NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of percutaneous retroperitoneal endoscopic necrosectomy

Keyhole removal of dead tissue to treat pancreatic necrosis

The pancreas produces juices that contain substances (enzymes) that help to digest food. Sometimes these substances can attack the pancreas itself. This can happen if the tube that normally takes the juices to the gut becomes blocked. This can cause swelling of the pancreas and severe pain in the abdomen (acute pancreatitis). Some patients with acute pancreatitis develop a complication called necrosis, when part of the pancreas is destroyed. This is a serious condition with high risk of death, and removal of the dead tissue is required as part of the management.

The usual way of removing the destroyed part of the pancreas is by open surgery. Percutaneous retroperitoneal endoscopic necrosectomy is an alternative treatment option where a thin telescope, inserted through a small cut in the side above the hip, is used to wash out and remove the dead tissue.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in September 2010.

Procedure name

Percutaneous retroperitoneal endoscopic necrosectomy

Specialty societies

- Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland

- Association of Laparoscopic Surgeons of Great Britain and Ireland
- The Pancreatic Society of Great Britain and Ireland

Description

Indications and current treatment

Pancreatic necrosis (also called necrotising pancreatitis) is a serious complication of acute pancreatitis that can occur in some patients (with or without the formation of a pseudocyst). It is a condition associated with significant morbidity, requiring prolonged hospitalisation, and it has a high mortality.

Traditionally pancreatic necrosis has been treated by open necrosectomy via laparotomy, but image guided drainage or laparoscopic drainage may also be used.

Disease severity instruments used in acute pancreatitis

As acute pancreatitis is associated with significant morbidity and mortality risks, different severity scores have been developed to aid prognosis.

One measure of severity of acute pancreatitis is the Ranson score which scores 11 criteria (higher scores worse).

At admission:

- age in years > 55 years
- white blood cell count > 16,000 cells/mm^3
- blood glucose > 10 mmol/litre (200 mg/100 ml)
- serum aspartate aminotransferase (AST) > 250 IU/litre
- serum lactate dehydrogenase (LDH) > 350 IU/litre.

At 48 hours:

- serum calcium < 2.0 mmol/litre (8.0 mg/100 ml)
- haematocrit fall > 10%
- hypoxemia PO_2 < 60 mmHg
- blood urea nitrogen (BUN) increase of 1.8 mmol/litre (5 mg/100 ml) or more after intravenous fluid hydration
- base deficit (negative base excess) > 4 mEq/litre
- sequestration of fluids > 6 litres.

An alternative system is the Acute physiology and chronic health evaluation II (APACHE II) score, which is an assessment of disease severity based on 12 routine physiological measurements scored 0 to 71 (higher scores worse).

What the procedure involves

Percutaneous retroperitoneal endoscopic necrosectomy aims to remove necrotic tissue under direct vision. The procedure is less invasive and may improve prognosis compared with traditional open surgery

Under general anaesthesia an endoscope, which may be rigid or flexible, is inserted postero-laterally into the retroperitoneal space to visualise the necrosis. Dead tissue is removed for example, using suction, lavage or forceps, and necrotic tissue is debrided where necessary using forceps. This is done by inserting two or three ancillary ports or keyholes. Drains may be placed for irrigation of the cavity in the post-operative period. The procedure may be repeated if required.

Percutaneous retroperitoneal endoscopic necrosectomy may also allow more complete removal of necrotic tissue than percutaneous drainage alone because it is performed under direct vision, thus allowing collected pus to drain more freely.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to percutaneous retroperitoneal endoscopic necrosectomy. Searches were conducted of the following databases, covering the period from their commencement to 20 September 2010 and updated to 29 November 2010: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with necrosis of the pancreas.
Intervention/test	Percutaneous retroperitoneal endoscopic necrosectomy
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on approximately 448 patients from 1 randomised controlled trial[1], and 4 non-randomised controlled studies[2,3,4,5].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on percutaneous retroperitoneal endoscopic necrosectomy

Abbreviations used: CI, confidence interval; CT, computed tomography; ICU, intensive care unit; NS, not significant;

Study details	Key efficacy findings	Key safety findings	Comments
Van Santvoort H C (2010)[1] PANTER **Randomised controlled trial** Holland Recruitment period: 2005 to 2008 Study population: patients with necrotising pancreatitis and suspected or confirmed infected necrotic tissue. ICU at time of randomisation = 50%, >50% pancreatic necrosis = 32% **n = 88 (43 minimally invasive, 45 open)** Age: 57 years (mean) Sex: 73% male Patient selection criteria: either positive culture of pancreatic / peri-pancreatic necrotic tissue, or suspected infected necrosis with persistent sepsis or clinical deterioration despite maximal support. No chronic pancreatitis, previous exploratory laparotomy during the current episode, previous drainage or surgery, pancreatitis due to abdominal surgery, or acute intra-abdominal event. Technique: step-up approach with percutaneous or endoscopic drainage followed up (if required) by minimally invasive retroperitoneal necrosectomy vs open necrosectomy. **Follow-up: 6 months (median)** Conflict of interest/source of funding: supported by a state grant.	Number of patients analysed: **n = 88 (43 minimally invasive, 45 open)** **Surgical parameters** In the open group there was a median of 1 necrosectomy procedure (range: 1 to 7). 42.2% (19/45) of patients required one or more additional laparotomies for ongoing sepsis, complications, or both. 33% required additional percutaneous drainage after laparotomy. 34.8% (15/43) of patients in the step-up group did not require necrosectomy, and 2 patients with multiple organ failure were deemed too unstable for surgery (both underwent endoscopic transgastric drainage; both subsequently died). The remaining 60.5% (26/43) of patients underwent necrosectomy at 10 days after drainage. A median of 1 video-assisted retroperitoneal debridement procedure (range: 0 to 3) were carried out. 32.6% (14/43) of patients required one or more additional operations for ongoing sepsis, complications, or both. ***In the tables below, 'minimally invasive' denotes the 'step-up' arm, involving trial of percutaneous or endoscopic drainage followed-up byas required minimally invasive retroperitoneal necrosectomy.*** Outcome | Minimally invasive | Open | Risk ratio (95% CI) | p= Median length of stay (range) | 50 days (1 to 287) | 60 days (1 to 247) | Not applicable | 0.53 **Treatment success** Outcome | Minimally invasive | Open | Risk ratio (95% CI) | p= Major complication or death | 39.5% (17/43) | 68.9% (31/45) | 0.57 (0.38 to 0.87) | 0.006 Death | 18.6% | 15.6% | 1.20 (0.48 | 0.70	***See note in efficacy section re use of the term 'minimally invasive'*** **Complications** During index treatment Outcome | Minimally invasive | Open | Risk ratio (95% CI) | p= New onset multiple organ failure or systemic complications | 11.6% (5/43) | 42.2% (19/45) | 0.28 (0.11 to 0.67) | 0.001 Bleeding requiring intervention | 16.3% (7/43) | 22.2% (10/45) | 0.73 (0.31to 1.75) | 0.48 Fistula or perforation requiring intervention | 32.6% (14/43) | 22.2% (10/45) | 0.63 (0.25 to 1.58) | 0.32 At 6-month follow-up Outcome | Minimally invasive | Open | Risk ratio (95% CI) | p= Pancreatic fistula | 27.9% (12/43) | 37.8% (17/45) | 0.74 (0.40 to 1.36) | 0.33 Incisional hernia | 7.0 (3/43) | 24.4% (11/45) | 0.29 (0.09 to 0.95) | 0.03 New-onset diabetes | 16.3% (7/43) | 37.8% (17/45) | 0.43 (0.20 to 0.94) | 0.02 Use of pancreatic enzymes | 7.0 (3/43) | 33.3% (15/45) | 0.21 (0.07 to 0.67) | 0.002	**Follow-up issues**: Analysis on intention-to-treat principle. **Study design issues**: 19 participating sites, some centres might have contributed only a very small number of patients. Block randomisation at central study centre with stratification for site, and access route for drainage – retroperitoneal, transabdominal, or endoscopic transgastric. Not powered to demonstrate improvement in mortality. **Study population issues**: Patients were assessed for randomisation by a panel of 8 experts. There were no significant differences between the groups in terms of demographic or clinical criteria at baseline. **Other issues**: Additional patients to those reported in van Santvoort (2007). Of the patients randomised to minimally invasive necrosectomy, 93% underwent retroperitoneal drainage, 2% transabdominal, and 5% endoscopic transgastric.

Abbreviations used: CI, confidence interval; CT, computed tomography; ICU, intensive care unit; NS, not significant;						
Study details	**Key efficacy findings**				**Key safety findings**	**Comments**
		(8/43)	(7/45)	to 3.01)		
	Median length of stay (range)	50 days (1 to 287)	60 days (1 to 247)	Not applicable	0.53	

Abbreviations used: CI, confidence interval; CT, computed tomography; ICU, intensive care unit; NS, not significant;

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Raraty M G T (2010)[5]

Non-randomised controlled study
UK
Recruitment period: 1997 to 2008
Study population: patients with pancreatic necrosis >50% pancreatic necrosis at 1st procedure = 59%. Infected necrosis = 57%.

n = 189 (137 minimally invasive, 52 open)
Age: 58 years (mean)
Sex: 62% male

Patient selection criteria: patients with positive culture or extraintestinal sag on CT scan, or sterile necrosis with persisting symptoms despite maximal conservative treatment for 3 to 4 weeks.

Technique: under general anesthesia with access via left flank and under nephroscopic guidance, piecemeal removal of necrosis with forceps followed by insertion of an irrigating drain vs. open necrosectomy.

Follow-up: not reported

Conflict of interest/source of funding: Unit funded by a national grant</td>
<td>Number of patients analysed: n = 189 (137 minimally invasive, 52 open)

Surgical parameters
In the minimally invasive group 13.9% (19/137) required conversion to open procedure or an additional open procedure. 6 patients due to inability to place guidewire or dilate the track, 4 for bleeding, 4 for remote collections not amenable to percutaneous drainage, 2 for secondary colonic necrosis, 2 for ischaemic colitis requiring resection, and 1 for colonic fistula
Group median (and range)
<table>
<tr><th>Outcome</th><th>Minimally invasive</th><th>Open</th><th>p=</th></tr>
<tr><td>Length of stay (days)</td><td>94.5 (16 to 300)</td><td>85 (8 to 222)</td><td>0.011</td></tr>
<tr><td>Time to discharge post surgery (days)</td><td>64 (15 to 272)</td><td>43 (5 to 158)</td><td>0.004</td></tr>
<tr><td>ICU stay</td><td>43.1% (59/137)</td><td>76.9% (40/52)</td><td><0.0001</td></tr>
<tr><td>Number of procedures</td><td>3 (1 to 9)</td><td>1 (1 to 9)</td><td><0.0001</td></tr>
</table>
Treatment success
<table>
<tr><th>Outcome</th><th>Minimally invasive</th><th>Open</th><th>p=</th></tr>
<tr><td>Death</td><td>19.0% (26/137)</td><td>38.5% (20/52)</td><td>0.009</td></tr>
<tr><td>Multisystem organ failure</td><td>31%</td><td>56%</td><td><0.0001</td></tr>
</table>
Patient age (p<0.0001), baseline multiple organ failure (p<0.0001), and Minimally invasive necrosectomy (p=0.016) were independent predictors of mortality.</td>
<td>Complications
<table>
<tr><th>Outcome</th><th>Minimally invasive</th><th>Open</th><th>p=</th></tr>
<tr><td>Myocardial infarction</td><td>2.9% (1/137)</td><td>9.6% (5/52)</td><td>0.122</td></tr>
<tr><td>Cerebrovascular event</td><td>1.5% (2/137)</td><td>3.8% (2/52)</td><td>0.652</td></tr>
<tr><td>Pseudocyst</td><td>2.2% (3/137)</td><td>9.6% (5/52)</td><td>0.063</td></tr>
<tr><td>Bleeding</td><td>11.7% (16/137)</td><td>17.3% (9/52)</td><td>0.436</td></tr>
<tr><td>Biliary stricture</td><td>2.2% (3/137)</td><td>9.6% (5/52)</td><td>0.253</td></tr>
<tr><td>Pancreatic fistula</td><td>3.6% (5/137)</td><td>7.7% (4/52)</td><td>0.434</td></tr>
<tr><td>Enteric fistula</td><td>7.3% (10/137)</td><td>9.6% (5/52)</td><td>0.865</td></tr>
<tr><td>Pulmonary embolus</td><td>0.7% (1/137)</td><td>1.9% (1/52)</td><td>0.621</td></tr>
<tr><td>Colonic necrosis</td><td>2.9% (4/137)</td><td>5.8% (3/52)</td><td>0.621</td></tr>
<tr><td>Vein thrombosis</td><td>5.1% (7/137)</td><td>7.7% (4/52)</td><td>0.741</td></tr>
<tr><td>Infection</td><td>2.9% (4/137)</td><td>1.9% (1/52)</td><td>0.893</td></tr>
<tr><td>Other</td><td>7.3% (10/137)</td><td>15.4% (8/52)</td><td>0.313</td></tr>
<tr><td>Any complication</td><td>54.7% (75/137)</td><td>82.7% (43/52)</td><td>0.0007</td></tr>
</table></td>
<td>Follow-up issues:
Retrospective analysis of prospective database

Intention to treat analysis.

Study design issues:
Selection criteria for open necrosectomy based on lack of safe percutaneous route in to the necrosis or other indication for open surgery.

Study population issues:
Prophylactic antibiotics not routinely used , number in each group not reported.
No significant difference between study groups in terms of demographics, aetiology, or clinical characteristics at baseline. Except for median baseline APACHE II score which was significantly lower in the minimally invasive group (p=0.038).

Other issues:
Percentages quoted for postoperative multiple organ failure do not resolve with the numerators stated.</td>
</tr>
</table>

Abbreviations used: CI, confidence interval; CT, computed tomography; ICU, intensive care unit; NS, not significant;

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Connor S C (2005)[2]

Non-randomised controlled study
UK
Recruitment period: 1997 to 2003
Study population: patients with pancreatic necrosis >50% pancreatic necrosis = 81%

n = 88 (47 minimally invasive, 41 open)
Age: 56 years (mean)
Sex: 61% male

Patient selection criteria: patients with positive culture, or sterile necrosis with persisting symptoms despite maximal conservative treatment.

Technique: minimally invasive necrosectomy (not otherwise defined) vs open necrosectomy. Prophylactic antibiotics in patients with proven infection in both groups.

Follow-up: 29 months (median)

Conflict of interest/source of funding: not reported.</td>
<td>Number of patients analysed: n = 88 (47 minimally invasive, 41 open)

Surgical parameters
In the minimally invasive necrosectomy group there was a median of 3 procedures per patient (range: 1 to 9), while in the open necrosectomy group there was a median of 1 procedure (range: 1 to 9) (measurement of significance not reported).
Group median scores
<table>
<tr><th>Outcome</th><th>Minimally invasive</th><th>Open</th><th>p=</th></tr>
<tr><td>ICU stay (range)</td><td>0 days (0 to 66)</td><td>4 days (0 to 56)</td><td><0.01</td></tr>
<tr><td>Length of stay (range)</td><td>64 days (15 to 272)</td><td>50 days (5 to 158)</td><td>0.04</td></tr>
</table>
Treatment success
Group medians and range or proportion of patients
<table>
<tr><th>Outcome</th><th>Minimally invasive</th><th>Open</th><th>p=</th></tr>
<tr><td>Death</td><td>19.1% (9/47)</td><td>39.0% (16/41)</td><td>0.06</td></tr>
<tr><td>Postoperative APACHE II score</td><td>7 (0 to 22)</td><td>10 (0 to 21)</td><td>0.02</td></tr>
</table>
</td>
<td>Complications
<table>
<tr><th>Outcome</th><th>Minimally invasive</th><th>Open</th><th>p=</th></tr>
<tr><td>Overall</td><td>91.4% (43/47)</td><td>95.1% (39/41)</td><td>NS</td></tr>
<tr><td>Organ failure</td><td>42.6% (20/47)</td><td>58.6% (24/41)</td><td>NS</td></tr>
<tr><td>Cardiovascular</td><td>14.9% (7/47)</td><td>17.1% (7/41)</td><td>NS</td></tr>
<tr><td>Pulmonary</td><td>2.1% (1/47)</td><td>7.3% (3/41)</td><td>NS</td></tr>
<tr><td>Bleeding</td><td>12.8% (6/47)</td><td>9.8% (4/41)</td><td>NS</td></tr>
<tr><td>Vein thrombosis</td><td>21.3% (10/47)</td><td>2.4% (1/41)</td><td><0.01</td></tr>
<tr><td>Colonic necrosis</td><td>4.3% (2/47)</td><td>0% (0/41)</td><td>NS</td></tr>
<tr><td>Gastrointestinal fistula</td><td>4.3% (2/47)</td><td>4.9% (2/41)</td><td>NS</td></tr>
</table>
Overall the rate of complications was not significantly lower in patients with sterile necrosis 89.5% (17/19) than in those with infected necrosis 92.6% (63/68) (p = 0.65).</td>
<td>Follow-up issues:
Retrospective database analysis.

Study design issues:
Selection criteria for minimally invasive or open necrosectomy not reported.
Study population issues:
66 patients received prophylactic antibiotics, number in each group not reported.
Significantly more patients in the minimally invasive group had >50% necrosis (p = 0.03).

Other issues:
Possibly some of the same patients reported in Raraty (2010)</td>
</tr>
</table>

Abbreviations used: CI, confidence interval; CT, computed tomography; ICU, intensive care unit; NS, not significant;

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Van Santvoort H C (2007)[3]

Non-randomised controlled study
Holland
Recruitment period: 1995 to 2005
Study population: patients with proven or suspected pancreatic and / or peripancreatic necrosis. Median time between admission and primary necrosectomy = 41 days.
n = 30 (15 percutaneous vs 15 open laparotomy)
Age: 52 years median
Sex: 44% male

Patient selection criteria: not reported.

Technique: 5 cm incision, retroperitoneal space entered. Debridement with forceps using a ‘videoscope’ and drains placed, vs laparotomy with blunt debridement and continuous postoperative lavage.

Follow-up: to discharge
Conflict of interest/source of funding: not reported.</td>
<td>Number of patients analysed: n = 30 (15 percutaneous, 15 open)

Surgical parameters
Conversion to open surgery was not required in any patients in the percutaneous group 0% (0/15). Additional treatment by laparotomy was required in 1 patient in the percutaneous group, where it was deemed that further debridement by this approach was not feasible.

Treatment success
Rate per patients treated or Group median (and range)
<table>
<tr><th>Outcome</th><th>Percutaneous</th><th>Laparotomy</th><th>p=</th></tr>
<tr><td>Reintervention for postoperative complication</td><td>20.0% (3/15)</td><td>40.0% (6/15)</td><td>0.427</td></tr>
<tr><td>Reintervention for further necrosectomy</td><td>73.3% (11/15)</td><td>86.7% (13/15)</td><td>0.651</td></tr>
<tr><td>Total necrosectomies</td><td>2 (1to 9)</td><td>2 (1 to 13)</td><td>0.624</td></tr>
<tr><td>Total surgical interventions</td><td>3 (1 to 11)</td><td>4 (1 -14)</td><td>0.345</td></tr>
<tr><td>Postoperative multiple organ failure</td><td>13.3% (2/15)</td><td>66.7% (10/15)</td><td>0.008</td></tr>
<tr><td>Postoperative ICU admission</td><td>73.3% (11/15)</td><td>80.0% (12/15)</td><td>1.000</td></tr>
<tr><td>Postoperative hospital stay (survivors)</td><td>57 days (18 to 162)</td><td>54 days (20 to 150)</td><td>0.926</td></tr>
<tr><td>Length of stay (survivors)</td><td>110 days (45 to 240)</td><td>106 (46 to 231)</td><td>0.600</td></tr>
<tr><td>In-hospital mortality</td><td>6.7% (1/15)</td><td>40.0% (6/15)</td><td>0.080</td></tr>
</table>
</td>
<td>Complications
Percutaneous group
26.7% (4/15) of patients required additional laparotomy during the postoperative course.
<table>
<tr><th>Complication</th><th>Percutaneous</th><th>Laparotomy</th></tr>
<tr><td>Total</td><td>53.3% (8/15)</td><td>46.7% (7/15)</td></tr>
<tr><td>Bowel perforation</td><td>6.7% (1/15)</td><td>13.3% (2/15)</td></tr>
<tr><td>Bleeding*</td><td>26.7% (4/15)</td><td>6.7% (1/15)</td></tr>
<tr><td>Colonic necrosis</td><td>0% (0/15)</td><td>6.7% (1/15)</td></tr>
<tr><td>Gastrointestinal fistula</td><td>6.7% (1/15)</td><td>20.0% (3/15)</td></tr>
<tr><td>Pancreatic fistula</td><td>13.3% (2/15)</td><td>0% (0/15)</td></tr>
</table>
Of the 4 bleeding events in the percutaneous group, 2 occurred after additional laparotomy procedures.

There were no statistically significant differences between the groups. Length of follow-up of event not reported.</td>
<td>Follow-up issues:
Retrospective database analysis.
Study design issues:
Pair-matched analysis. Overlapping recruitment period, percutaneous technique introduced in 2001. Possibility of confounding from a historical control was assessed.
Matching of cases based on organ failure, infection, timing of surgery, age, and severity of condition on CT imaging.
Surgical strategy was based on the surgeon’s preference.
Study population issues:
Patients were matched on all criteria used, and there were no differences between the groups in terms of sex, aetiology, organ failure, ICU admission, white blood cell count, or APACHE II score.
Other issues:
Preoperative percutaneous drainage was used in 6 patients in the open group, and 22 patients in the percutaneous group.</td>
</tr>
</table>

Abbreviations used: CI, confidence interval; CT, computed tomography; ICU, intensive care unit; NS, not significant;			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Gambiez L P (1998)[4] **Non-randomised controlled study** France Recruitment period: 1990 to 1995 Study population: Patients with acute necrotising pancreatitis, mean Ranson score 3.3 points. Cause alcohol (n = 24), Gallstones (n = 17), Other (n = 12). n = **53 (20 PPN)** Age: 49 years (mean) Sex: 66% Male Patient selection criteria: pancreatic necrosis demonstrated on CT scan, and microbiologic examination. Technique: Endoscopic retroperitoneal necrosectomy by retroperitoneal approach through a short lumbotomy using a direct vision endoscope. Necrotic tissue and collections removed by blunt debridement using a suction metal tube that was also equipped for electrocoagulation. After debridement, a drain allowing continuous irrigation was left in the retroperitoneal space. **Follow-up: to discharge** Conflict of interest/source of funding: not reported.	Number of patients analysed: **53 (20 percutaneous)** **Survival** (follow-up period not reported): 100% (14/14) with supportive therapy 80.0% (8/10) with percutaneous drainage 90.0% (18/20) with PPN 66.7% (6/9) with open necrosectomy Mortality was significantly higher in patients with infected necrosis 31.8% (7/22) than in those with sterile collections 0% (0/17) ($p < 0.05$). **Length of stay** Group mean (standard deviation) inpatient stay: 23 (± 9) days with supportive therapy 89 (± 24) days with percutaneous drainage 62 (± 21) days with PPN 86 (± 32) days with open necrosectomy The mean hospital length of stay was significantly shorter in the PPN group than the percutaneous drainage, or the open necrosectomy groups ($p < 0.05$).	**Complications** Percutaneous drainage: Incisional hernia 10.0% (1/10) PPN: Colonic fistula 5.0% (1/20) Splenic bleed 5.0% (1/20) Subsequent laparotomy 10% (2/20) Pancreatic fistula to skin 10% (2/20) Incisional hernia 10% (2/20) Open necrosectomy: Incisional hernia 22.2% (2/9)	**This study was included in the original overview.** **Follow-up issues**: Single study centre retrospective analysis. **Study design issues**: Patients received one of the four different management strategies according to their clinical features, including severity of disease. **Study population issues**: Patients who had PPN are likely to differ in prognostic factors from people who had open necrosectomy or percutaneous drainage. AGE, Ranson score, CT assessed grade, and clinical features were significantly different between the groups at baseline. **Other issues**: Operator experience with the four treatment types is not reported.

Efficacy

Mortality

A randomised controlled trial of 88 patients reported that there was no statistically significant difference in the rate of mortality between patients treated by a step-up protocol with minimally invasive retroperitoneal necrosectomy where percutaneous drainage failed (19% [8/43]) and those treated by open necrosectomy (16% [7/45]) (p = 0.70); length of follow-up for this specific outcome is not explicitly reported, but patients in the study were followed-up for up to 6 months from hospital discharge[1]. In this study 60% (26/43) of patients underwent percutaneous retroperitoneal endoscopic necrosectomy, 35% (15/43) of patients required drainage alone and 5% (2/43) of patients with multiple organ failure were too unstable for surgery**.** A non-randomised controlled study of 189 patients reported mortality in 19% (26/137) of patients treated by minimally invasive pancreatic necrosectomy and 38% (20/52) of patients undergoing open necrosectomy (p=0.009) (follow up not reported)[5]. A non-randomised controlled study of 30 patients reported that there was no statistically significant difference in the rate of in-hospital mortality between patients treated by percutaneous retroperitoneal endoscopic necrosectomy (7% [1/15]) and those receiving open necrosectomy (40% [6/15]) (p = 0.08)[3].

A non-randomised controlled study of 53 patients reported a survival rate of 90% (18/20) following percutaneous retroperitoneal endoscopic necrosectomy, 80% (8/10) following percutaneous drainage alone, and 67% (6/9) following open necrosectomy (measurement of significance not reported); follow-up to discharge[4].

Clinical outcome

The non-randomised controlled study of 30 patients reported that there was significantly less postoperative multiple organ failure following percutaneous retroperitoneal endoscopic necrosectomy (13% [2/15]) than following open necrosectomy via laparotomy (67% [10/15]) (p = 0.008)[3].

Composite endpoint

The randomised controlled trial of 88 patients reported that the rate of major complication or death was significantly lower in patients treated by a step-up protocol with minimally invasive retroperitoneal necrosectomy where percutaneous drainage failed (40% [17/43]) than in patients undergoing open necrosectomy (69% [31/45]) (p = 0.006); length of follow up not reported[1].

Safety

Fistula / perforation

The randomised controlled trial of 88 patients reported that there was no statistically significant difference in the rate of fistula formation or perforation requiring intervention between patients treated by a step-up protocol with minimally invasive retroperitoneal necrosectomy where percutaneous drainage failed (33% [14/43]) and those treated by open necrosectomy (22% [10/45]) (p = 0.32); length of follow-up not reported[1]. A non-randomised controlled trial of 30 patients reported that bowel perforation occurred in 7% (1/15) of patients treated by percutaneous retroperitoneal endoscopic necrosectomy and in 13% (2/15) of matched patients treated by open necrosectomy (p = not significant); follow-up to discharge[3]. In the same study, the rate of pancreatic fistula was 13% (2/15) and 0% (0/15) respectively (p = not significant).

Bleeding

The randomised controlled trial of 88 patients reported that bleeding requiring intervention occurred in 16% (7/43) of patients treated by a step-up protocol with minimally invasive retroperitoneal necrosectomy, and in 22% (10/45) of patients treated by open necrosectomy (p = 0.48); length of follow-up not reported[1]. A non randomised controlled study of 189 patients reported that bleeding occurred in 12% (16/137) patients treated by minimally invasive pancreatic necrosectomy and 17% (9/52) undergoing open necrosectomy (p=0.44) (follow up not reported)[5].

Other

The randomised controlled trial of 88 patients reported that new-onset diabetes occurred in 16% (7/43) of patients treated by a step-up protocol with minimally invasive retroperitoneal necrosectomy where percutaneous drainage failed and in 38% (17/45) of those treated by open necrosectomy (p = 0.02) at a median 6-month follow-up[1].

A non-randomised controlled study of 88 patients reported that portal vein or splenic vein thrombosis occurred significantly more often in patients treated by percutaneous retroperitoneal endoscopic necrosectomy (21% [10/47]) than in patients treated by open necrosectomy (2% [1/41]) (p < 0.01); median follow-up of 29 months[2].

Validity and generalisability of the studies

- The available evidence reports on a range of minimally invasive techniques, some with endoscopic visualisation alone, some with transgastric laparoscopy

and some with purely external imaging. This makes comparison of studies difficult.

- Follow-up is not well reported in the studies available, and is only usually to the time of discharge.
- No randomised comparative data are available that compare percutaneous retroperitoneal endoscopic necrosectomy with open necrosectomy.
- The degree of dissection and lavage employed during the procedure varied within and between the studies.
- The indications for patients included in the studies available varied within and between studies. Some had infected pancreatic necrosis and some non-infected necrosis but with progressive organ failure. This makes comparison of outcomes difficult.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Interventional procedures

- Percutaneous pancreatic necrosectomy. NICE interventional procedures guidance 33 (2003). Available from www.nice.org.uk/guidance/IPG33.

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Mr D Berry (Association of Laparoscopic Surgeons of Great Britain and Ireland), Mr R Carter, Mr A Siriwardena and Mr M Deakin (Pancreatic Society of Great Britain and Ireland), Mr M Raraty (Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland)

- Four out of five of the specialist advisors categorised the procedure as established and no longer new.

- The procedure is also known as minimal access retroperitoneal pancreatic necrosectomy.
- The main comparators are open necrosectomy, percutaneous drainage or other minimally invasive techniques such as endoscopic debridement or laparoscopic debridement.
- Adverse events reported following the procedure include bleeding, incomplete drainage / sepsis control, intraperitoneal rupture, colonic fistula, gastric fistula, iatrogenic injury to kidney or spleen, venous thrombosis, colonic necrosis, pseudocyst formation and death.
- Theoretical adverse events might include post-procedural multiple organ dysfunction
- It is a relatively simple procedure for hepato-pancreato-biliary (HPB) surgical trainees to learn. Training should be undertaken in units with sufficient pancreatic throughput to see numbers of patients with infected necrosis.
- The key efficacy outcomes for this procedure are mortality, requirement for ICU post-op, reduction in morbidity, number of interventions required and length of hospital stay.
- All the Specialist Advisors thought that if found to be safe and efficacious it is likely to be made available at a minority of UK hospitals but at least ten.
- The procedure requires a long hospital stay and often multiple operative procedures are needed. Patients with severe acute pancreatitis are among the most expensive for the NHS to treat due to a high requirement for sometimes prolonged critical care.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme was unable to gather patient opinion for this procedure.

Issues for consideration by IPAC

- Most patients included in the studies had failed previous percutaneous drainage.
- Existing IP guidance states that: ’The Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland has agreed to set up a registry for the procedure. All patients undergoing this procedure should be entered into the registry.’ No such registry was established and therefore no data are available.
- No issues relating to equality and diversity were raised during the scoping process.
- A large number of small case series are listed in appendix A.

References

1 van Santvoort HC, Besselink MG, Bakker OJ et al. (2010) A step-up approach or open necrosectomy for necrotizing pancreatitis. New England Journal of Medicine 362:1491-1502.

2 Connor S, Alexakis N, Raraty MG et al. (2005) Early and late complications after pancreatic necrosectomy. Surgery 137:499-505.

3 van Santvoort HC, Besselink MG, Bollen TL et al. (2007) Case-matched comparison of the retroperitoneal approach with laparotomy for necrotizing pancreatitis. World Journal of Surgery 31:1635-1642.

4 Gambiez LP, Denimal FA, Porte HL et al. (1998) Retroperitoneal approach and endoscopic management of peripancreatic necrosis collections. Arch Surg 133:66-72.

5 Raraty MGT, Halloran CM, Dodd S et al (2010) Minimal access retroperitoneal pancreatic necrosectomy. Improvement in morbidity and mortality with a less invasive approach. Annals of Surgery 251: 787-793

Appendix A: Additional papers on percutaneous retroperitoneal endoscopic necrosectomy

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Bruennler, T., Langgartner, J., Lang, S., et al (1008) Percutaneous necrosectomy in patients with acute, necrotizing pancreatitis. European Radiology 18 (8) 1604-1610	n = 18 Follow-up = not reported	Percutaneous minimally invasive necrosectomy can be regarded as a safe and effective complementary treatment modality in patients with necrotising pancreatitis.	Larger studies are included in table 2
Cheung, M.-T., Ho, C. N. S., Siu, K.-W et al (2005) Percutaneous drainage and necrosectomy in the management of pancreatic necrosis. ANZ Journal of Surgery 75 (4) 204-207.	n = 8 Follow-up = to discharge	Those patients who had 'organized necrosis' after the acute episode of pancreatitis could receive benefit from percutaneous necrosectomy. The persistent symptoms could be alleviated after the removal of the residual necrotic material.	Larger studies are included in table 2
Connor, S., Ghaneh, P., Raraty, M (2003) Minimally invasive retroperitoneal pancreatic necrosectomy. Digestive Surgery 20 (4) 270-277	n = 24 Follow-up = to discharge	A new technique that has shown promising results, and could be preferable to open pancreatic necrosectomy in selected patients.	Larger studies are included in table 2 Potentially some of the same patients are reported in Connor (2005) in table 2
Cuschieri SA, Jakimowicz JJ, Stultiens G. Laparoscopic infracolic approach for complications of acute pancreatitis. Semin Laparosc Surg 1998;5:189-194	n = 3 Follow-up = not reported	The infracolic laparoscopic approach seems to be a useful technique for internal drainage of pancreatic pseudocysts. Its use for necrosectomy, drainage, and irrigation of the lesser sac merits further evaluation.	Larger studies are included in table 2
el Yassini AE, Hoebeke Y, Keuleneer RD. Laparoscopic treatment of secondary infected pancreatic collections after an acute pancreatitis: two cases. Act Chirurg Belg 1996; 96:226-228	n = 1 Follow-up = not reported	The treatment consisted of a necrosectomy and the installation of a system of drainage and lavage.	Larger studies are included in table 2
Endlicher, E., Volk, M., Feuerbach, S., Scholmerich, J., et al (2003) Long-term follow-up of patients with necrotizing pancreatitis treated by percutaneous necrosectomy.	n = 9 Follow up = 30 months	Percutaneous drainage of infected necrotising pancreatitis has given good long-term results with regard to quality of life, endocrine and exocrine pancreatic function, and	Larger studies are included in table 2

Hepato-Gastroenterology 50 (54) 2225-2228.		may be an alternative to surgical treatment.	
Gagner M. Laparoscopic treatment of acute necrotizing pancreatitis. Semin Laparosc Surg 1996;3:21-28	n = 8 Follow-up = not reported	No local complications described.	Larger studies are included in table 2
Oria A, Ocampo C, Zandalazini H, et al. Internal drainage of giant acute pseudocysts: the role of video-assisted pancreatic necrosectomy. Arch Surg 2000;135:136-140.	n = 10 Follow-up = not reported	Depending on appropriate surgical timing, video-assisted necrosectomy is a feasible and safe procedure.	Larger studies are included in table 2
Risse, O., Auguste, T., Delannoy, P et al (2004) Percutaneous video-assisted necrosectomy for infected pancreatic necrosis. Gastroenterologie Clinique et Biologique 28 (10:Pt 1) t-71.	n = 6 Follow-up = 7 months	Early experience in 6 patients has shown that percutaneous video-assisted necrosectomy is feasible, safe and efficient.	Larger studies are included in table 2
Zorger, N., Hamer, O. W., Feuerbach, S et al (2004) Percutaneous treatment of a patient with infected necrotizing pancreatitis. Nature Clinical Practice Gastroenterology & Hepatology 2 (1) 54-57.	n = 1 Follow-up = 3 years	Interventional treatment using large-bore percutaneous catheters to perform percutaneous necrosectomy, fragmentation of necrotic pancreatic tissue with a snare catheter and dormia basket, and aspiration.	Larger studies are included in table 2

Appendix B: Related NICE guidance for percutaneous retroperitoneal endoscopic necrosectomy

There is currently no NICE guidance related to this procedure.

Appendix C: Literature search for percutaneous retroperitoneal endoscopic necrosectomy

Database	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	20/09/2010	September 2010
Database of Abstracts of Reviews of Effects – DARE (CRD website)	20/09/2010	-
HTA database (CRD website)	20/09/2010	-
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	20/09/2010	September 2010
MEDLINE (Ovid)	20/09/2010	1950 to September Week 1 2010
MEDLINE In-Process (Ovid)	20/09/2010	September 17, 2010
EMBASE (Ovid)	20/09/2010	1980 to 2010 Week 37
CINAHL (NLH Search)	20/09/2010	-
Zetoc	20/09/2010	-
BLIC (Dialog DataStar)	04/03/2009	-

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	Pancreatitis, Acute Necrotizing/
2	(acute adj3 pancreatitis).tw.
3	or/1-2
4	(pancrea$ or peripancreatic or peri-pancreatic).tw.
5	Necrosis/
6	(necrosis or nectroti?ing).tw.
7	5 or 6
8	Infection/
9	infect$.tw.

10	or/8-9
11	4 and 7 and 10
12	3 or 11
13	percutaneous.tw.
14	retroperitone$.tw.
15	Endoscopes/
16	endoscop$.tw.
17	Surgical Procedures, Minimally Invasive/
18	(minimally invasive adj3 (surgery or technique or procedure)).tw.
19	Laparoscopes/
20	laparoscop$.tw.
21	nephroscop$.tw.
22	Video-Assisted Surgery/
23	((video-assist$ or video assist$) adj3 (surgery or technique or procedure)).tw.
24	Debridement/
25	debridement.tw.
26	lavage.tw.
27	or/13-26
28	necrosectomy.tw.
29	27 and 28
30	PPN.tw.
31	29 or 30
32	12 and 31
33	Animals/ not Humans/
34	32 not 33