

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of endoscopic transluminal pancreatic necrosectomy

Pancreatitis causes the pancreas to become inflamed, resulting in severe pain and illness. Sometimes the tissue of the pancreas starts to die (necrosis) and may become infected. It can be removed by open surgery or suction through a needle. In this procedure an endoscope (a thin tube with a camera on the end) is inserted through the mouth and instruments are passed through the stomach wall to wash out and remove the dead tissue.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) 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 IP overview was prepared in February 2016 and updated in September 2016.

Procedure name

- Endoscopic transluminal pancreatic necrosectomy

Specialist societies

- British Society for Gastroenterology
- Association of Upper Gastrointestinal Surgeons
- Pancreatic Society of Great Britain and Ireland

Description

Indications and current treatment

Pancreatic necrosis (also called necrotising pancreatitis) is a serious complication of pancreatitis that can occur in some patients. It can occur with or without the formation of pseudocysts and is associated with significant morbidity and high mortality, particularly if it becomes infected. Patients usually need a long stay in hospital with treatment in intensive care.

Current treatment options for pancreatic necrosis include conventional open or laparoscopic necrosectomy.

What the procedure involves

Endoscopic transluminal pancreatic necrosectomy is done with the patient under sedation or general anaesthesia, using upper gastrointestinal endoscopy and endosonographic or fluoroscopic guidance or both. The stomach is distended with carbon dioxide. The area where the necrotic tissue has collected is usually identified as a bulge in the stomach wall. An opening is made in the posterior wall of the stomach. The opening is dilated with a balloon over a guide wire to allow the endoscope to pass through into the area of necrotic tissue. Any fluid that has collected is drained. Necrotic tissue is removed through the endoscope using suction, forceps and irrigation. One or more self-expanding stents or irrigation catheters may be left in place in the stomach wall to help further drainage from the retroperitoneal space into the stomach. Repeated sessions may be needed over many days until the cavity is clean and lined with granulation tissue. The procedure aims to avoid the need for open or laparoscopic necrosectomy and its associated morbidity.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to endoscopic transluminal pancreatic necrosectomy. The following databases were searched, covering the period from their start to 3 June 2016: 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 pancreatic necrosis.
Intervention/test	Endoscopic transluminal pancreatic 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 IP overview

This IP overview is based on approximately 940 patients from 2 systematic reviews, 1 randomised controlled trial (also included in the systematic reviews), 3 non-randomised controlled trials (included in 1 of the systematic reviews), 2 case series (included in 1 of the systematic reviews) and 1 case report¹⁻⁹.

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 endoscopic transluminal pancreatic necrosectomy

Study 1 Luigiano C (2016)

Details

Study type	Systematic review
Country	Italy
Recruitment period	Search date: December 2015
Study population and number	n=938 (46 studies) Patients treated by endoscopic necrosectomy
Age and sex	Not reported
Patient selection criteria	Search terms used were 'endoscopy', 'endosonography', endoscopic transluminal necrosectomy', 'endoscopic necrosectomy', 'endoscopic debridement', 'drainage', 'endoscopic drainage', 'transluminal drainage', 'transgastric necrosectomy', 'transgastric debridement', 'pancreatitis', 'pancreatic', 'pancreas', 'infected necrosis', 'acute necrotizing pancreatitis' and 'treatment outcome'. Case reports, case series with fewer than 4 patients, studies in which the outcomes could not be determined from the text, commentaries, non-English language articles, congress proceedings and abstracts were not included.
Technique	Transmural (transgastric or transduodenal) endoscopic ultrasound-guided or non-endoscopic ultrasound guided access to the necrotic area, followed by balloon dilation of the tract between the peripancreatic collection and gastrointestinal tract lumen to allow passage of a gastroscope into the collection.
Follow-up	Not reported
Conflict of interest/source of funding	Not reported

Analysis

Study design issues: There was 1 randomised controlled trial included in the review (Bakker et al, 2012). Most of the studies included small numbers of patients, were retrospective and had low to moderate overall levels of evidence.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: 938 Mean technical success rate=99% (range 75–100%) Mean clinical success rate=89% (range 50–100%)	Complications Mean overall complication rate=22% (range 0–48%) Most common complications: • Bleeding=11% (103/938) • Perforations or pneumoperitoneum=3% (26/938) • Air embolism=0.4% (4/938) Mean overall mortality=5% (range 0–25% per study)

Study 2 Van Brunschot (2014)

Details

Study type	Systematic review
Country	The Netherlands
Recruitment period	Search date: January 2005–June 2013
Study population and number	n=455 (14 studies) Patients with necrotising pancreatitis
Age and sex	Mean 56 years; 63% male
Patient selection criteria	Inclusion criteria for review: consecutive series of patients with necrotising pancreatitis having endoscopic necrosectomy for (suspected) infected necrosis or symptomatic sterile pancreatic necrosis; the following outcomes were reported: percentage of infected peripancreatic collections, number of interventions, endoscopic necrosectomy success rate, mortality, and complications. Exclusion criteria: studies with fewer than 5 patients; studies also including patients with chronic pancreatitis with results for acute pancreatitis not reported separately; studies on a selected subgroup of patients with acute pancreatitis, classified as 'pseudocysts' or 'pancreatic abscesses' as defined by the 1992 Atlanta classification with results of these subgroups not reported separately; studies including sterile pancreatic necrosis with results of infected pancreatic necrosis not reported separately or, otherwise uncomplicated sterile pancreatic necrosis.
Technique	Endoscopic transluminal necrosectomy was done under sedation in 11 of the 14 studies, 1 study used moderate sedation or general anaesthesia, 1 study used conscious sedation with oral intubation, and 1 study did not report the type of sedation used.
Follow-up	Mean 23 months
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Patients lost to follow-up were excluded (number not stated).

Study design issues: There was 1 randomised controlled trial included in the review. Seven studies were retrospective, non-controlled cohort studies; 4 were retrospective, non-controlled cohort studies with prospective databases; and 1 was a retrospective, non-controlled cohort study in a partially prospective database. For 4 studies, results were only included from a subgroup of patients. Overall methodological quality of the studies was considered to be moderate to low. The number of patients per study ranged from 5 to 104. There was a lack of uniform patient selection. The primary end point in most studies was radiological findings, which does not necessarily correlate with current disease stage and outcome in every patient.

Study population issues: Aetiology was reported in 12 studies (52% biliary, 19% alcoholic, 29% other). Infected necrosis was proven by a positive bacteriological culture of pancreatic or peripancreatic necrosis before or at first necrosectomy in 57% (261/455) of patients. Baseline data on disease severity before intervention and clear definitions for organ failure and complications were poorly reported. When reported, scores were relatively low compared with most surgical series, suggesting a less ill patient population. At baseline, the mean Acute Physiology and Chronic Health Evaluation (APACHE-II; range 0–71, with higher scores indicating more severe disease) score was 8, CT severity index (range 0–10, with higher scores indicating more severe disease) was 7, organ failure was present in 23% of patients (14/62), and 32% (62/195) of patients were admitted to the intensive care unit before intervention.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: 455 Primary endoscopic necrosectomy was successful as definitive treatment in 81% (372/455) of patients. On average, 4 (range 1–23) endoscopic sessions were done per patient. 84% (382/455) of patients were treated by endoscopy alone; the remaining patients had 1 or more additional percutaneous or surgical interventions. Additional interventions: • Percutaneous, n=18 • Surgical, n=46 • Percutaneous and surgical, n=7 • Other, n=2 The main indications for intervention were persistent collections, recurrent collections, extended necrosis, perforation of a hollow organ, and bleeding.	Complications Total=36% (163/455) • Bleeding=18% (76/420) (treated endoscopically by coagulation, epinephrine injections or clips in 93% of patients; 7% of patients needed angiography with coiling or surgery) • Pancreatic fistula=5% (9/187) • Spontaneous perforation of a hollow organ (apart from the stomach or duodenum because of the intervention)=4% (9/249) • Air embolism=1% (2/207) The other complications were not described. Overall mortality=6% (28/455) (range 0–15% per study; 2 studies reported the in-hospital mortality and 12 studies reported mortality within the follow-up period) (no substantial heterogeneity: $I^2 < 30\%$, $p = 0.93$)

Study 3 Bakker OJ (2012) – study also included in Van Brunschot (2014) and Luigiano C (2016) systematic reviews

Details

Study type	Randomised controlled trial (Pancreatitis, Endoscopic Transgastric vs Primary Necrosectomy in Patients with Infected Necrosis [PENGUIN] trial)
Country	The Netherlands
Recruitment period	2008–10
Study population and number	n=20 (10 endoscopic necrosectomy versus 10 surgical necrosectomy; 22 were randomised originally, but 2 were withdrawn from the ‘surgery’ group as they had percutaneous drainage prior to surgery) Patients with infected necrotising pancreatitis.
Age and sex	Median 62 years (endoscopic necrosectomy) versus 64 years (surgical necrosectomy); 70% (14/20) male
Patient selection criteria	Adult patients needing necrosectomy for suspected or confirmed infected necrotising pancreatitis who could have either endoscopic or surgical necrosectomy, based on CT imaging. Infected necrosis was defined as a positive culture of pancreatic or peripancreatic necrosis obtained from fine-needle aspiration or the first drainage procedure or operation or by the presence of gas in the collection on contrast-enhanced CT scan. Suspected infected pancreatic necrosis was defined as persisting sepsis or progressive clinical deterioration despite maximal support on the intensive care unit without documented infected necrosis. Exclusion criteria were previous surgical or endoscopic necrosectomy, previous exploratory laparotomy, pancreatitis as a consequence of abdominal surgery, a flare-up of chronic pancreatitis, abdominal compartment syndrome, perforation of a visceral organ, or bleeding as indication for intervention.
Technique	Endoscopic transgastric necrosectomy: all procedures were done with the patient under conscious sedation. The procedure consisted of transgastric puncture, balloon dilatation, retroperitoneal drainage, and necrosectomy. Surgical necrosectomy: all procedures were done with the patient under general anaesthesia. Technique was video-assisted retroperitoneal debridement (n=6) or open necrosectomy through laparotomy (n=4). Continuous postoperative lavage was done using 2 large bore drains.
Follow-up	6 months
Conflict of interest/source of funding	No potential conflicts of interest were reported.

Analysis

Follow-up issues: There were no losses to follow-up. Follow-up visits took place 3 and 6 months after discharge.

Study design issues: Two patients who were assigned to surgical necrosectomy had percutaneous catheter drainage after randomisation and improved so that necrosectomy was no longer needed. These patients were excluded from the analysis. The method of randomisation is not described. An experienced radiologist blinded for treatment allocation evaluated all CT scans for the presence and extent of necrosis before randomisation and persisting fluid collections at 6 months after discharge. An adjudication committee consisting of 5 gastrointestinal surgeons and 2 gastroenterologists independently reviewed all clinical end points and performed a blinded outcome assessment. The primary end point was the pro-inflammatory response after necrosectomy, as measured by the serum level of the pro-inflammatory cytokine interleukin-6 (IL-6). Secondary end points included a composite clinical end point of death or major complications. Sample size calculation of 10 patients per group was based on detecting a reduction of 45% in pro-inflammatory response, with 30% within-group standard deviation, with 80% power. The study was not powered to show a difference in death rate.

IP overview: endoscopic transluminal pancreatic necrosectomy

Study population issues: Baseline characteristics were similar between the 2 treatment groups. 95% (19/20) of patients had proven infected necrosis at the first intervention. In the acute phase before randomisation, 40% of all patients had organ failure and 30% had multiple organ failure. The median APACHE II scores were 10 (interquartile range 6–14) in the endoscopic group and 11 (interquartile range 7–14) in the surgical treatment group ($p=0.76$).

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: 20 (10 versus 10) Median number of necrosectomies: - Endoscopic=3 (IQR 2–6) - Surgical=1 (IQR 1–2) Serum interleukin-6 (IL-6) levels were statistically significantly lower in the endoscopic group compared with the surgical group; the largest difference between the 2 groups was seen at 24 hours after the procedure (approximate values estimated from graphical presentation: 32 pg/ml versus 220 pg/ml; $p=0.005$) New intensive care unit admission after randomisation: - Endoscopic=10% (1/10) - Surgical=50% (5/10), $p=0.14$ Days in hospital after randomisation (surviving patients only), median (IQR): - Endoscopic=45 (12–69) - Surgical=36 (17–74), $p=0.91$	Major complications or death: - Endoscopic=20% (2/10) - Surgical=80% (8/10), $p=0.03$ Risk difference 0.60 (95% CI 0.16 to 0.80) (major complications comprised new-onset multiple organ failure, intra-abdominal bleeding needing intervention, enterocutaneous fistula or perforation of a visceral organ needing intervention, and pancreatic fistula) Major complications <i>New-onset multiple organ failure:</i> - Endoscopic=0% (0/10) - Surgical=50% (5/10), $p=0.03$ <i>Intra-abdominal bleeding needing intervention:</i> - Endoscopic=0% (0/10) - Surgical=0% (0/10) <i>Enterocutaneous fistula or perforation of a visceral organ needing intervention:</i> - Endoscopic=0% (0/10) - Surgical=20% (2/10), $p=0.47$ <i>Pancreatic fistula:</i> - Endoscopic=10% (1/10) - Surgical=70% (7/10), $p=0.02$ Death: - Endoscopic=10% (1/10; 8 days after randomisation) - Surgical=40% (4/10; 21, 29, 79 and 155 days after randomisation) Risk difference 0.30 (95% CI -0.08 to 0.60, $p=0.30$) All deaths were attributable to persistent multiple organ failure. Long-term complications (assessed 6 months after discharge) <i>New-onset diabetes:</i> - Endoscopic=22% (2/9) - Surgical=50% (3/6), $p=0.33$ <i>Use of pancreatic enzymes:</i> - Endoscopic=0% (0/9) - Surgical=50% (3/6), $p=0.04$ <i>Persisting fluid collections seen on CT scan:</i> - Endoscopic=22% (2/9) - Surgical=50% (3/6), $p=0.33$
Abbreviations used: IQR, interquartile range	

Study 4 Khreiss M (2015) – study also included in Luigiano C (2016) systematic review

Details

Study type	Non-randomised comparative study
Country	USA
Recruitment period	2008–13
Study population and number	n=40 (20 endoscopic necrosectomy versus 20 minimally invasive surgical cyst gastrostomy and necrosectomy) Patients with sterile walled-off pancreatic necrosis.
Age and sex	Median 55 years; 63% (25/40) male
Patient selection criteria	All patients had a diagnosis of walled-off necrosis based on a documented episode of necrotising pancreatitis and a CT or MRI scan confirming a well-encapsulated retrogastric pancreatic or peripancreatic collection persisting for more than 4 weeks after the index episode of necrotising pancreatitis. All patients with any septic features (defined as fever, white blood cell count, presence of gas in the collection, or any features of the systemic inflammatory response) were excluded from the analysis.
Technique	The comparator of minimally invasive surgery included robotic (n=14) and laparoscopic surgery (n=6).
Follow-up	Median 16 months for the endoscopic group and 6 months for the surgical group (p=0.027)
Conflict of interest/source of funding	None

Analysis

Follow-up issues: The follow-up period was statistically significantly longer in the endoscopic group than the surgical group (median 16 months versus 6 months, p=0.027).

Study design issues: Retrospective review. The treatment was decided by a multidisciplinary team; patients with gallstone pancreatitis were offered surgical cyst gastrostomy to allow concomitant removal of the gallbladder. The surgical approach (laparoscopic or robotic) was based on the surgeon's preference. An additional 4 patients were treated by minimally invasive surgery during the study period but were excluded because of clinical sepsis presumed to be from an infected walled-off necrosis.

Study population issues: The 2 treatment groups were similar with regard to age, race, body mass index, aetiology of pancreatitis and location of the walled-off necrosis. The endoscopic treatment group had a higher proportion of females (55% versus 20%, p=0.048), a lower Charlson comorbidity index (0.95 versus 1.5, p=0.03) and a smaller median cyst size compared with the surgical group (11.2 cm versus 15.2 cm, p=0.008).

Other issues: Although the intention was to exclude infected walled-off necrosis, some of the cultured debris was positive for microorganisms and a large number of patients did not have bacteriological assessment of the collected debris.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: 40 (20 versus 20) Failure rate (defined as any reintervention in the surgical group versus the need for surgical intervention in the endoscopic group): - Endoscopic=10% (2/20) (1 leak at the endoscopic cyst gastrostomy site causing an acute abdomen; 1 sepsis due to incomplete debridement after endoscopic cyst gastrostomy. Both patients were treated by laparotomy with cyst gastrostomy and pancreatic debridement, with good outcomes.) - Surgical=15% (3/20), $p=0.661$ (all were salvaged by endoscopy) Reintervention rate: - Endoscopic=45% (9/20) (8 endoscopic reinterventions and 1 percutaneously placed drain) - Surgical=15% (3/20), $p=0.08$ Index procedure length of stay: - Endoscopic=2 days - Surgical=7 days, $p=0.003$ Total length of stay (including the index procedure and any reinterventions and readmissions needed to resolution: - Endoscopic=3 days - Surgical=7 days, $p=0.032$ Time to resolution: - Endoscopic=3.6 months - Surgical=0.42 months, $p=0.001$ Reintervention in the endoscopic group was associated with increased body mass index ($p=0.043$) and tended to occur in patients with larger walled-off necrosis size ($p=0.110$).	Complications – endoscopic cohort Total=20% (4/20) - Infection, $n=2$ - Bleeding, $n=1$ - Perforation, $n=1$ (not further described) Complications – surgical cohort Total=20% (4/20) - Pulmonary embolus, $n=1$ - Infected port site, $n=1$ - Splenic artery pseudoaneurysm, $n=1$ (treated by coil embolisation) - Infected residual collection, $n=1$ (treated by endoscopic debridement and placement of a nasogastric tube) 90-day mortality=0% (0/40)

Study 5 Tan V (2014) – study also included in Luigiano C (2016) systematic review

Details

Study type	Non-randomised comparative study (retrospective)
Country	France (2 centres)
Recruitment period	2005–11
Study population and number	n=32 (11 endoscopic necrosectomy versus 21 surgical necrosectomy) Patients with infected acute necrotising pancreatitis.
Age and sex	Median 51 versus 52 years; 72% (23/32) male
Patient selection criteria	Patients with proved infected necrosis (defined by either a positive culture of peripancreatic necrosis, harvested by fine needle aspiration or by the presence of gas bubbles in the area of pancreas on a CT scan study associated with a septic status).
Technique	Endoscopic transgastric necrosectomy: double pigtail stents were left for drainage between the necrotic cavity and the stomach for at least 6 months. A long first procedure was done to ensure that necrosectomy was as complete as possible.
Follow-up	Median 483 days
Conflict of interest/source of funding	None

Analysis

Follow-up issues: There were no losses to follow-up.

Study design issues: Endoscopic necrosectomy was not available in 1 of the centres, which only offered surgical anterior necrosectomies. The other centre was the first French centre to use endoscopic necrosectomies. Patients from the 2 centres were compared retrospectively. The primary end point of the study was the hospital length of stay.

Study population issues: Baseline characteristics of the patients were similar between the 2 groups (age, sex ratio, American Society of Anesthesiologists [ASA] class, diabetes, obesity, proportion of patients with >1 cardiovascular risk). The proportion of patients with organ failure was statistically significantly lower in the endoscopic group than the surgical group (9% [1/11] versus 60% [13/21], $p=0.007$). Disease severity scores (Ranson, SAPS II, APACHE II) were statistically significantly lower in the endoscopic group but the radiological severity of pancreatitis graded by CTSI (CT severity index) did not differ. The distribution of peripancreatic collections differed in that all patients presenting with necrosis in the mesentery's root were in the surgical treatment group ($p=0.0006$).

Key efficacy and safety findings

Efficacy	Safety																																																																
Number of patients analysed: 32 (11 versus 21) 1 patient needed 3 successive endoscopic necrosectomies, all others were treated by a single procedure. Median hospital stay in intensive care unit: - Endoscopic=9 days - Surgical=30 days, p=0.008 Median total hospitalisation stay: - Endoscopic=32 days - Surgical=74 days, p=0.006	Complications Postoperative complications, n (%) <table><tr><th></th><th>Endoscopic n=11</th><th>Surgical n=21</th><th>p value</th></tr><tr><td>Patient with ≥1 complication</td><td>3 (27)</td><td>18 (86)</td><td>0.002</td></tr><tr><td>Death</td><td>0 (0)</td><td>3 (14)</td><td>0.53</td></tr><tr><td>New-onset organ failure</td><td>2 (18)</td><td>5 (17)</td><td>0.99</td></tr><tr><td>Bleeding</td><td>0 (0)</td><td>3 (14)*</td><td>0.53</td></tr><tr><td>Enterocutaneous fistula (needing intervention)</td><td>0 (0)</td><td>2 (9)</td><td>0.54</td></tr><tr><td>Pancreatic fistula (all grades)</td><td>0 (0)</td><td>8 (38)</td><td>0.03</td></tr><tr><td>Pancreatic fistula grade C</td><td>0 (0)</td><td>2 (9)</td><td>0.54</td></tr><tr><td>Late postoperative hernias (needing reoperation)</td><td>0 (0)</td><td>9 (43)</td><td>0.01</td></tr><tr><td>Bowel obstruction</td><td>0 (0)</td><td>4 (19)</td><td>0.27</td></tr><tr><td>Bowel perforation</td><td>1 (4.5)</td><td>0 (0)</td><td>0.34</td></tr><tr><td>Stent complication</td><td>2 (9)</td><td>0 (0)</td><td>0.11</td></tr></table> *including 2 deaths The cause of death was multiple organ failure for all 3 deaths. 5 patients in the surgical group needed relaparotomy, 3 for haemoperitoneum (2 died) and 2 for enterocutaneous fistula. Long-term pancreatic complications, n (%) <table><tr><th></th><th>Endoscopic n=11</th><th>Surgical n=21</th><th>p value</th></tr><tr><td>Diabetes</td><td>1 (9)</td><td>4 (19)</td><td>0.98</td></tr><tr><td>Use of pancreatic extracts</td><td>3 (27)</td><td>4 (19)</td><td>0.64</td></tr><tr><td>Pseudocysts</td><td>3 (27)</td><td>6 (29)</td><td>0.29</td></tr></table>		Endoscopic n=11	Surgical n=21	p value	Patient with ≥1 complication	3 (27)	18 (86)	0.002	Death	0 (0)	3 (14)	0.53	New-onset organ failure	2 (18)	5 (17)	0.99	Bleeding	0 (0)	3 (14)*	0.53	Enterocutaneous fistula (needing intervention)	0 (0)	2 (9)	0.54	Pancreatic fistula (all grades)	0 (0)	8 (38)	0.03	Pancreatic fistula grade C	0 (0)	2 (9)	0.54	Late postoperative hernias (needing reoperation)	0 (0)	9 (43)	0.01	Bowel obstruction	0 (0)	4 (19)	0.27	Bowel perforation	1 (4.5)	0 (0)	0.34	Stent complication	2 (9)	0 (0)	0.11		Endoscopic n=11	Surgical n=21	p value	Diabetes	1 (9)	4 (19)	0.98	Use of pancreatic extracts	3 (27)	4 (19)	0.64	Pseudocysts	3 (27)	6 (29)	0.29
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Study 6 Kumar N (2014) – study also included in Luigiano C (2016) systematic review

Details

Study type	Non-randomised comparative study
Country	USA
Recruitment period	2009–10
Study population and number	n=24 (12 endoscopic necrosectomy versus 12 step-up approach) Patients with acute pancreatitis and symptomatic walled-off pancreatic necrosis.
Age and sex	Mean 59 years (endoscopic necrosectomy) and 53 years (step-up approach); 71% (17/24) male
Patient selection criteria	Patients with acute pancreatitis and symptomatic walled-off pancreatic necrosis with suspected or confirmed infected necrosis. Patients with other prior intervention for walled-off pancreatic necrosis were excluded.
Technique	Endoscopic necrosectomy was done with the patient under general anaesthesia, and using CO ₂ insufflation. 3 double-pigtail stents were left in place. Follow-up endoscopy was done for repeat necrosectomy or stent removal as indicated. Patients in the step-up group had primary percutaneous catheter drainage under conscious sedation. Those patients with a lack of response to drainage or with clinical signs or symptoms of infection or abdominal pain were taken to surgery at the discretion of the surgical team. Surgical necrosectomy included both open and minimally invasive techniques.
Follow-up	1.9±0.3 years (endoscopic necrosectomy) and 2.5±0.8 years (step-up approach)
Conflict of interest/source of funding	None

Analysis

Study design issues: Matched cohort study using a prospective registry. Patients were matched based on collection size and Charlson comorbidity Index. The primary outcome was clinical resolution of symptomatic walled-off pancreatic necrosis after the primary therapeutic modality. Clinical resolution was defined as resolution of primary symptom and absence of abdominal pain, nausea, vomiting, fever, leucocytosis, and sepsis.

Study population issues: There were no significant differences in baseline characteristics between the 2 groups. No patients had multiple organ failure before the procedure.

Key efficacy and safety findings

Efficacy	Safety																
Number of patients analysed: 24 (12 versus 12) Number of procedures: - Patients in the endoscopic necrosectomy group each had 1.4±0.2 necrosectomies. - Patients in the step-up approach group each had 2.0±0.2 catheter placements, p=0.015 Clinical resolution after primary therapeutic modality: - Endoscopic necrosectomy=91.7% (11/12) - Step-up approach (after percutaneous catheter drainage)=25.0% (3/12), p=0.0028 Intravenous antibiotic use after the procedure: - Endoscopic necrosectomy=25.0% (3/12) - Step-up approach=91.7% (11/12), p=0.003 Intensive care unit length of stay (days): - Endoscopic necrosectomy=0.2 - Step-up approach=5.4±2.5, p=0.04 1 patient in the endoscopic necrosectomy group had percutaneous catheter drainage at 26 weeks follow-up because of a persistent collection that was not endoscopically accessible, with evidence of infection. 75% (9/12) of patients in the step-up approach group proceeded to minimally invasive surgical necrosectomy after 3.4±0.9 weeks for persistent signs or symptoms of infection. All 9 patients had resolution of symptoms after 1 surgical procedure.	Procedural complications: - Endoscopic necrosectomy=8.3% (1/12) (bleeding) - Percutaneous catheter drainage=8.3% (1/12) (wound infection) 7 of the 9 patients treated by surgical necrosectomy had a total of 8 complications: 6 patients had bleeding that needed transfusion and 1 patient had both wound infection and enterocutaneous fistula. Organ failure No patients in the endoscopic necrosectomy group developed organ failure after the procedure. In the step-up group, 2 patients had organ failure after the primary procedure and 3 developed new organ failure after surgical necrosectomy. In-hospital mortality: - Endoscopic necrosectomy=0% (0/12) - Step-up approach=8.3% (1/12) – patient died with pulseless electrical activity arrest 28 days after percutaneous catheter drainage. The patient was receiving intravenous antibiotics but not vasopressors or total parenteral nutrition, and did not have organ failure. Long-term follow-up, n (%) <table><tr><th></th><th>Endoscopic n=12</th><th>Step-up approach n=11</th><th>p value</th></tr><tr><td>New endocrine insufficiency</td><td>0 (0)</td><td>7 (63.6)</td><td><0.01</td></tr><tr><td>New exocrine insufficiency</td><td>3 (25.0)</td><td>5 (45.5)</td><td>not reported</td></tr><tr><td>Mortality</td><td>0 (0)</td><td>0 (0)</td><td></td></tr></table>		Endoscopic n=12	Step-up approach n=11	p value	New endocrine insufficiency	0 (0)	7 (63.6)	<0.01	New exocrine insufficiency	3 (25.0)	5 (45.5)	not reported	Mortality	0 (0)	0 (0)	
	Endoscopic n=12	Step-up approach n=11	p value														
New endocrine insufficiency	0 (0)	7 (63.6)	<0.01														
New exocrine insufficiency	3 (25.0)	5 (45.5)	not reported														
Mortality	0 (0)	0 (0)															

Study 7 Schmidt PN (2015) – study also included in Luigiano C (2016) systematic review

Details

Study type	Case series
Country	Denmark
Recruitment period	2005–11
Study population and number	n=81 Patients with acute pancreatitis and walled-off necrosis.
Age and sex	Median 54 years; 64% (52/81) male
Patient selection criteria	Patients with persistently symptomatic collections despite either optimal conservative treatment, percutaneous drainage, or in a few cases also surgical treatment. Symptoms included infection, pain, gastric outlet obstruction, bile duct obstruction, and leakage.
Technique	Endosonography-guided, transgastric or transduodenal drainage followed by endoscopic debridement of loose necrotic material using a therapeutic gastroscope and either tripod, stone retrieval basket or polypectomy snare. Endoscopic necrosectomy was usually not done during the index procedure. Percutaneous catheters were placed when there were widely expanding peripancreatic collections that were not accessible by the endoscopic route alone. All endoscopies were done with CO ₂ insufflation. The endoscopic sessions with redilatation of the transmural tract and debridement were repeated at weekly intervals until the necrotic cavity was free of debris and granulation tissue was seen. At that time, the nasocystic catheter was removed. The pigtail stents were removed 1 year after the index procedure.
Follow-up	Median 41 months (range 14–91)
Conflict of interest/source of funding	None

Analysis

Follow-up issues: No patients were lost to follow-up.

Study design issues: The aim of the study was to assess the outcome and safety profile of the procedure in the patient cohort.

Study population issues: 71% of patients had culture-proven infected walled-off necrosis at the index endoscopy. Percutaneous fine-needle aspiration or drainage were done before the index endoscopy in 35 patients (43%) and 6 patients had been treated by surgery before referral to the study centre. 30% of patients had organ failure (multiple organ failure in 23%; respiratory 27%, circulatory 19%, renal 17%, and gastrointestinal 9%) and 28% needed treatment in the intensive care unit. Pancreatic parenchymal necrosis was present in 92% (73/81) of patients.

Other issues: The number of endoscopies ranged from 1–8, which suggests that some patients may not have been treated by endoscopic necrosectomy after the index endoscopy. The paper does not specifically state how many patients were treated by endoscopic necrosectomy.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: 81 Median number of endoscopies=4 (range 1–8) Clinical success rate of endoscopic transmural drainage and necrosectomy=89% (72/81) (defined as the proportion of patients surviving with complete resolution of their walled-off necrosis and concomitant resolution of their clinical symptoms without need of surgical necrosectomy) Recurrence 4.2% (3/72) of patients had recurrence of small symptomatic collections and needed additional endoscopic treatment, which resulted in complete resolution.	Procedure-related complications • None=88% (71/81) • Death as a consequence of periprocedural septic shock=1.2% (1/81) • Bleeding from necrosis cavity managed by embolisation=4.9% (4/81) • Pneumoperitoneum without the need for intervention or treated by needle aspiration=4.9% (4/81) • Bleeding from transmural tract treated with epinephrine injection and transfusion=1.2% (1/81) In-hospital mortality=11.1% (9/81) (4 multiple organ failure because of sepsis, 2 circulatory failure caused by arterial bleeding unrelated to endoscopy, 2 respiratory failure, 1 septic shock and multiple organ failure considered as immediate complication to endoscopic procedure) 1-year mortality=0% (defined as death within 1 year from the date of discharge) Long-term mortality=4.2% (3/72) (1 patient died from pancreatic cancer 22 months after discharge)

Study 8 Yasuda I (2013) – study also included in Luigiano C (2016) systematic review

Details

Study type	Case series (retrospective)
Country	Japan (16 centres)
Recruitment period	2005–11
Study population and number	n=57 Patients with infected walled-off pancreatic necrosis.
Age and sex	Median 58 years (range 19–81); 81% (46/57) male
Patient selection criteria	Not reported
Technique	Endoscopic necrosectomy was done on the same day as the initial drainage in 19% (11/57) of patients, and between 1 and more than 15 days later in the remaining patients. CO ₂ gas was used instead of room air for insufflation in 39 patients. Endoscopic necrosectomy was done 1–4 times a week until all necrotic tissue had been removed. The route to the necrotic cavity was maintained by placing stents or a nasocystic drainage catheter. Endoscopic necrosectomy was continued until the majority of necrotic tissue was removed and pink granulation tissue lining the wall was observed. At the final endoscopic necrosectomy session, stents were sometimes placed depending on each institution's protocol.
Follow-up	Median 27 months
Conflict of interest/source of funding	None

Analysis

Follow-up issues: Follow-up data were obtained by interviews at the outpatient clinic. If patients had not been followed up periodically, the physician contacted the patients or their family by telephone. There were no losses to follow-up.

Study design issues: The primary outcomes were successful resolution of pancreatic necrosis by endoscopic necrosectomy and the associated mortality and complications. Successful resolution was defined as remission of clinical symptoms and the disappearance of the necrotic cavity on endoscopic necrosectomy imaging. Incomplete resolution was defined as the need for surgery or additional non-surgical treatments to cure the infected walled-off necrosis. The secondary outcome was prognosis after endoscopic necrosectomy.

Study population issues: Of the 57 patients, 10 were in very poor health before the procedure (grade 4 or 5 on the American Society of Anaesthesiologists [ASA] physical status classification). In 6 patients, the necrotic cavity extended to the pelvis.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: 57 Median number of endoscopic necrosectomy sessions=5 (range 1–20) Median length of hospital stay=21 days (range 10–101) Successful resolution=75% (43/57) All patients initially received parenteral nutrition; 12 patients recommenced normal food intake within 7 days and another 12 patients received enteral feeding of an elemental diet. Of the 14 patients for whom treatment was unsuccessful, 6 (11%) died during the treatment period before resolution and 8 (14%) were converted to other treatments (3 additional percutaneous drainage and 5 surgery) because of persistent sepsis, after a mean endoscopic necrosectomy treatment period of 29 days (range 2–59 days). Of these 8 patients, 6 eventually had successful resolution but 2 died after further treatment. Patients in poor medical health (ASA classification ≥ 3) were significantly more likely to have an unsuccessful endoscopic necrosectomy ($p=0.0437$). Recurrence 5.3% (3/57) of patients had a recurrent cavity after 2–8 months: 2 with infection and 1 without. These patients were successfully treated by endoscopic or percutaneous drainage. Comparison with surgical necrosectomy The number of surgical necrosectomies at the study centres was 21, and treatment was successful in 71.4%. The associated morbidity and mortality were 52.3% and 28.6% respectively. The median hospital stay was 140 days (range 30–304).	Complications=33% (19/57) Complications during the procedure • Bleeding from the fistula=8.8% (5/57) • Bleeding from the cavity wall=5.3% (3/57) • Perforation=5.3% (3/57) • Air embolism=1.8% (1/57) - the patient died Complications between treatment sessions • Rupture of splenic aneurysm=3.5% (2/57) – 1 patient died • Mallory-Weiss tear=1.8% (1/57) – the patient died • Bleeding from the fistula=1.8% (1/57) • Aspiration pneumonia=1.8% (1/57) • Ileus=1.8% (1/57) • Sudden cardiorespiratory arrest (unknown cause)=1.8% (1/57) – the patient died Mortality during the treatment period=11% (6/57) (in addition to the 4 deaths described above, 2 patients died from multiple organ failure secondary to sepsis). 2 patients died during follow-up because of unrelated causes: 1 from bile duct cancer after 6 months and 1 from pneumonia after 14 months.

Study 9 Bonnot B (2014)

Details

Study type	Case report
Country	France
Recruitment period	Not reported
Study population and number	n=1 Patient with severe acute pancreatitis and infected necrosis.
Age and sex	63-year old woman
Patient selection criteria	Not reported
Technique	Endoscopic transgastric necrosectomy with carbon dioxide insufflation under general anaesthesia. Endoscopic necrosectomy was repeated 4 more times.
Follow-up	None
Conflict of interest/source of funding	None

Key efficacy and safety findings

Fatal gas embolism

The patient was admitted with severe acute pancreatitis and moderate respiratory failure. On day 22, sepsis developed and CT showed gas within peripancreatic and retrogastric heterogeneous collections consistent with infected necrosis. CT-guided percutaneous drainage was done. Culture was positive for *Enterobacter cloacae*. Endoscopic transgastric necrosectomy was done on day 29 because of persistent sepsis. This was repeated on days 34, 37, 47 and 55. Gas was visible in the venous portal system on day 47 but not 7 days later. On day 63, a sixth necrosectomy procedure was started but bradycardia developed, followed by asystolic cardiac arrest. Immediate CT of the chest and abdomen showed massive gas embolism in the venous portal system and the right and left cardiac chambers. The patient died despite prolonged resuscitation.

Efficacy

Clinical success

In a systematic review of 938 patients, the mean clinical success rate was 89% (range 75–100%)¹. In a systematic review of 455 patients, primary endoscopic necrosectomy was successful as definitive treatment in 81% (372/455) of patients². In a non-randomised comparative study, 24 patients were treated by endoscopic necrosectomy or a step-up approach (percutaneous catheter drainage with possible surgery). Clinical resolution (defined as resolution of primary symptoms and no abdominal pain, nausea, vomiting, fever, leucocytosis or sepsis) was reported in 92% (11/12) of patients after endoscopic necrosectomy and 25% (3/12) of patients after percutaneous catheter drainage in the step-up approach group ($p=0.0028$)⁶. In a case series of 81 patients, clinical success (defined as the proportion of patients surviving with complete resolution of their necrosis and concomitant resolution of their clinical symptoms without needing surgical necrosectomy) was reported in 89% (72/81) of patients⁷. In a case series of 57 patients, successful resolution was reported in 75% (43/57) of patients⁸.

In the systematic review of 455 patients, 16% (73/455) of patients needed additional interventions after endoscopic necrosectomy (18 percutaneous, 46 surgical, 7 percutaneous and surgical, 2 other)². In the non-randomised comparative study of 40 patients treated by endoscopic or surgical necrosectomy re-intervention rates of 45% (9/20) and 15% (3/20) were reported respectively ($p=0.08$)⁴. This study also reported failure rates (defined as any re-intervention in the surgical group versus the need for surgical intervention in the endoscopic group) of 10% (2/20) and 15% (3/20) respectively ($p=0.661$)⁴. In the case series of 81 patients, small collections of necrotic tissue and fluid that caused symptoms recurred in 4% (3/72) of patients. These patients needed additional endoscopic treatment, which resulted in complete resolution⁷. In the case series of 57 patients, 5% (3/57) of patients had a recurrent cavity after 2–8 months; they were successfully treated by endoscopic or percutaneous drainage⁸.

Length of hospital stay

In a randomised controlled trial of 20 patients treated by endoscopic or surgical necrosectomy (included in the systematic review) hospital stays after randomisation were 45 and 36 days respectively ($p=0.91$)³. In a non-randomised comparative study of 40 patients treated by endoscopic or surgical necrosectomy the length of stay for the index procedure was 2 and 7 days respectively ($p=0.003$). The total length of stay was 3 days for patients treated by endoscopic necrosectomy compared with 7 days for patients treated by surgical necrosectomy ($p=0.032$)⁴. In a non-randomised comparative study of 32 patients treated by endoscopic or surgical necrosectomy, median length of hospital stay was 32 and 74 days respectively ($p=0.006$)⁵.

Safety

Death

The mean overall mortality rate after this procedure was reported as 5% (range 0–25% per study) in a systematic review of 938 patients¹. Overall mortality after this procedure was reported as 6% (28/455; range 0–15% per study) in a systematic review of 455 patients; this included both in-hospital mortality and mortality within the follow-up period². Death was reported in 10% (1/10) of patients treated by endoscopic necrosectomy and 40% (4/10) of patients treated by surgical necrosectomy ($p=0.30$) in a randomised controlled trial of 20 patients (included in the systematic review)³. The death rate was 0% (0/11) in patients treated by endoscopic necrosectomy compared with 14% (3/21) of patients treated by surgical necrosectomy ($p=0.53$) in a non-randomised comparative study of 32 patients⁵. In-hospital mortality was 0% (0/12) for patients treated by endoscopic necrosectomy compared with 8% (1/12) for patients treated by a step-up approach in a non-randomised comparative study of 24 patients⁶. A case series of 81 patients reported in-hospital mortality of 11% (9/81): 4 multiple organ failure because of sepsis, 2 circulatory failure because of arterial bleeding unrelated to endoscopy, 2 respiratory failure, 1 septic shock and multiple organ failure considered as immediate complication to endoscopic procedure⁷. A case series of 57 patients reported mortality during the treatment period of 11% (6/57): 2 multiple organ failure secondary to sepsis, 1 air embolism, 1 splenic aneurysm rupture, 1 Mallory-Weiss tear, and 1 sudden cardiorespiratory arrest of unknown cause⁸.

Air or gas embolism

Fatal gas embolism after endoscopic transgastric necrosectomy with carbon dioxide insufflation was described in a case report⁹. Air embolism was reported in 0.4% (4/938) of patients in the systematic review of 938 patients¹. Air embolism was reported in 1 patient in the case series of 57 patients: the patient died (also included in the deaths described previously)⁸.

Bleeding

Bleeding was reported in 11% (103/938) of patients in the systematic review of 938 patients¹. It was reported in 18% (76/420) of patients in the systematic review of 455 patients². This was treated endoscopically by coagulation, epinephrine injections or clips in 93% of patients; 7% of patients needed angiography with coiling or surgery². Bleeding was reported in 1 patient treated by endoscopic necrosectomy in a non-randomised comparative study of 40 patients⁴. Bleeding was reported in 8% (1/12) of patients treated by

endoscopic necrosectomy and 50% (6/12) of patients treated by surgical necrosectomy in the non-randomised comparative study of 24 patients⁶. Bleeding from the necrosis cavity, managed by embolisation, was reported in 5% (4/81) of patients in the case series of 81 patients. Bleeding from the transmural tract, treated with epinephrine injection and transfusion, was reported in 1 patient in the same study⁷. Bleeding from the cavity wall and bleeding from the fistula during the procedure were reported in 5% (3/57) and 9% (5/57) of patients respectively in the case series of 57 patients⁸.

Pancreatic fistula

Pancreatic fistula was reported in 5% (9/187) of patients in the systematic review of 455 patients². It was also reported in 10% (1/10) of patients treated by endoscopic necrosectomy and 70% (7/10) of patients treated by surgical necrosectomy ($p=0.02$) in the randomised controlled trial of 20 patients (included in the systematic review)³. Pancreatic fistula was reported in 0% (0/11) in patients treated by endoscopic necrosectomy compared with 38% (8/21) of patients treated by surgical necrosectomy ($p=0.03$) in a non-randomised comparative study of 32 patients⁵.

Perforation or pneumoperitoneum

Perforation or pneumoperitoneum was reported in 3% (26/938) of patients in the systematic review of 938 patients¹. Spontaneous perforation of a hollow organ (apart from the stomach or duodenum because of the intervention) was reported in 4% (9/249) of patients in the systematic review of 455 patients². Perforation (not further described) was reported in 1 patient treated by endoscopic necrosectomy in the non-randomised comparative study of 40 patients⁴. Bowel perforation was reported in 1 patient treated by endoscopic necrosectomy in the non-randomised comparative study of 32 patients⁵. Perforation was reported in 5% (3/57) of patients in the case series of 57 patients⁸. Pneumoperitoneum, without the need for intervention or treated by needle aspiration, was reported in 5% (4/81) of patients in the case series of 81 patients⁷.

Organ failure

New-onset organ failure was reported in 18% (2/11) of patients treated by endoscopic necrosectomy and 17% (5/21) of patients treated by surgical necrosectomy ($p=0.99$) in the non-randomised comparative study of 32 patients⁵.

Infection

Infection was reported in 2 patients treated by endoscopic necrosectomy in the non-randomised comparative study of 40 patients⁴.

Stent complication

Stent complication (not further described) was reported in 9% (2/11) of patients treated by endoscopic necrosectomy in the non-randomised comparative study of 32 patients⁵.

Diabetes

New-onset diabetes (assessed 6 months after hospital discharge) was reported in 22% (2/9) of patients treated by endoscopic necrosectomy and 50% (3/6) of patients treated by surgical necrosectomy ($p=0.33$) in the randomised controlled trial of 20 patients³.

Validity and generalisability of the studies

- The systematic reviews include a retrospective cohort study from the UK.
- The patient populations are heterogeneous. The systematic reviews included patients with infected necrotising pancreatitis^{1,2}. One non-randomised comparative study only included patients with sterile walled-off pancreatic necrosis⁴.
- In 1 of the non-randomised comparative studies, disease severity scores were statistically significantly lower in the endoscopic treatment group than in the surgical treatment group⁵.
- The technique varied between studies. One study specifically aimed to complete the necrosectomy in a single procedure⁵, but most studies completed the treatment over a number of sessions.
- Most of the studies are retrospective and there is only 1 small randomised controlled trial.

Existing assessments of this procedure

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

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Percutaneous retroperitoneal endoscopic necrosectomy. NICE interventional procedure guidance 384 (2011). Available from <http://www.nice.org.uk/guidance/IPG384>

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 is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. Three Specialist Advisor Questionnaires for endoscopic transluminal pancreatic necrosectomy were submitted and can be found on the [NICE website](#).

Patient commentators' opinions

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

Issues for consideration by IPAC

None other than those described above.

References

1. Luigiano C, Pellicano R, Fusaroli P et al. (2016) Pancreatic necrosectomy: an evidence-based systematic review of the levels of evidence and a comparison of endoscopic versus non-endoscopic techniques. *Minerva Chirurgica* 71: 262–9
2. van Brunschot S, Fockens P, Bakker OJ et al. (2014) Endoscopic transluminal necrosectomy in necrotising pancreatitis: a systematic review. *Surgical Endoscopy* 28: 1425–38
3. Bakker OJ, van Santvoort HC, van Brunschot S et al. (2012) Endoscopic transgastric vs surgical necrosectomy for infected necrotizing pancreatitis: a randomized trial. *JAMA* 307: 1053-1061
4. Khreiss M, Zenati M, Clifford A et al. (2015) Cyst Gastrostomy and Necrosectomy for the Management of Sterile Walled-Off Pancreatic Necrosis: a Comparison of Minimally Invasive Surgical and Endoscopic Outcomes at a High-Volume Pancreatic Center. *Journal of Gastrointestinal Surgery* 19: 1441–48
5. Tan V, Charachon A, Lescot T et al. (2014) Endoscopic transgastric versus surgical necrosectomy in infected pancreatic necrosis. *Clinics & Research in Hepatology & Gastroenterology* 38: 770-776
6. Kumar N, Conwell DL, Thompson CC. (2014) Direct endoscopic necrosectomy versus step-up approach for walled-off pancreatic necrosis comparison of clinical outcome and health care utilization. *Pancreas* 43: 1334–39
7. Schmidt PN, Novovic S, Roug S et al. (2015) Endoscopic, transmural drainage and necrosectomy for walled-off pancreatic and peripancreatic necrosis is associated with low mortality--a single-center experience. *Scandinavian Journal of Gastroenterology* 50: 611–18
8. Yasuda I, Nakashima M, Iwai T (2013) Japanese multicenter experience of endoscopic necrosectomy for infected walled-off pancreatic necrosis: The JENIPaN study. *Endoscopy* 45: 627-634

Appendix A: Additional papers on endoscopic transluminal pancreatic necrosectomy

The following table outlines the studies that are considered potentially relevant to the IP 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.

Studies with fewer than 10 patients were excluded.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Abdelhafez M, Elnegouly M, Hasab Allah MS et al. (2013) Transluminal retroperitoneal endoscopic necrosectomy with the use of hydrogen peroxide and without external irrigation: a novel approach for the treatment of walled-off pancreatic necrosis. Surgical Endoscopy 27: 3911-3920	Case series n=10 Median follow-up=289 days	Complete radiological success and long-term clinical efficacy was achieved in nine patients (1 patient had an inaccessible left paracolic gutter collection and died 62 days after endotherapy). Mean number of sessions was 1.4 (range 1-2). Complications included bleeding, which was self-limited in three patients and endoscopically controlled in one. All patients avoided surgery, and no recurrence was reported.	Included in Van Brunschot (2014) systematic review.
Albers D, Toermer T, Charton JP et al. (2016) Endoscopic therapy for infected pancreatic necrosis using fully covered self-expandable metal stents: combination of transluminal necrosectomy, transluminal and percutaneous drainage. Zeitschrift fur Gastroenterologie 54: 26-30	Case series n=13 Mean follow-up=8.5 months	A sustained clinical success was achieved in 12 of 13 cases. Discharge occurred after 2.5 +/- 22.4 days. The self-expanding metal stent was extracted after 82.5 +/- 56.6 days. Mean follow up was 8.5 +/- 5.9 months	Studies with more patients or longer follow-up are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Attam R, Trikudanathan G, Arain M et al. (2014) Endoscopic transluminal drainage and necrosectomy by using a novel, through-the-scope, fully covered, large-bore esophageal metal stent: preliminary experience in 10 patients. <i>Gastrointestinal Endoscopy</i> 80: 312-318	Case series n=10	Resolution of walled-off necrosis was achieved in 9 of the 10 patients (90%) after a median of 3 endoscopic sessions. There were no early adverse events. Late adverse events occurred in 3 patients (30%); worsening of infection from stent migration and occlusion of cystogastrostomy (2 patients), and fatal pseudoaneurysmal bleeding from erosion of infected necrosis into a major artery distant from the stent (1 patient). The stent was easily removed in all the cases after resolution or improvement of the necrotic cavity.	Larger studies are included.
Babu BI, Siriwardena AK (2009) Current status of minimally invasive necrosectomy for post-inflammatory pancreatic necrosis. <i>HPB</i> 11: 96-102	Review n=344 patients (157 endoscopic necrosectomy)	Overall, 157 patients underwent endoscopic necrosectomy; major complications were reported in 31 (20%) and death in seven (5%).	A more recent systematic review is included.
Bausch D, Wellner U, Kahl S et al. (2012) Minimally invasive operations for acute necrotizing pancreatitis: comparison of minimally invasive retroperitoneal necrosectomy with endoscopic transgastric necrosectomy. <i>Surgery</i> 152: S128-34	Non-randomised comparative study n=32 (18 endoscopic necrosectomy)	Problems after open necrosectomy (ONE) and minimally invasive retroperitoneal necrosectomy (MINE) were ongoing sepsis (ONE 73% vs MINE 29% vs endoscopic transgastric necrosectomy [ETG] 11%) and bleeding requiring intervention (ONE 26% vs MINE 21% vs ETG 17%). A specific complication of ETG was gastric perforation into the peritoneal cavity during the procedure (28%), requiring immediate open pseudocystogastrostomy. Laparotomy was necessary in 21% after MINE and 28% after ETG owing to specific complications or persistent infected necrosis. Overall mortality was greatest after ONE (ONE 63% vs MINE 21% vs ETG 6%; $p<0.05$).	Included in Van Brunschot (2014) systematic review.
Bello B, Matthews JB (2012) Minimally invasive treatment of pancreatic necrosis. <i>World Journal of Gastroenterology</i> 18: 6829-6835	Systematic review n=947 patients (27 studies, including 10 on endoscopic necrosectomy)	Each minimally invasive approach though was found to be safe and feasible in multiple reports. With these new techniques, treatment of infected pancreatic necrosis remains a challenge. We advocate a multidisciplinary approach to this complex problem with treatment individualised to each patient.	A more recent systematic review is included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Coelho D, Ardengh JC, Eulalio JM et al. (2008) Management of infected and sterile pancreatic necrosis by programmed endoscopic necrosectomy. Digestive Diseases 26: 364–9	Case series n=56 Mean follow-up=21 months	There were 2 (11%) pseudocyst recurrences and 1 (5%) recurrence of new episodes of pancreatic necrosis. All were managed clinically and/or endoscopically. No mortality was related to the procedure.	Included in Van Brunschot (2014) systematic review.
Charnley RM, Lochan R, Gray H et al. (2006) Endoscopic necrosectomy as primary therapy in the management of infected pancreatic necrosis. Endoscopy 38: 925–28	Case series n=13 Median follow-up=16 months	Necrosis was successfully treated endoscopically in 12 patients, requiring a mean of 4 endoscopic interventions (range 1-10); 1 patient needed open surgery; 2 had additional percutaneous necrosectomy and 1 needed laparoscopic drainage. Two patients died of complications unrelated to the procedure.	Included in Van Brunschot (2014) systematic review.
Cho JH, Kim YJ, Kim YS. (2014) Paradigm shift away from open surgical necrosectomy toward endoscopic interventions for necrotizing pancreatitis. Gastrointestinal Intervention 3: 84-88	Review 14 studies	Interventions for infected and symptomatic walled-off pancreatic necrosis (WOPN) have undergone a paradigm shift away from open surgical necrosectomy toward endoscopic intervention such as transmural drainage and necrosectomy. Recent multicentre studies and evidence-based guidelines have suggested the safety and efficacy of endoscopic transmural necrosectomy (ETN) for management of complicated WOPN. In consideration of the inherent properties and the risks associated with this procedure, ETN should be performed by expert endoscopists who are well-versed in management of necrotizing pancreatitis and supported by a special multidisciplinary team.	No meta-analysis.
Escourrou J, Shehab H, Buscail L et al. (2008) Peroral transgastric/transduodenal necrosectomy: success in the treatment of infected pancreatic necrosis. Annals of Surgery 248 (6) 1074–1080	Case series n=13 Follow-up=20 months	This technique is highly effective and safe in the treatment of infected organised pancreatic necrosis. Results are achievable and sustainable with a limited number of sessions.	Larger studies are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Gardner TB, Coelho-Prabhu N, Gordon SR et al. (2011) Direct endoscopic necrosectomy for the treatment of walled-off pancreatic necrosis: results from a multicenter U.S. series. <i>Gastrointestinal Endoscopy</i> 73: 718–26	Case series n=104 Mean follow-up=19.5 months	Successful resolution=91% (95/104) Of the patients in whom it failed, 5 died during follow-up before resolution, 2 had operative drainage for persistent walled-off pancreatic necrosis, 1 needed surgery for massive bleeding on fistula tract dilation, and 1 died periprocedurally. The mean time to resolution was 4 months after treatment. The median number of procedures was 3 with 2 debridements. Complications occurred in approximately 14% and included 5 retrogastric perforations or pneumoperitoneum, which were managed nonoperatively. Univariate analysis identified a body mass index >32 as a risk factor for failed necrosectomy.	Included in Van Brunschot (2014) systematic review. <i>(Included in table 2 of 2011 overview)</i>
Gardner TB, Chahal P, Papachristou GI et al. (2009) A comparison of direct endoscopic necrosectomy with transmural endoscopic drainage for the treatment of walled-off pancreatic necrosis. <i>Gastrointestinal Endoscopy</i> 69: 1085-1095	Non-randomised comparative study n=45 Mean follow-up=14 months	Successful resolution was accomplished in 88% of patients who had direct endoscopic necrosectomy versus 45% who had standard drainage ($p<0.01$), without a change in the total number of procedures. The maximum size of tract dilation was larger in the direct endoscopic necrosectomy group (17mm vs 14mm, $p<0.02$). Complications were limited to mild periprocedural bleeding with equivalent rates between groups.	Included in Van Brunschot (2014) systematic review. <i>(Included in table 2 of 2011 overview)</i>
Gornals JB, Consiglieri CF, Busquets J et al. (2016) Endoscopic necrosectomy of walled-off pancreatic necrosis using a lumen-apposing metal stent and irrigation technique. <i>Surgical Endoscopy</i> 30: 2592-2602	Case series n=12 Mean follow-up=13 months	This new variant of irrigation endoscopic transmural necrosectomy without mechanical debridement helps to simplify the technique, is feasible, and has excellent outcomes in walled-off pancreatic necrosis treatment.	Studies with more patients or longer follow-up are included.
Gurusamy KS, Belgaumkar AP, Haswell A et al. (2016) Interventions for necrotising pancreatitis. <i>Cochrane Database of Systematic Reviews</i> 4 CD011383-2016.	Systematic review n=311 (8 RCTs)	Very low quality evidence suggested that the endoscopic minimally invasive step-up approach resulted in fewer adverse events than the video-assisted minimally invasive step-up approach but increased the number of procedures required for treatment.	Review only included 1 RCT on endoscopic transluminal pancreatic necrosectomy, which is already included in table 2.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Haghshenasskashani, A, Laurence JM, Kwan V et al. (2011) Endoscopic necrosectomy of pancreatic necrosis: a systematic review. Surgical Endoscopy 25: 3724-3730	Systematic review n=260 patients (10 case series)	The overall mortality rate was 5%. The mean procedure-related morbidity rate was 27%. The rate of complete resolution of pancreatic necrosis with the endoscopic method alone was 76%.	A more recent systematic review is included.
Huggett MT, Oppong KW, Pereira SP et al. (2015) Endoscopic drainage of walled-off pancreatic necrosis using a novel self-expanding metal stent. Endoscopy 2015	Case series n=19 (14 necrosectomy)	Resolution or reduction in the size of collection by at least 80% was achieved in all patients. Percutaneous or surgical drainage was required in 3 patients. Five stents migrated or dislodged. One patient had abdominal pain post-procedure. Five patients died during follow-up 3 from multi-organ failure, and 2 unrelated to pancreatitis).	Larger studies are included.
Isayama H, Nakai Y, Rerknimitr R et al. (2016) The Asian consensus statements on endoscopic management of walled-off necrosis Part2: Endoscopic management. J Gastroenterol Hepatol 2016	Review	An endoscopic (transgastric/retroperitoneal) approach with or without necrosectomy is associated with lower morbidity when compared to open surgery. Endoscopic necrosectomy is associated with definite risks of morbidity (bleeding, perforation, air embolism, etc.) and mortality.	Consensus statements based on literature review.
Jurgensen C, Naser F, Boese-Landgraf J et al. (2012) Endoscopic ultrasound-guided endoscopic necrosectomy of the pancreas: is irrigation necessary? Surgical Endoscopy 26: 1359-1363	Case series n=35 Median follow-up=23 months	An average of 6.2 endoscopy sessions per patient were needed for access, necrosectomy, and stent management. The in-hospital mortality rate was 6% (2/35), including one procedure-related death resulting from postinterventional aspiration. The immediate morbidity rate was 9% (3/35). It was possible to achieve clinical remission for all the surviving patients with no additional surgery needed for management of the necroses.	Larger studies are included.
Mukai S, Itoi T, Sofuni A et al (2015) Expanding endoscopic interventions for pancreatic pseudocyst and walled-off necrosis. Journal of Gastroenterology 50: 211-221	Case series n=89 (32 endoscopic necrosectomy)	Even complicated walled-off necrosis cases can be treated using combination endotherapies, although a surgical approach as well as a percutaneous approach should be considered in the cases refractory to endoscopic therapies.	Study includes a combination of interventions.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Papachristou GI, Takahashi N, Chahal P et al. (2007) Peroral endoscopic drainage/debridement of walled-off pancreatic necrosis. <i>Annals of Surgery</i> 245:943-951	Case series n=53 Mean follow-up=6 months	81% (43/53) of patients had successful drainage/debridement (defined as complete or almost complete resolution of the collection and resolution of clinical symptoms). Complete resolution of walled-off pancreatic necrosis in 23 patients and marked improvement in 20. 40% (21/53) of patients required concurrent percutaneous drainage. 23% (12/53) of patients required open intervention at a median of 47 days follow-up.	Included in Van Brunschot (2014) systematic review. <i>(Included in table 2 of 2011 overview)</i>
Puli SR, Graumlich JF, Pamulaparthi SR et al. (2014) Endoscopic transmural necrosectomy for walled-off pancreatic necrosis: A systematic review and meta-analysis. <i>Canadian Journal of Gastroenterology and Hepatology</i> 28: 50–3	Systematic review n=233 patients (8 studies)	Pooled proportion of successful resolution of pancreatic necrosis using endoscopic transmural necrosectomy (ETN) was 81.8% (95% CI 76.7% to 86.4%). The pooled proportion of recurrence in the form of necrotic cavity or pseudocyst after ETN was 10.9% (95% CI 7.3% to 15.1%). Complications were noted in 21.3% (95% CI 16.4% to 26.7%) of patients and included bleeding, sepsis and perforation. The weighted mean number of days in hospital after ETN was 32.9 days (95% CI 10.5 to 55.2 days). For pancreatic necrosis that did not resolve, surgery had to be performed in 13.0% (95% CI 9.1% to 17.5%) of patients.	A systematic review with a more recent search date is included (Van Brunschot, 2014).
Rinninella E, Kunda R, Dollhopf M et al. (2015) EUS-guided drainage of pancreatic fluid collections using a novel lumen-apposing metal stent on an electrocautery-enhanced delivery system: a large retrospective study (with video). <i>Gastrointestinal Endoscopy</i> 82: 1039–46	Case series n=93 (33 endoscopic necrosectomy)	EUS-guided drainage with the electrocautery-enhanced delivery system is a safe, easy to perform, and a highly effective minimally invasive treatment modality for pancreatic fluid collections.	Study includes patients with mixed indications and only a small proportion of patients were treated by endoscopic necrosectomy; the results are not reported separately.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Rische S, Riecken B, Degenkolb J et al. (2013) Transmural endoscopic necrosectomy of infected pancreatic necroses and drainage of infected pseudocysts: a tailored approach. Scandinavian Journal of Gastroenterology 48: 231–40	Case series n=40	Transgastric endoscopy is an effective minimally invasive procedure even in patients with advanced pancreatic necroses. Complication rate is low particularly in patients with sole pseudocysts or localized necroses. The extent of the fluid collections and necroses is a new predictive parameter for the outcome of the patients.	Included in Van Brunschot (2014) systematic review.
Sarkaria S, Sethi A, Rondon C et al. (2014) Pancreatic necrosectomy using covered esophageal stents: A novel approach. Journal of Clinical Gastroenterology 48 145-152)	Case series n=17 Follow-up=238±165 days	Two patients failed endoscopic intervention and required surgery. The only complication was a perforation during tract dilation, which was managed conservatively. Fifteen patients (88%) achieved complete resolution.	Larger studies are included.
Seewald S, Ang TL, Richter H et al. (2012) Long-term results after endoscopic drainage and necrosectomy of symptomatic pancreatic fluid collections. Digestive Endoscopy 24: 36-41	Case series n=80 (49 endoscopic necrosectomy) Mean follow-up=31 months	Endoscopic drainage of symptomatic pancreatic fluid collections is safe and effective, with excellent immediate and long-term results. Endoscopic necrosectomy has a risk of serious complications. The underlying pancreatic duct abnormalities must be addressed to prevent recurrence of fluid collections.	Results are not presented separately for endoscopic necrosectomy.
Seifert H, Biermer M, Schmitt W et al. (2009) Transluminal endoscopic necrosectomy after acute pancreatitis: A multicentre study with long-term follow-up (the GEPARD Study). Gut 58:1260-1266.	Case series n=93 Mean follow-up=43 months	Long-term clinical success was achieved in 68% (63/93) of all patients. One patient died in late follow-up relating to pancreatitis, and 12% (11/93) had recurrence.	Included in Van Brunschot (2014) systematic review. (Included in table 2 of 2011 overview)
Sharaiha RZ, Tyberg A, Khashab MA et al. (2016) Endoscopic Therapy With Lumen-apposing Metal Stents is Safe and Effective for Patients With Pancreatic Walled-off Necrosis. Clinical Gastroenterology and Hepatology DOI: 10.1016/j.cgh.2016.05.011	Case series n=124 (78 direct endoscopic necrosectomy) Median follow-up=4 months	Clinical success was achieved in 107 patients (86%) after 3 months of follow up. Thirteen patients required a percutaneous drain and 3 required a surgical intervention to manage their walled-off necrosis. The stents remained patent in 94% of patients (117/124) and migrated in 6% of patients (7/124). The median number of endoscopic interventions was 2 (range 1-9 interventions).	Studies with more patients or longer follow-up are included.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Siddiqui AA, Easler J, Strongin A et al. (2014) Hydrogen peroxide-assisted endoscopic necrosectomy for walled-off pancreatic necrosis: a dual center pilot experience. Digestive Diseases & Sciences 59: 687-690	Case series n=14	Hydrogen peroxide irrigation facilitates necrotic tissue dislodgement, debridement, and debris extraction during endoscopic therapy of walled-off necrosis.	Larger studies are included.
Smoczyński M, Rompa G, Marek I et al. (2008) Complications of endoscopic therapy of pancreatic organized necrosis. Gastroenterologia Polska 15: 15–19	Case series n=46	Endoscopic treatment of organised pancreatic necrosis is preferable if cooperation with surgeons and radiologists is accessible. It should be stressed that the risk of complications related to this method of management does not endanger patient's life.	Larger studies are included.
Storm AC, Thompson CC (2016) Safety of direct endoscopic necrosectomy in patients with gastric varices. World J Gastrointest Endosc 8: 402-408	Case series n=15	Successful resolution of walled-off necrosis does not appear to be compromised by the presence of gastric varices, with similar rates of resolution and only minor bleeding events. Experienced centres should not consider gastric varices a contraindication to direct endoscopic necrosectomy.	Studies with more patients or longer follow-up are included.
Thompson CC, Kumar N, Slattery J et al. (2016) A standardized method for endoscopic necrosectomy improves complication and mortality rates. Pancreatology 16: 66-72	Case series n=60 Mean follow-up=68 weeks	60 consecutive patients underwent 1.58 +/- 0.1 necrosectomies, with debridement accomplished on the initial procedure in 98%. 39 patients (65%) required only 1 session. Clinical resolution occurred in 87%, with radiologic confirmation. Percutaneous drainage was required in 8 patients during follow-up, and 4 of these later required surgery. Serious adverse events occurred in 3% of patients, and there was no mortality.	Studies with more patients or longer follow-up are included.
van Santvoort HC, Bakker OJ, Bollen TL et al. (2011) A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. Gastroenterology 141: 1254-1263	Case series n=639 (11 endoscopic necrosectomy)	A total of 208 patients (33%) received interventions for infected necrosis, with 19% mortality. Catheter drainage was most often performed as the first intervention (63% of cases), without additional necrosectomy in 35% of patients. Primary catheter drainage had fewer complications than primary necrosectomy (42% vs 64%, p=0.003). Patients with pancreatic parenchymal necrosis (n=324), compared with patients with only peripancreatic necrosis (n=315), had a higher risk of organ failure (50% vs 24%, p<0.001) and mortality (20% vs 9%, p<0.001).	Only a small proportion of patients were treated by endoscopic necrosectomy.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Voermans RP, Veldkamp MC, Rauws EA et al. (2007) Endoscopic transmural debridement of symptomatic organized pancreatic necrosis (with videos). Gastrointestinal Endoscopy 66: 909–16	Case series n=25 Median follow-up=16 months	There was no mortality. Severe complications that required surgery occurred in 2 patients: haemorrhage in 1 case and perforation of cyst wall in the other. During a median follow-up of 16 months (range 3-38 months), the overall clinical success rate with resolution of the collection and related symptoms was 93%.	Included in Van Brunschot (2014) systematic review.

Appendix B: Related NICE guidance for endoscopic transluminal pancreatic necrosectomy

Guidance	Recommendations
Interventional procedures	Percutaneous retroperitoneal endoscopic necrosectomy. NICE interventional procedure guidance 384 (2011) 1.1 Current evidence on the safety and efficacy of percutaneous retroperitoneal endoscopic necrosectomy is adequate to support the use of this procedure provided that normal arrangements are in place for clinical governance, consent and audit. 1.2 The procedure should only be carried out by a team experienced in the management of complex pancreatic disease.

Appendix C: Literature search for endoscopic transluminal pancreatic necrosectomy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	03/06/2016	Issue 6 of 12, June 2016
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	03/06/2016	Issue 5 of 12, May 2016
HTA database (Cochrane Library)	03/06/2016	Issue 2 of 4, April 2016
MEDLINE (Ovid)	03/06/2016	1946 to May Week 4 2016
MEDLINE In-Process (Ovid)	03/06/2016	June 02, 2016
EMBASE (Ovid)	03/06/2016	1974 to 2016 Week 22
CINAHL (NLH Search 2.0)	27/08/2015	n/a
PubMed	27/08/2015	n/a
JournalTOCS	28/08/2015	n/a

Trial sources searched on 06 May 2015

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched on 06 May 2015

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

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

1	exp Pancreatic Cyst/
2	(pancreat* adj3 (cyst* or pseudocyst* or necros*)).tw.
3	Pancreatitis, Acute Necrotizing/

IP overview: endoscopic transluminal pancreatic necrosectomy

4	(Pancreatit* adj3 Acute Necrot*).tw.
5	(pancreat* adj3 abscess*).tw.
6	or/1-5
7	Necrosis/
8	Pancreatitis/
9	7 and 8
10	6 or 9
11	Pancreatitis/
12	10 or 11
13	((endoscop* or translum* or transgast*) adj3 (drain* or necrosect* or debridement or surg*)).tw.
14	Natural Orifice Endoscopic Surgery/
15	NOTES.tw.
16	(minimal access adj3 necrosect*).tw.
17	or/13-16
18	12 and 17
19	limit 11 to yr="1990-1996"
20	10 or 19
21	17 and 20
22	Animals/ not Humans/
23	21 not 22
24	limit 23 to ed=20150507-20150831