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Endoscopic ultrasound-guided endoscopic necrosectomy of the pancreas: is irrigation necessary?

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Abstract
Background Findings have shown endoscopic necrosectomy to be beneficial for patients with symptomatic pancreatic necrosis accessible for an endoscopic approach. The available studies show that endoscopic necrosectomy requires a multitude of subsequent procedures including repeat irrigation for removal of the necrotic material. This study aimed to investigate the need for additional irrigation in patients with necrotizing pancreatitis treated by endoscopic necrosectomy.
Methods The study enrolled 35 consecutive patients (27 men) with a median age of 59 years who had pancreatic necrosis treated with endoscopic necrosectomy. Endoscopic ultrasound–guided internal drainage and consecutive endoscopic necrosectomy was combined with interval multistenting of the cavity. Neither endoscopic nor external irrigation was part of the procedure.
Results 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. The median follow-up period was 23 months.
Conclusion Neither endoscopic nor external flushing is needed for successful endoscopic treatment of symptomatic necroses. Even without irrigation, the outcome for patients treated with endoscopic necrosectomy is comparable to that described in the published data.

Keywords Pancreatic · Therapeutic/palliation · Endoscopy · Ultrasonography

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Infected necrosis of the pancreas is a serious condition. Surgery is the gold standard treatment, but it has a high mortality rate of 25–34% [1–3]. In 2000, Seifert et al. [4] introduced an alternative endoscopic method using transgastric access and debridement of the necrotic material in three patients. Subsequently, endoscopic necrosectomy using endoscopic ultrasound guidance (EUS-G) was performed in single-center series of up to 54 patients [5–13]. Compared with surgery, EUS-G was associated with a relatively low complication rate and a significantly lower mortality rate. A recent multicenter study based on 93 patients confirmed the data for these cohorts with a 30-day mortality rate of only 7.5% [14].

Endoscopic necrosectomy generally is performed mechanically (e.g., using the endoscopic retrograde cholangiopancreatography [ERCP] basket) and with additional flushing of the cavity. Subsequent repeat irrigation, assumed to be necessary for a successful outcome, was part of treatment for almost all the published patients (Table 1). To our knowledge, no study has evaluated whether endoscopic debridement alone combined with interval multistenting is sufficient or even superior to this treatment. Therefore, we retrospectively analyzed our results for endoscopic necrosectomy without multisession irrigation. Debridement of all floating and rather loosely attached necrotic material plus multistenting of the access to the cavity was performed. Flushing was used only to allow appropriate vision during the procedure.

Patients and methods

Patients

This study enrolled 35 consecutive patients (27 men), who underwent endoscopic necrosectomy. The median age of the patients was 59 years (range, 21–85 years). Of the 35 patients, 12 were reported earlier in the multicenter necrosectomy study with a focus on long term follow-up evaluation [14]. For all the patients, demographics such as age, sex, presenting symptoms, and comorbidities were recorded. The location and size of the necrotic cavity were documented by transabdominal ultrasound, computed tomography (CT), or both, and further confirmed by pretherapeutic EUS. Endoscopic necrosectomies were performed after informed consent, with the number of procedures and any related complications recorded over the following 0–78 months (mean follow-up period, 28 months).

Similar to the accepted indications for surgical interventions, the indications for endoscopic treatment were uncontrolled infection ($n = 19$), sustained pain or symptomatic gastroduodenal compression ($n = 13$), jaundice ($n = 1$), or progressively increasing size of the necrotic area ($n = 2$).

Exclusion criteria

Patients were excluded from the study if they had a prothrombin time exceeding 1.5 times normal unless substituted, a platelet count lower than 50,000/μl unless substituted, necrotic cavities endoscopically inaccessible from the stomach or duodenum (e.g., with a distance between the gastric and necrotic cavities exceeding 15 mm), an age younger than 18 years, or no informed consent.

After an overnight fast, the patients were examined under conscious sedation with midazolam, pethidin, or ketanest while in the left lateral position. During and after the procedure, they were monitored with pulse oxymetry by a physician or nurse. Prophylactic or therapeutic broad-spectrum antibiotics such as imipenem or ciprofloxacin in combination with metronidazol were administered before and during the intervention.

Table 1 Review of prior studies (only publications with >10 patients) with regard to outcome

	n	Mortality/surgery	Mean no. of endoscopies for EN + EL (range)	Use of irrigation
Seewald et al. [11]	13	0/4	23.6 (4–64)	Endoscopic 13/13 Nasocystic 12/13
Charnley et al. [5]	13	2/4	4 (1–6)	Endoscopic 13/13 Nasocystic 5/13
Papachristou et al. [9]	22	1/NS	3 (1–12)	Nasocystic 22/22 + external in parts
Voermans et al. [12]	25	0/2	1.7 (1–4)	Nasocystic 20/25
Hocke et al. [8]	19	2/2	NS	Endoscopic 19/19
Escourrou et al. [6]	13	0/0	1.8 (1–3)	Endoscopic 13/13 Nasocystic 13/13
Coelho et al. [13]	36	2/6	4 (2–8)	Endoscopic 36/36
Gardner et al. [7]	17	0/1	2.2 (NS)	Nasocystic 14/17
Seifert et al. [14]	93	7/11	NS	NS
Current data (2002–2009)	35	2/0	2.9 (1–11)	None

Required numbers of endoscopy sessions for EN + EL and use of irrigation by endoscopy or via nasocystic/external drainage

EN endoscopic necrosectomy; *EL* endoscopic lavage; *NS* not specified

Initial drainage technique

Under EUS guidance, puncture of the cavity was performed with a 19-gauge EUS needle (Echotip; Wilson-Cook Co, Winston Salem, NC, USA) before a 0.035-in. guidewire was inserted under fluoroscopic guidance. Bile duct dilators and Soehandra retrievers were used to dilate the pathway to the cavity to a diameter of 10 Fr. Subsequent balloon dilation (CRE; Boston Scientific, Microvasive, Cork, Ireland) to a diameter of 20 mm enabled broad access.

Initially, the first session was restricted to insertion of one or two stents, but with increasing experience, balloon dilation usually was carried out during the first session. Access was kept open by insertion of at least three double-pigtail stents (e.g., 10-Fr Gastrosoft biliary endoprosthesis; OptiMed, Ettlingen/Germany). The number of endoscopy sessions for "access" was defined as the number of endoscopies before the necrosectomy itself.

Endoscopic necrosectomy

A therapeutic gastroscope (GIF-1T140; Olympus Medical Systems Corp, Tokyo, Japan) was used to enter the cavity. Floating and loosely adherent material was removed predominantly by tripod polyp-grasping forceps (Medwork, Höchstadt, Germany), whereas broadly wall-adherent necroses were left in place. During the procedure, minimal irrigation (5–10 ml of NaCl 0.9%) was used to maintain vision.

At the end of each session, up to seven additional stents were placed to secure broad access and outflow. Necrosectomy sessions were planned in 2- to 3-day intervals until a grossly cleared cavity finally was achieved. Neither nasocystic catheters nor percutaneous irrigation tubes were placed. No endoscopic flushing sessions were carried out.

Postnecrosectomy

After a grossly cleared cavity had been achieved with removal of all floating and loosely adherent material, the patients were discharged home once their clinical condition had improved sufficiently. The stents were removed after 4–6 weeks. If at that time complete collapse of the cyst had not been achieved, new stents were reintroduced for another 4–6 weeks. This procedure was carried on until collapse of the cavity was proven.

Any session performed only to exchange or remove the stents subsequent to the last endoscopic necrosectomy was accounted for as "stent management." Follow-up assessment included regular telephone calls with patients, their physicians, or both. In case of recurrent symptoms, patients were reevaluated by transabdominal ultrasound, CT, or EUS. Pancreatography was not performed routinely.

Results

A total of 35 patients (27 men and 8 women) treated with endoscopic necrosectomy were identified in our database. Biliary ($n = 13$) and alcoholic ($n = 11$) pancreatitis were the leading causes for pancreatic necrosis, whereas its origin was related to prior ERCP in two patients, to medication in one patient, and to an unknown cause in five patients. For two patients, endoscopic necrosectomy was performed subsequent to pancreatic surgery: after pancreatic tail resection for nesidioblastosis in the first patient and after incomplete surgical necrosectomy for severe biliary pancreatitis in the second patient. A cancer of the pancreatic head was identified in one patient as the underlying cause for his necrotizing pancreatitis of the pancreas body and tail. Another four patients had simultaneous (lung, $n = 1$) or metachronous (throat, lymphoma, prostate, $n = 3$) malignant diseases limiting long-term survival.

The indications for treatment were infections or size-related symptoms such as pain, jaundice, or gastroduodenal compression, with compromise of adequate food intake. For two patients, an asymptomatic but steady increase in the necrotic cavity was the reason for intervention. The one patient had a palpable mass larger than 14 cm in diameter. For the other patient, who had lung cancer, a necrosectomy was thought to be mandatory before adjuvant chemotherapy. The interval between acute pancreatitis or exacerbation of chronic pancreatitis and the first endoscopic drainage procedure was 18–383 days (mean 48 days). For six patients, the onset of the pancreatitis could not be specified.

For 22 (63%) of the 35 patients, the course of the disease was complicated by severe preexisting comorbidities such as a recent history of myocardial infarction, stroke, or diabetes. Three patients (9%) had a spontaneous perforation with an open fistula into the stomach ($n = 1$) or duodenum ($n = 2$). These perforation sites were used for sole or supplementary access to the necrotic cavity.

An average of 6.2 endoscopy sessions per patient were needed for access, necrosectomy, and stent management (Table 2). From the first to the second half of the patients, the mean number of procedures for access (1.9 sessions/patient)

Table 2 Mean number of endoscopy sessions per patient

Endoscopy sessions/patient	All patients	Patients 1–17	Patients 18–35
For access	1.9	2.5	1.3
For necrosectomy	2.9	2.5	3.3
For stent management	1.5	1.8	1.2
Total	6.2	6.7	5.8

and for stent management (1.5 sessions/patient) decreased with time by 49 and 33%, respectively. On the other hand, the mean number of procedures needed for necrosectomy (2.9 sessions/patient) increased. The increase was due to two patients (patients 25 and 26) who respectively required 10 and 11 sessions for necrosectomy due to the dimensions of the necrotic cavity (diameter > 10 cm), comprising predominantly solid material in each case.

The short-term mortality rate was 6% (2/35) (involving 1 pulmonary aspiration of cystic fluid and necrotic material in a 71-year-old 1 h after the intervention and 1 cardiac low output failure in a 65-year-old). The latter of these two cases was not judged to be procedure-related because the patient's hospital admission was due to severe pressor-dependent heart failure after an acute myocardial infarction that preceded the pancreatitis for several days. In this patient, rapid decrease of C-reactive protein (CRP) and the size of the (superinfected) necrotic cyst after drainage indicated success of the endoscopic treatment. The immediate morbidity rate was 9% (1 case due to arterial and 2 cases due to venous bleeding, all successfully treated by endoscopy using injection of adrenalin at 1:10,000 and/or fibrin glue, respectively).

Additional surgery for the management of the endoscopically treated necroses was not required for any of the 35 patients. Additional external drainage was necessary for one patient, with extension of endoscopic transgastric necrosectomy into the pelvis when regression of the cavity led to pelvic sequestration weeks later.

Complete resolution of the necrotic cavity without symptoms indicative of recurrence during the follow-up period was achieved for all the surviving patients (94%). No late complications related to the endoscopic necrosectomy procedure were noted.

Cholecystectomy was scheduled in every case of biliary pancreatitis 4 to 6 weeks after removal of the last drainage. Two cases of acute cholecystitis required emergency surgery, whereas prophylactic biliary sphincterotomy before discharge prevented recurrence of biliary pancreatitis or symptomatic bile duct stones during the interval before planned cholecystectomy.

Two patients experienced symptomatic intestinal stenoses requiring surgery during the late follow-up period. The one patient had intestinal stenosis due to adhesions 17 months after necrosectomy, and the other patient had duodenal stenosis after 5 months due to inflammation of the adjacent pancreatic head, which finally lead to death due to septic postoperative complications. Additional mortality during the follow-up period was related to synchronous or metachronous neoplasia ($n = 3$), suicide ($n = 1$), cardiac arrest ($n = 1$), and variceal bleeding ($n = 1$).

Discussion

Endoscopic necrosectomy has been established as a treatment method for symptomatic pancreatic necroses [4–14]. However, it was presumed, that subsequent repeat endoscopic irrigation or external nasocystic or percutaneous drainages were necessary (Table 1). Dissolution of necroses was thought to be achieved by liquefying the necrotic material through constant flushing and subsequent drainage of the debris [15]. This assumption leads back to the time when abscess drainage by single stenting alone led to frequent reinfection, which initiated the introduction of nasocystic drainage and repeated daily flushing of the cavities [16]. This irrigation procedure then was transferred to the endoscopic treatment of necrosectomies. However, to date, this has never proved to be necessary.

The available studies show that endoscopic necrosectomies are time consuming and require a multitude of subsequent complex procedures for removal of the necrotic material. This aspect limited the practicability of the method and demanded simplification.

Our study demonstrates that neither endoscopic nor external flushing is needed for successful endoscopic treatment of symptomatic necroses. Once they are grossly cleared mechanically by endoscopy, minor remnants are obviously resorbed or migrate into the gut through the artificial access. We therefore suggest that nasocystic tubes, endoscopic flushing, or external drainages do not add benefit to the procedure.

Drainage of the necrotic cavities was achieved by the transgastric access and alongside the multiple stents, which prevented the dreaded risk of occlusion seen with the single-stent techniques. Although small in number, the results of our study show that nasocystic or percutaneous drainages with the associated patient unease can be avoided.

When the endoscopic necrosectomy method was introduced, dilation of the track was performed stepwise, with an increasing number of stents resulting in several endoscopy sessions required for access. Despite increasing experience with balloon dilation even at the first session, we saw the necessity to allow time for a stable channel to build up to prevent possible peritonitis. Therefore, we did not start endoscopic necrosectomy before the second session (Table 2). Necrosectomy during the first session may require different techniques to avoid leakage of potentially infectious fluid and solids into the peritoneal cavity. The use of coated stents, described in a single case [17], may offer an alternative approach without the risk of lateral leakage. If a standard endoscope can pass through, endoscopic necrosectomy may be safe even during the first endoscopy session.

The number of procedures and their duration are related to the size and location of the necrotic cavity in addition to

technical aspects. These include the location and diameter of the access channel and methods of debris removal. A straight angle and a proximal access facilitate easier removal of necrotic material than a more distal access resulting in retroflexion. The transgastric approach generally is easier to handle even if there is a preexisting track due to spontaneous transduodenal perforation.

For debris removal, we prefer the use of a polyp grasper, which is easier to control and to free from necrotic material than the polyp snare or the stone removal basket recommended by other groups [4, 5, 8–12]. Nonetheless, a perfect tool for grasping and removing necrotic material in the stomach still is lacking. Avoidance of additional drainages has the potential benefits of easing mobilization and reducing the hospital stay.

With increasing experience, stent management was reduced to one session for most patients (Table 2). Above all, further improvements in the necrosectomy technique have the potential for optimization in view of this resource-intensive technique. But even with a reduced number of endoscopic interventions, the demand for specialized interventional endoscopy skills and financial resources will limit its general use outside specialized endoscopic centers.

Conclusion

In this retrospective study, endoscopic necrosectomy with stenting alone demonstrated good short- and long-term results. Avoidance of repeated and lengthy endoscopic procedures for flushing of the necrotic cavity, immediate mobilization, better tolerance by patients, and the potential for a reduced hospital stay are clear benefits. As shown by our study, endoscopic necrosectomy without irrigation may be comparable with additional internal or external flushing described in the published data.

Disclosures Christian Jürgensen, Frank Neser, Joachim Boese-Landgraf, Detlef Schuppan, Ulrich Stölzel, and Annette Fritscher-Ravens have no conflicts of interest or financial ties to disclose.

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