscellaneous	10 (7.3%)	8 (15.4%)	0.313
Total	69 in 75 patients (55% of patients)	52 in 43 patients (83% of patients)	

TABLE 6. Univariable Logistic Regression: Risk Factors for Death

Variable	Odds Ratio (95% Confidence Interval)	*P*
Age (yr)	1.06 (1.03, 1.09)	<0.0001
Sex	1.37 (0.68, 2.74)	0.376
Tertiary referral	1.06 (0.49, 2.46)	0.825
Pancreatic infection	1.39 (0.67, 2.91)	0.379
>50% necrosis	0.75 (0.32, 1.77)	0.509
ICU preoperatively	2.4 (1.16, 4.95)	0.018
Preoperative multiorgan failure	6.62 (3.02, 14.51)	<0.0001
MARPN	0.385 (0.19, 0.78)	0.008
Preoperative APACHE II score	1.13 (1.05, 1.22)	0.001

however, all of these patients are included in the MARPN group on an intention-to-treat basis. Three patients had had a previous laparotomy at the referring hospital prior to transfer: in one, the diagnosis of pancreatitis was only made at emergency laparotomy but no necrosectomy was performed; in the second, a laparostomy was performed for abdominal compartment syndrome, but again, no necrosectomy was performed; in the third, an open necrosectomy had been performed but there was evidence of residual infected necrosis on transfer. In all 3 patients, it was felt that a minimal access route to the residual necrosis would be easier and safer than a further attempt at laparotomy.

Postoperatively, 73 patients (38.6%) had multisystem organ failure with a median (range) postoperative APACHE II score of 8 (1–24) and median (range) postoperative CRP of 174 (8–443) (Table 4). Ninety-nine patients (52.4%) required ICU treatment postoperatively with a median (range) ICU stay postsurgery of 13 (1–118) days. Forty-six patients (24.3%) died a median (range) of 37 (1–220) days after surgery. Patients undergoing minimal access retroperitoneal pancreatic necrosectomy required more procedures than those having an open necrosectomy: median (range), 3 (1–9 procedures) versus 1 (1–9) by open surgery; $P < 0.0001$; and MARPN was associated with a longer overall hospital stay and a longer stay postsurgery: median (range); 94.5 (16–300) versus 85, (8–222) $P = 0.011$ and 60 (5–272) versus 36, (1–164) $P = 0.0002$, respectively. The survivors left hospital a median (range) of 57 (5–272) days after surgery. Deaths were due to multisystem organ failure in 32 cases, myocardial infarction in 4 cases, bleeding in 4 cases, colonic necrosis in 2 cases and 1 each of: cerebrovascular incident, perforated colon cancer, necrotising fasciitis, and multiple metastases.

The MARPN patients had a much lower incidence of postoperative organ failure (34/137, 31% vs. 39/52, 56%; $P < 0.0001$) and a lower postoperative APACHE II score (median 8 vs. 11; $P = 0.0006$) than those patients undergoing open necrosectomy. Fewer of the MARPN patients required ICU care postoperatively (59/137, 43% vs. 40/52, 77%; $P < 0.0001$). In particular, the mortality in the MARPN group was significantly lower than in the open necrosectomy group (26/137, 19% vs. 20/52, 38%; $P = 0.009$) (Table 4). Overall, 118 (62.4%) of patients developed complications (Table 5). More patients in the open group suffered complications (43/52, 82.7% vs. 75/137, 54.7%; $P = 0.0007$). Six of the 137 patients who had MARPN had the initial procedure under local anesthetic as they were deemed too unwell for a general anesthetic. Of these patients, 5 survived.

Table 6 shows the results of the univariable logistic regression analysis. Age, preoperative ICU admission and multiorgan failure were highly significant predictors of mortality along with MARPN at the univariable level. When these variables were assessed in the multivariable backward selection procedure (with preoperative APACHE II scores forced into the model because of baseline imbalance between groups), all except preoperative ICU admission, and APACHE II (because of their high correlation with preoperative multiorgan failure) remained highly significant (Table 7). Thus MARPN was found to be an independent predictor of mortality ($P = 0.016$) along with age ($P < 0.0001$) and preoperative multiorgan failure ($P < 0.0001$).

TABLE 7. Multivariable Logistic Regression: Independent Risk Factors for Death (With Forced Entry of Variables Imbalanced Between Groups at Baseline)

Variable	Odds Ratio (95% Confidence Interval)	*P*
Age (yr)	1.07 (1.04, 1.11)	<0.0001
Preoperative multiorgan failure	8.67 (3.01, 25.0)	<0.0001
MARPN	0.31 (0.12, 0.81)	0.016
Preoperative APACHE II score	1.00 (0.90, 1.10)	0.939

DISCUSSION

Although there is some anecdotal evidence that selected patients can be managed conservatively,[26,58] the gold standard of treatment for patients with infected pancreatic necrosis remains open pancreatic necrosectomy. Open necrosectomy for infected necrosis carries substantial risks, however, with mortality rates of up to 40% to 50% reported even from specialist centers (Table 1).[19,24,27,38-48,59-61] The physiological stress to the patient of severe acute pancreatitis with infected necrosis is further exacerbated by the 'second hit' of a laparotomy and open necrosectomy.

A number of less invasive surgical techniques have therefore been developed in an attempt to minimize the excess disturbance of necrosectomy. A laparoscopic approach with 3 different approaches (retrogastric retrocolic debridement, a full retroperitoneoscopic approach, and transgastric drainage) was first used in the early 1990'sand subsequently used in conjunction with radiologic, percutaneous drainage or hand-assisted laparoscopy.[32–34,62–66] A variety of endoscopic, transgastric,[35,37,67–70] and percutaneous radiologic[71–75] approaches have also been used for drainage/removal of pancreatic necrosis. To obtain good access, percutaneous procedures have often required general anesthetic and dilatation of the track up to 28F with multiple procedures being required—averaging 17 (range, 7–32) in the series by Echenique et al.[73] A variety of instruments passed along access tracks have been used to examine the debrided cavity to ensure completeness of removal of necrosis including a bronchoscope,[75] a mediastinoscope,[76] laparoscope,[77,78] a flexible endoscope,[79,80] and as in our practice an operating nephroscope.[81–86]

It is difficult to compare the different series because key predictors of mortality such as extent of pancreatic necrosis, infection (at the first procedure), and presence of multiorgan dysfunction are usually lacking and there is still confusion in the literature between pancreatic necrosis and acute fluid collections and pseudocysts.[6,16–18] The present series represents a high mortality-risk group based on the high frequency of these factors along with advanced age, high CRP levels,[56] and high APACHE II scores,[54] organ dysfunction,[55] and Balthazar radiologic severity scores.[53] We have demonstrated that the percutaneous, retroperitoneal approach may be employed in up to 85% of patients requiring surgery for pancreatic necrosis (Fig. 1). In a nonrandomized comparison with patients who had traditional open pancreatic necrosectomy, the minimal access technique resulted in less postoperative physiological disturbance, a reduced need for intensive care, fewer complications, and a significantly reduced in-hospital mortality rate.

It is noted that the MARPN group had a significantly ($P = 0.038$) lower preoperative APACHE II score than the open group, whereas APACHE II scores were similar on admission. Unfortunately, the APACHE II system takes no account of treatment effects, and is therefore a poor scoring system once intensive treatment, such as ventilatory or circulatory support has been instituted. In view of the discrepancy, however, this baseline imbalance was corrected for by forcing this variable into the multivariate analysis, thus removing potential bias because of more favorable APACHE II scores in the MARPN group. This multivariable logistic regression analysis showed that MARPN remained an independent predictor of mortality ($P = 0.011$) even when APACHE II scores were adjusted for, along with age ($P < 0.0001$) and preoperative presence of multiorgan failure ($P < 0.0001$), which is consistent with our previously published results.[8]

This is a nonrandomized retrospective review of a prospectively maintained database and as such, there were baseline differences between the 2 groups of patients and therefore potential biases. Minimization of these biases was undertaken by using 3 simultaneous approaches: reporting consecutive cases, analysis by intention to treat, and statistical correction of baseline differences using forced multivariate statistical modeling. Whereas the open technique has been long-term established, the results include the learning curve and inevitably inferior results of the new technique during this early period. Intention to treat also minimizes potential outcome differences from baseline differences between the groups. General improvements in patient care over time will tend to favor the predominant (newer) technique but relevant conclusions may still be drawn by using statistical modeling made possible by the large numbers in this study. Over the period of the study, the Liverpool Pancreas Unit has received an increasing number of referrals of patients with severe pancreatitis and pancreatic necrosis because of a policy of centralization of specialist services. The series therefore includes a high proportion of tertiary referrals, but this is comparable with other high-volume specialist centers. We have deliberately chosen to treat as many patients as possible using a minimal access approach, and therefore the patients from later years treated by open necrosectomy have tended to be those with necrosis restricted to the head/uncinate region of the pancreas, with no feasible access route for MARPN. Nevertheless, the extent of necrosis did not differ statistically between the 2 groups of patients, nor was there any difference in the proportion with infected necrosis. We have further endeavored to correct for any imbalance in the baseline severity of illness in the 2 groups (such as the APACHE II scores) in the statistical analysis by forcing imbalanced criteria into the multifactorial model. Despite these imbalances, age, preoperative multiorgan failure, and MARPN remained significant predictors of mortality.

In this series, 107 (64.5%) of 166 patients had a proven positive bacteriological culture at the first procedure although following surgical intervention all invariably became infected. Fungal infection was found in 18 (10.7%) patients of whom 9 (50%) died. Based on earlier findings of a high mortality associated with fungal infection, this is now aggressively treated.[87–89] The widespread use of broad-spectrum antibiotics may have contributed to an increase in the incidence of primary fungal infection.[20,88,90] We, therefore, recommend a particularly aggressive policy of antifungal therapy and debridement in the presence of fungal infection, but try to avoid the use of prophylactic broad-spectrum antibiotics.

Patients undergoing MARPN required more procedures than those requiring open surgery, and therefore had a slightly longer overall hospital stay. On the other hand, although the initial MARPN procedure involving dilatation of the track was performed under general anesthetic, unless contraindicated subsequent procedures could be performed using local anesthetic with or without light sedation. Five of the 6 patients who also had the initial procedure under local anesthetic having been deemed too unwell for a general anesthetic (and therefore would not have been offered open necrosectomy) survived.

In summary, we report the outcome of a series of 137 patients undergoing a minimal access retroperitoneal approach to the treat-

ment of infected pancreatic necrosis. We have shown that this approach is practicable and may offer significant benefits for the patient when compared with a traditional open necrosectomy.

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