

## Surgery for pancreatic necrosis: "Whom, when and what"

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Acute pancreatitis is a common condition in which 70% of patients will recover with simple medical management. For patients who develop extensive or infected pancreatic necrosis the outcome is significantly different with a high morbidity and mortality<sup>[1]</sup>. Surgery is the mainstay of treatment for these patients but several unresolved issues remain including *who requires surgery, when is the optimal time to intervene and what technique should be used*.

Infected necrosis is generally accepted as a strong indication for surgery<sup>[2]</sup>. This has developed not from randomised data but observational studies over time that seemed to show a reduction in the previously reported mortality<sup>[3-5]</sup>. A small number of recent reports<sup>[6-8]</sup> have attempted to cast doubt on whether all patients with infected pancreatic necrosis should undergo surgery. So should a randomised controlled trial be undertaken? On the available evidence most surgeons and gastroenterologists would lack the "equipoise" required to perform such a trial. The number of patients successfully responding to conservative treatment remains small compared to the overall population with infected pancreatic necrosis. Further identification of factors associated with spontaneous resolution of infected necrosis needs to be identified before conservative treatment can be recommended as an acceptable alternative.

With the main indication for surgery being infected necrosis, the absence of infection is not an absolute contraindication. Over 90% of patients with sterile necrosis can be successfully treated without surgical intervention<sup>[9,10]</sup>, but a small subset with extensive necrosis warrants surgery. Indications in this setting include deteriorating organ failure despite maximal support<sup>[10,11]</sup> or persisting symptoms which preclude hospital discharge despite several weeks of optimum conservative treatment<sup>[9,12]</sup>.

The timing of surgery is an important determinant of outcome with early surgery (within the first week) associated with a high mortality<sup>[13,14]</sup>. The development of infected necrosis is time dependant, increasing to a peak in weeks 2-4<sup>[15]</sup>. Some studies have suggested that antibiotics may reduce the incidence of infected necrosis<sup>[16-22]</sup> but other recent large randomized controlled trials now reject this notion<sup>[23,24]</sup>. Moreover whether prophylactic antibiotics can delay the onset of infected necrosis or the need for intervention is unknown. Another unknown factor is whether those patients who develop infected necrosis within the first 14 d of their illness should continue to be managed conservatively to allow the necrotic tissue to demarcate the reduction of complications associated with early debridement. Infected necrosis is almost universally associated with the progressive escalation of organ failure<sup>[17]</sup>.

Increasing pre-operative organ dysfunction scores have been associated with an increase in mortality<sup>[25,26]</sup> and thus any delay in surgery following the diagnosis of infected necrosis is likely to be detrimental.

The aim of intervention in those with pancreatic necrosis is to remove the necrotic tissue and to provide adequate drainage for the remaining debris while preserving viable pancreatic tissue with minimal morbidity and mortality. It is generally accepted that debridement is preferable to resection<sup>[2]</sup> and the approaches to the pancreatic necrosis include trans-peritoneal, retro-peritoneal, minimally invasive and percutaneous techniques<sup>[4,12,14,25-32]</sup>. Post operative management includes laparostomy, packing, closed retroperitoneal lavage and repeat debridement<sup>[4,12,14,25-32]</sup>. There is no standardised optimal technique as there are no randomised trials that compared surgical techniques. In the largest reported series<sup>[17]</sup> the mortality was 39% but it has been reported as low as 6-8%<sup>[12,28]</sup>, which was the same as that for the overall mortality associated with pancreatitis in the United Kingdom<sup>[33]</sup>. The reason for this wide inter-study variation is likely to be due to a number of factors. Firstly, there was an inter-study heterogeneity in both the reporting and the frequency of adverse patient prognostic factors. Secondly, intervention rates varied 10-fold<sup>[34,35]</sup>, suggesting that the indications for intervention provided by guidelines are not uniformly interpreted. Thirdly, many studies were relatively small, retrospective or based over long time periods during which there was often a change in management.

The Regional Pancreas Centre at the Royal Liverpool University Hospital has adopted a minimally invasive approach in preference to an open approach because it was associated with a very high mortality despite expert surgery and intensive care<sup>[26,27]</sup>. Minimally, invasive retroperitoneal pancreatic necrosectomy has the dual advantages of removal of the solid necrotic material under direct vision through a wide bore tract<sup>[27,31,32]</sup> and the use of high volume post-operative lavage through the wide tract<sup>[27]</sup>. Moreover minimally invasive retroperitoneal pancreatic necrosectomy can be performed under local anaesthesia and reduces the need for post-operative intensive care, by avoiding an escalation in organ dysfunction which is usually seen after open surgery<sup>[26,31]</sup>. The disadvantages of minimally invasive retroperitoneal pancreatic necrosectomy include an increase in the number of procedures and possible increase in hospital stay<sup>[26,27]</sup>. Minimally invasive retroperitoneal pancreatic necrosectomy has not yet been shown to significantly reduce mortality although the trend is strong in this direction. Further experience with this technique and possible multi-centre randomised trials are needed.

Future studies on the outcome from intervention for pancreatic necrosis should incorporate standardised reporting of the precise profile of patients to allow for more valid comparisons between the different surgical techniques. In particular, there should be a clear description of the indications for intervention, the overall sample size from which the patients are selected, key prognostic indicators including age, organ dysfunction scores, extent of necrosis and the incidence of primary infection of the necrosis. It is notable that most studies failed to provide these critical factors and did not distinguish primary from secondary infection. Improving the reporting of studies will lead to the identification of the optimal patient at the optimal time undergoing the optimal procedure.

## REFERENCES

- 1 **Neoptolemos JP**, Raraty M, Finch M, Sutton R. Acute pancreatitis: the substantial human and financial costs. *Gut* 1998; **42**: 886-891
- 2 **Uhl W**, Warshaw A, Imrie C, Bassi C, McKay CJ, Lankisch PG, Carter R, Di Magno E, Banks PA, Whitcomb DC, Dervenis C, Ulrich CD, Satake K, Ghaneh P, Hartwig W, Werner J, McEntee G, Neoptolemos JP, Buchler MW. International Association of Pancreatologists. IAP Guidelines for the surgical management of acute pancreatitis. *Pancreatology* 2002; **2**: 565-573
- 3 **Altemeier WA**, Alexander JW. Pancreatic abscess. *Arch Surg* 1963; **87**: 80-85
- 4 **Bradley EL**. Management of infected pancreatic necrosis by open drainage. *Ann Surg* 1987; **204**: 542-549
- 5 **Sarr M**. Invited Commentary. *Dig Surg* 2003; **20**: 300
- 6 **Dubner H**, Steinberg W, Hill M, Bassi C, Chardavoigne R, Bank S. Infected pancreatic necrosis and peripancreatic fluid collections: Serendipitous response to antibiotic and medical therapy in three patients. *Pancreas* 1996; **12**: 298-302
- 7 **Salas CJ**, Gallego RFJ, Sanchez SJC, Diez GF. Medical treatment of infected pancreatic necrosis. *Gastroenterol Hepatol* 2001; **24**: 268-269
- 8 **Ramesh H**, Prakash K, Lekha V, Jacob G, Venugopal A. Are some cases of infected pancreatic necrosis treatable without intervention. *Dig Surg* 2003; **20**: 296
- 9 **Ashley SW**, Perez A, Pierce EA, Brooks DC, Moore FD Jr, Whang EE, Banks PA, Zinner MJ. Necrotising pancreatitis. *Ann Surg* 2001; **234**: 572-580
- 10 **Buchler MW**, Gloor B, Muller CA, Friess H, Seiler CA, Uhl W. Acute necrotising pancreatitis: treatment strategy according to status of infection. *Ann Surg* 2000; **232**: 619-626
- 11 **Beger HG**, Isenmann R. Acute pancreatitis: Who needs an operation? *J Hepatobiliary Pancreat Surg* 2002; **9**: 436-442
- 12 **Fernandez-del Castillo C**, Rattner DW, Makary MA, Mostafavi A, McGrath D, Warshaw A. Debridement and closed packing for the treatment of necrotising pancreatitis. *Ann Surg* 2000; **228**: 676-684
- 13 **Mier J**, Leon EL, Castillo A, Robledo F, Blanco R. Early versus late necrosectomy in severe pancreatitis. *Am J Surg* 1997; **173**: 71-75
- 14 **Gotzinger P**, Wamser P, Exner R, Schwanzler E, Jakesz R, Fugger R, Sautner T. Surgical treatment of severe acute pancreatitis: timing of operation is crucial for survival. *Surg Infect* 2003; **4**: 205-211
- 15 **Beger HG**, Bittner R, Block S, Buchler M. Bacterial contamination of pancreatic necrosis. A prospective clinical study. *Gastroenterology* 1986; **91**: 433-438
- 16 **Pederzoli P**, Bassi C, Vesentini S, Campedelli A. A randomised multicentre clinical trial of antibiotic prophylaxis of septic complications in acute necrotising pancreatitis with imipenem. *Surg Gynecol Obstet* 1993; **176**: 480-483
- 17 **Gotzinger P**, Sautner T, Kriwanek S, Beckerhinn P, Barlan M, Armbruster C, Wamser P, Fugger R. Surgical treatment for severe acute pancreatitis: Extent and surgical control of necrosis determine outcome. *World J Surg* 2002; **26**: 474-478
- 18 **Pederzoli P**, Bassi C, Vesentini S, Girelli R, Cavallini G, Falconi M, Nifosi F, Riela A, Dagradi A. A randomised multi-centre clinical trial of antibiotic prophylaxis of septic complications in acute necrotising pancreatitis with imipenem. *Surg Gynecol Obstet* 1993; **176**: 480-483
- 19 **Sainio V**, Kempainen E, Puolakkainen P, Taavitsainen M, Kivisaari L, Valtonen V, Haapiainen R, Schroder T, Kivilaakso E. Early antibiotic treatment in acute necrotising pancreatitis. *Lancet* 1995; **346**: 663-667
- 20 **Delcenserie R**, Yzet T, Ducroix JP. Prophylactic antibiotics in treatment of severe acute alcoholic pancreatitis. *Pancreas* 1996; **13**: 198-201
- 21 **Schwarz M**, Isenmann R, Meyer H, Beger HG. Antibiotic use in necrotizing pancreatitis. Results of a controlled study. *Dtsch Med Wochenschr* 1997; **122**: 356-361
- 22 **Nordback I**, Sand J, Saaristo R, Paajanen H. Early treatment with antibiotics reduces the need for surgery in acute necrotizing pancreatitis-a single-center randomized study. *J Gastrointest Surg* 2001; **5**: 113-118
- 23 **Isenmann R**, Runzi M, Kron M, Kahl S, Kraus D, Jung N, Maier L, Malfertheiner P, Goebell H, Beger HG. Prophylactic antibiotic treatment in patients with predicted severe acute pancreatitis: A placebo-controlled, double-blind trial. *Gastroenterology* 2004; **126**: 997-1004
- 24 **Spicak J**, Hejtmanekova S, Cech P, Hoskovec D, Kostka R, Leffler J, Kasalicky M, Svoboda P, Bartova J. Antibiotic prophylaxis in severe acute pancreatitis: randomized multicenter prospective trial with meropenem. *Pancreatology* 2003; **3**: 220
- 25 **Beattie GC**, Mason J, Swan D, Madhavan KK, Siriwardena AK. Outcome of necrosectomy in acute pancreatitis. *Scand J Gastroenterol* 2002; **12**: 1450-1453
- 26 **Connor S**, Ghaneh P, Raraty M, Rosso E, Hartley MN, Garvey C, Hughes M, McWilliams R, Evans J, Rowlands P, Sutton R, Neoptolemos JP. Increasing age and APACHE II scores are the main determinants of outcome from pancreatic necrosectomy. *Br J Surg* 2003; **90**: 1542-1548
- 27 **Connor S**, Ghaneh P, Raraty M, Sutton R, Rosso E, Garvey CJ, Hughes ML, Evans JC, Rowlands P, Neoptolemos JP. Minimally invasive retroperitoneal pancreatic necrosectomy. *Dig Surg* 2003; **20**: 270-277
- 28 **Beger HG**, Buchler M, Bittner R, Block S, Nevalainen T, Roscher R. Necrosectomy and post-operative local lavage in necrotising pancreatitis. *Br J Surg* 1988; **75**: 207-212
- 29 **Lasko DS**, Habib FA, Sleeman D, Levi J, Shatz D, Livingstone A. Percutaneous lavage for infected pancreatic necrosis. *J Gastrointest Surg* 2003; **7**: 288-289
- 30 **Tzovaras G**, Parks RW, Diamond T, Rowlands BJ. Early and long term results of surgery for severe necrotising pancreatitis. *Dig Surg* 2004; **21**: 41-47
- 31 **Carter RC**, McKay CJ, Imrie CW. Percutaneous necrosectomy and sinus tract endoscopy in the management of infected pancreatic necrosis: An initial experience. *Ann Surg* 2000; **232**: 175-180
- 32 **Gambiez LP**, Denimal FA, Porte HL, Saudemont A, Chambon JP, Quandalle PA. Retroperitoneal approach and endoscopic management of peripancreatic necrosis collections. *Arch Surg* 1998; **133**: 66-72
- 33 **Winslet M**, Hall C, London NJ, Neoptolemos JP. Relation serum amylase levels to aetiology and severity of acute pancreatitis. *Gut* 1992; **33**: 982-986
- 34 **Oleynikov D**, Cook C, Sellers B, Mone MC, Barton R. Decreased mortality from necrotising pancreatitis. *Am J Surg* 1998; **176**: 648-653
- 35 **Branum G**, Galloway J, Hirchowitz W, Fendley M, Hunter J. Pancreatic necrosis: results of necrosectomy, packing and ultimate closure over drains. *Ann Surg* 1998; **227**: 870-877

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