Official Organ of the European Society of Gastrointestinal Endoscopy (ESGE) and affiliated societies

Endoscopy

Publishers

Georg Thieme Verlag KG
Ruedigerstraße 14
D-70469 Stuttgart
P.O. Box 30 11 20
70451 Stuttgart
Germany

Thieme Medical Publishers, Inc.
333 Seventh Avenue
USA, New York, NY 10001

For subscription information
please contact: endoscopy@thieme.de

Reprint

Volume 45 · 2013

Japanese multicenter experience of endoscopic necrosectomy for infected walled-off pancreatic necrosis: The JENIPaN study

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submitted
18. November 2012
accepted after revision
26. March 2013

Bibliography
DOI http://dx.doi.org/10.1055/s-0033-1344027
Published online: 27.6.2013
Endoscopy 2013; 45: 627–634

ISSN 0013-726X

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Background and study aims: Only a few large cohort studies have evaluated the efficacy and safety of endoscopic necrosectomy for infected walled-off pancreatic necrosis (WOPN). Therefore, a multicenter, large cohort study was conducted to evaluate the efficacy and safety of endoscopic necrosectomy and to examine the procedural details and follow-up after successful endoscopic necrosectomy.

Patients and methods: A retrospective review was conducted in 16 leading Japanese institutions for patients who underwent endoscopic necrosectomy for infected WOPN between August 2005 and July 2011.The follow-up data were also reviewed to determine the long-term outcomes of the procedures.

Results: Of 57 patients, 43 (75 %) experienced successful resolution after a median of 5 sessions of endoscopic necrosectomy and 21 days of treatment. Complications occurred in 19 patients (33 %) during the treatment period. Six patients died (11 %): two due to multiple organ failure and one patient each from air embolism, splenic aneurysm, hemorrhage from a Mallory – Weiss tear, and an unknown cause. Of 43 patients with successful endoscopic necrosectomy, recurrent cavity formation was observed in three patients during a median follow-up period of 27 months.

Conclusions: Endoscopic necrosectomy can be an effective technique for infected WOPN and requires a relatively short treatment period. However, serious complications can arise, including death. Therefore, patients should be carefully selected, and knowledgeable, skilled, and experienced operators should perform the procedure. Further research into safer technologies is required in order to reduce the associated morbidity and mortality.

Introduction

Acute post-necrotic pancreatic/peripancreatic fluid collection occurs because of liquefaction of necrotic tissue. Over 4 weeks, a thick wall without an epithelial lining can form over the fluid collection, developing into walled-off pancreatic necrosis (WOPN) with variable fluid and solid components [1]. Infected pancreatic necrosis, which is a major risk factor for sepsis-related multiple organ failure, is the main life-threatening complication in the late phase of acute pancreatitis. The associated mortality is at least 20 %, and up to 80 % of deaths result from septic complications [2]. Therefore, patients with infected WOPN require timely and effective interventions. Open necrosectomy with drainage has been the standard of treatment for infected WOPN, but carries significant morbidity (13 % – 53 %) and high mortality (6 % – 34 %) [3,4]. In addition, patients experience a prolonged recovery. These limitations have led to investigations of alternative techniques.

In 1996, Baron et al. [5] were the first to report successful endoscopic drainage of WOPN, wherein several transgastric or transduodenal drainage catheters and a nasopancreatic irrigation tube were placed into the retroperitoneum and lavage was continued until the collection successfully resolved. In 2000, Seifert et al. [6] performed a more aggressive technique of inserting the endoscope directly into the necrotic cavity and removing the necrotic tissue. Several subsequent reports have described initial experiences with direct endoscopic necrosectomy for WOPN [3,7 – 12]. More recently, two large multicenter studies demonstrated the efficacy and safety of endoscopic necrosectomy for WOPN [13,14]. However, indications and techniques vary between studies. Therefore, a multicenter, large cohort study was conducted to evaluate the efficacy and safety of endoscopic necrosectomy in a carefully selected

population of patients with infected WOPN and to examine the procedural details and follow-up after successful endoscopic necrosectomy.

Patients and methods

Patients

A total of 16 leading Japanese institutions participated in this study. The participating institutions were: Gifu University Hospital (Gifu); Kitasato University East Hospital (Sagamihara); The University of Tokyo (Tokyo); Tokyo Medical University (Tokyo); Date Red Cross General Hospital (Date); Mie University Hospital (Tsu); Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences (Okayama); Tohoku University Graduate School of Medicine (Sendai); Yokohama City University School of Medicine (Yokohama); Fukushima Medical University (Fukushima); Kyushu University (Fukuoka); Kurume University School of Medicine (Fukuoka-Kurume); Kinki University School of Medicine (Sayama); Hokkaido University Graduate School of Medicine (Sapporo); Sapporo Medical University School of Medicine (Sapporo); and Gifu Municipal Hospital (Gifu). Institutional review board approval was obtained at each institution for participation in the study.

A standardized data collection form was sent to each institution. Each institution retrospectively reviewed their database and data for patients who underwent endoscopic necrosectomy for infected WOPN between August 2005 and July 2011 were included in the study. Follow-up data for patients who underwent successful endoscopic necrosectomy treatment were obtained by interviews at the outpatient clinic. However, if patients had not been followed periodically, each institutional attending physician contacted the patients or their family by telephone. The data were completely updated in January 2013.

Procedures

The standard technique for endoscopic necrosectomy involves the following steps. First, a curvilinear array endoscopic ultrasound (EUS) is used to visualize the extent of the necrosis and determine the optimal puncture site. Before puncture, color Doppler is used to confirm that there are no interposed vessels on the puncture line. The cavity is then punctured with a 19-gauge EUS needle. After withdrawing the inner stylet, a guide wire is inserted through the needle into the necrotic cavity under fluoroscopic guidance. The puncture site is then dilated using a dilator and/or a balloon catheter. Then, one or more double pigtail stent(s) and/or a nasocystic drainage catheter are inserted. In a few select cases, endoscopic necrosectomy is performed on the same day.

In most cases, the tract is dilated using a large balloon (12–20 mm) several days after stent placement or insertion of the drainage catheter (**Fig. 1**). A conventional forward-viewing endoscope is subsequently advanced into the cavity and endoscopic accessories are used to remove necrotic tissue with forceful irrigation of normal saline (**Fig. 2**). Endoscopic necrosectomy is performed 1–4 times per week, until all necrotic tissue has been removed. In anticipation of a subsequent endoscopic necrosectomy, the route to the necrotic cavity is maintained by placing stents and/or a nasocystic drainage catheter. Daily irrigation using 500–1000 mL of normal saline through a nasocystic drainage catheter is performed between endoscopic necrosectomy sessions at some institutions. Endoscopic necrosectomy is continued until the majority of necrotic tissue is removed and pink granulation tissue lining the wall is observed. At the final endoscopic necrosectomy session, stents may be placed depending on each institution's protocol.

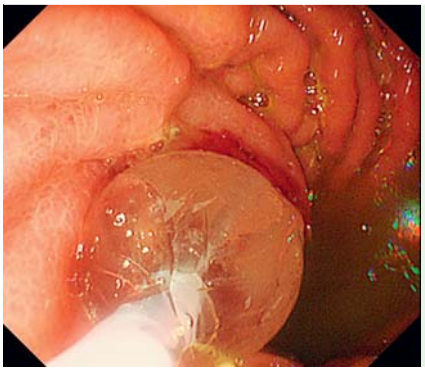

Fig. 1 Dilation of the transgastric entry tract into the necrotic cavity using a large balloon.

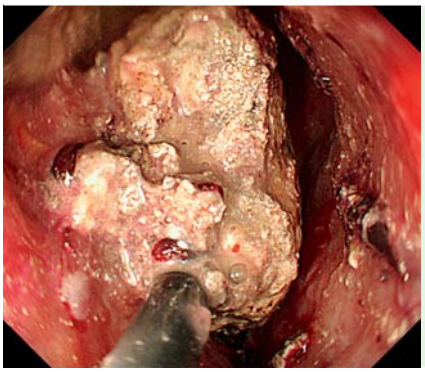

Fig. 2 Endoscopic removal of necrotic material using pentapod forceps.

Outcomes

The primary outcomes were successful resolution of pancreatic necrosis by endoscopic necrosectomy and the mortality and complication rates associated with endoscopic necrosectomy. 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 WOPN. The secondary outcome was prognosis after endoscopic necrosectomy.

Statistical analysis

Statistical comparisons were performed to determine the factors associated with successful resolution of the necrotic cavity. Continuous variables with Gaussian distribution were tested using the Student's *t*-test and those with non-Gaussian distributions were analyzed using the non-parametric Wilcoxon rank-sum test. Categorical and binary variables were tested using the chi-squared test with Yates' correction or Fisher's exact test for small-expected frequencies. All statistical tests were two tailed at the probability level of 0.05. Statistical analyses were performed using JMP software, version 8.0 (SAS Institute, Inc., Cary, North Carolina, USA).

Table 1 Patient demographics.

Female/male	11/46
Age, median (range), years	58 (19 – 81)
BMI, median (range), kg/m^2	21.3 (16.2 – 38.9)
Etiological factors, n (%)	
Idiopathic	20 (35)
Alcohol	18 (32)
Gallstone	8 (14)
Post-ERCP	7 (12)
Others*	4 (7)
ASA classification, n	
Grade 2	18
Grade 3	29
Grade 4	8
Grade 5	2
CT findings	
Main location, n	
Head and body	2
Body and tail	30
Entire pancreas	25
Lower extremity of the necrotic cavity, n	
Peripancreatic region	29
Beyond the lower extremity of the left kidney	22
Pelvic cavity	6
Form, n	
Simple	38
Multiple	19
Size, median (range), cm	
Long axis	14.0 (4.0 – 30.5)
Short axis	7.0 (2.0 – 22.0)

ASA, American Society of Anesthesiologists physical status classification; BMI, body mass index; ERCP, endoscopic retrograde cholangiopancreatography.

* Other etiological factors included pancreas divisum, anomalous connection of pancreatobiliary ducts, hypertriglyceridemia, and ampullary tumors.

Results

Patients

From August 2005 to July 2011, 57 patients underwent endoscopic necrosectomy for infected WOPN at the 16 institutions. Patient demographics are shown in **Table 1**.

Of the 57 patients, 10 were in very poor health (grade 4 or 5 in the American Society of Anesthesiologists (ASA) physical status classification) [15]. In six patients, the necrotic cavity extended to the pelvis.

Initial outcomes of endoscopic necrosectomy

Initial drainage was performed after a median duration of 50 days (range 13 – 436 days) from the onset of pancreatitis. The initial puncture was performed using a conventional 19-gauge EUS needle, and in most cases the tract was then dilated using a dilator and balloon catheter. Subsequently, a single nasocystic catheter and one or two indwelling stents were placed in the necrotic cavity (**Table 2**).

Endoscopic necrosectomy was performed on the same day as the initial drainage in 11 patients (19 %), and the remaining 46 patients (81 %) underwent initial endoscopic necrosectomy some days after the initial drainage. A gastroscope with water-jet function was used in 37 patients (65 %), and carbon dioxide (CO_2) gas was used instead of room air for insufflation in 39 patients (68 %) during endoscopic necrosectomy. Various endoscopic devices were used to remove the necrotic tissue, with the majority being pentapod forceps, rat-tooth forceps, and polypectomy snares.

Table 2 Initial drainage.

Time from onset of pancreatitis to initial drainage, median (range), days	50 (13 – 436)
Puncture needle, n	
Electrocautery needle	2
Non-electrocautery 19-G needle	55
Dilator, n	
NA	7
6 or 7 Fr	39
10 Fr	11
Diameter of dilation balloon, n	
NA	7
≤ 10 mm	41
≥ 15 mm	9
Placed drain, n	
Single nasocystic catheter	4
Single nasocystic catheter with a single stent	25
Single nasocystic catheter with 2 stents	18
Single nasocystic catheter with 3 or 4 stents	4
Two stents	4
Three stents	2

NA, not applicable.

Table 3 Endoscopic necrosectomy.

Timing of the first endoscopic necrosectomy, n	
At the initial drainage	11
After the initial drainage	46
1 – 7 days	20
8 – 14 days	20
≥ 15 days	6
Diameter of dilation balloon, n	
12 – 15 mm	16
18 mm	16
20 mm	25
Type of endoscope, n	
Conventional gastroscope	20
With water-jet function	37
Devices for necrosectomy, n*	
Pentapod forceps	30
Tripod forceps	3
Rat-tooth forceps	28
Biopsy forceps	7
Polypectomy snare	15
Basket catheter	5
Net catheter	3
Insufflation during the procedure, n	
Room air	18
CO_2 gas	39
Daily saline irrigation between sessions, n	
Done	25
Not done	25
NA	7

NA, not applicable.

* Multiple devices used per patient.

Daily irrigation with normal saline solution from a nasocystic drainage catheter was performed between endoscopic necrosectomy sessions in 25 patients (44 %) (**Table 3**).

Successful resolution was achieved in 43 patients (75 %) following a median of 5 (range 1 – 20) endoscopic necrosectomy sessions. Endoscopic necrosectomy was typically performed twice a week. The median duration of one endoscopic necrosectomy ses-

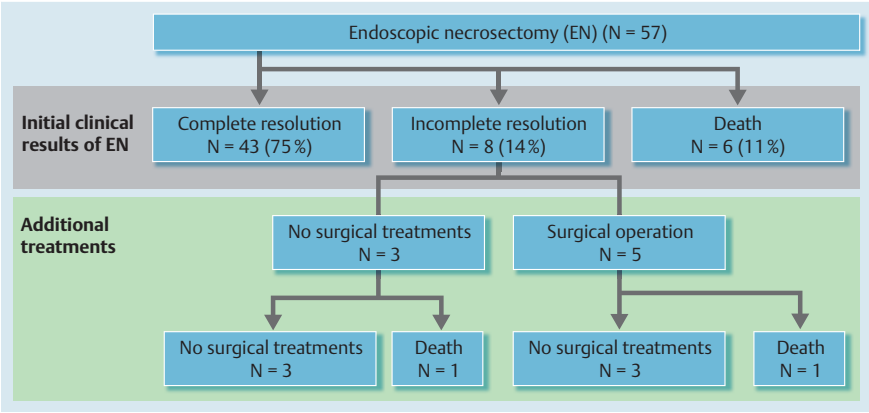

Fig. 3 Initial clinical results of endoscopic necrosectomy.

Table 4 Factors associated with failed cavity resolution by endoscopic necrosectomy.

Factor	Successful endoscopic necrosectomy (n = 43)	Failed endoscopic necrosectomy (n = 14)	*P* value
Female, n (%)	6 (14)	5 (36)	0.1155
Age, median (range), years	59 (19 – 81)	53 (22 – 74)	0.1445
BMI, median (range), kg/m^2	21.0 (16.2 – 38.9)	22.9 (17.4 – 26.3)	0.5920
Etiology (gallstone), n (%)	5 (12)	3 (21)	0.3912
ASA classification ≥ 3, n (%)	26 (60)	13 (93)	0.0437
Lower extremity of the cavity extended beyond the lower extremity of the left kidney, n (%)	20 (47)	8 (57)	0.5497
Size of necrosis, long axis, median (range), cm	14.0 (4.0 – 30.5)	14.5 (7.0 – 24.0)	0.6626
Multilocular form, n (%)	12 (28)	7 (50)	0.1916
Time from onset of pancreatitis to initial drainage < 6 weeks, n (%)	17 (40)	8 (57)	0.5441
Number of sessions, median (range)	5 (1 – 17)	4.5 (1 – 20)	0.9330
Maximum number of stents placed, median (range)	2 (1 – 7)	1.5 (1 – 4)	0.1223
Enteral feeding, n (%)	8 (19)	4 (29)	0.4631

ASA, American Society of Anesthesiologists physical status classification; BMI, body mass index.

sion was 63 minutes (range 27 – 173 minutes). The median duration of the treatment period was 21 days (range 10 – 101 days). The patients initially received parenteral nutrition. However, 12 patients recommenced normal food intake within 7 days. Another 12 patients received enteral feeding of an elemental diet. Only six patients underwent endoscopic retrograde cholangiopancreatography (ERCP) after the completion of endoscopic necrosectomy, and four patients received pancreatic stenting for pancreatic duct leakage.

Of the 14 patients for whom treatment was unsuccessful, six (11%) died during the treatment period before resolution and eight (14%) were converted to other treatments because of persistent sepsis after a median endoscopic necrosectomy treatment period of 29 days (range 2 – 56 days) and required surgery (n = 5) or additional percutaneous drainage (n = 3). Of these eight patients, six eventually experienced successful resolution, but two died after further treatment (**Fig. 3**).

Baseline characteristics were compared between the successful and failed endoscopic necrosectomy groups (**Table 4**). Patients in poor medical health (ASA classification ≥ 3) were significantly more likely to experience an unsuccessful endoscopic necrosectomy ($P = 0.0437$). The success rate was not significantly different between the group of institutions with more than two treatment cases and the group of institutions with only one or two treatment cases; the mean success rates (range) were 70.0% (0% – 100%) and 78.6% (0% – 100%), respectively ($P = 0.1726$).

Complications arose in 19 patients (33%) during the treatment period. They occurred during endoscopic necrosectomy in 12 patients and between sessions in 7 (**Table 5**). Bleeding from the fistula occurred during endoscopic necrosectomy in five patients following large balloon dilation. Hemostasis was achieved using endoscopic procedures in four patients (clipping in two patients and balloon compression by re-inflation of the balloon in the other two patients), while the remaining patient required coil embolization of a branch of the inferior pancreaticoduodenal artery under interventional radiologic guidance. Another three patients bled from the cavity wall during removal of the necrotic tissue. Conservative management and blood transfusion were sufficient for one patient. Compression by the tip of the endoscope was successful in another patient, and the remaining patient required coil embolization under interventional radiologic guidance. Perforation occurred in another three patients. In two patients, abdominal free air was found following dilation of the large balloon and in the remaining one patient, the cavity wall was perforated during removal of the necrotic tissue. In all three patients, the procedure was immediately terminated and a nasocystic tube and stents were placed. All patients recovered with conservative management and without any sequelae. One patient developed an air embolism. Following insertion of the endoscope into the necrotic cavity, the patient manifested the clinical picture of shock and was diagnosed with air embolism on computed tomography (CT). Brain death occurred and the patient died after 32 days.

Of the seven patients who experienced complications between endoscopic necrosectomy sessions, four experienced massive hematemesis. Rupture of a splenic pseudoaneurysm occurred in two patients, and coil embolization under interventional radiologic guidance was attempted for both. Although one patient was successfully treated, the other died. In the third case of bleeding, the patient was successfully treated with a local epinephrine injection. In the remaining case, the patient vomited frequently following the 4th endoscopic necrosectomy and massive hematemesis occurred several hours later. The patient's hemodynamic status rapidly deteriorated and she died before any interventions could be attempted. An autopsy showed the presence of a Mallory–Weiss tear, but the cause of vomiting remained unclear. Other complications arising between endoscopic necrosectomy sessions included aspiration pneumonia and ileus. Both patients were successfully treated by conservative treatments such as antibiotic therapy and bowel rest. Another patient experienced sudden cardiorespiratory arrest in the ward at 32 hours after completion of the 8th endoscopic necrosectomy. Despite resuscitation, the patient developed brain death and died after 40 weeks. The cause of the sudden cardiorespiratory arrest was not known.

Six patients (11%) died during the treatment period of endoscopic necrosectomy. Multiple organ failure secondary to sepsis resulted in two deaths, and one patient each died because of air embolism, rupture of a splenic aneurysm, a Mallory–Weiss tear, and an unknown cause.

Table 5 Complications during the treatment period of endoscopic necrosectomy.

During the procedure, n	12 (21%)
Bleeding from the fistula	5
Bleeding from the cavity wall	3
Perforation	3
Air embolism	1[1]
Between sessions, n	7 (12%)
Rupture of splenic aneurysm	2[2]
Mallory–Weiss tear	1[1]
Bleeding from the fistula	1
Aspiration pneumonia	1
Ileus	1
Sudden cardiorespiratory arrest (unknown cause)	1[1]
Total	19 (33%)

[1] Fatal cases.
[2] One patient died.

Table 6 Follow-up of 43 patients following successful endoscopic necrosectomy.

Follow-up period after completion of endoscopic necrosectomy, median (range), months	27 (5–59)
Removal of stents, n	
Removed at final session	7
Removed later	23
Spontaneously dislodged	9
Still in situ	4
Recurrent cavity	3 (7%)
Without infection	1
With infection	2
Died	2 (4%)*

* Two patients died due to unrelated causes: 1 from the bile duct cancer after 6 months and another from pneumonia after 14 months.

Follow-up results

Complete follow-up data were obtained for all 43 patients who were successfully treated with endoscopic necrosectomy. A total of 32 patients were regularly followed every 3–6 months, with blood tests performed as appropriate at each institution. Follow-up abdominal CT (every 3–6 months) was obtained until 1 year after the endoscopic necrosectomy in 37 patients, 2 years in 20 patients, and more than 3 years in 10 patients. The median follow-up period for these 43 patients was 27 months (range 5–59 months). Stents were removed at the final endoscopic necrosectomy session in 7 patients, whereas 23 patients had their stents removed after a median duration of 13 weeks (range 3 weeks–17 months). Another nine patients experienced spontaneous dislodgement of the stents after a median duration of 15 weeks (range 8 weeks–9 months). In the remaining four patients, the stents were still in situ at the time of the last follow-up (median 22 months; range 11–30 months) (▶ **Table 6**).

Two patients died due to causes unrelated to the endoscopic necrosectomy procedure or pancreatitis. One died from bile duct cancer after 6 months and another from pneumonia after 14 months. Cavity recurrence was observed in three patients after 2–8 months: in one patient, the cavity was sterile but the cavity was infected in the other two patients (▶ **Table 6**). These patients were successfully treated by endoscopic or percutaneous drainage.

Discussion

In a multicenter randomized controlled trial, the Dutch Pancreatitis Study Group compared standard open necrosectomy with a step-up approach that involved percutaneous drainage followed by minimally invasive retroperitoneal necrosectomy if necessary [16]. Major complications occurred less frequently in the step-up approach compared with open necrosectomy (40% vs. 69%; P=0.006), and 35% of patients in the step-up group were successfully treated with percutaneous drainage alone. In a subsequent study, the same group prospectively examined 639 consecutive patients with necrotizing pancreatitis and found that patients whose first intervention was catheter drainage had fewer complications than those undergoing primary necrosectomy (42% vs. 64%; P=0.003) [17]. Furthermore, in a retrospective study, Gardner et al. [18] compared direct endoscopic necrosectomy with conventional transmural endoscopic drainage for WOPN and found that the former procedure achieved higher rates of successful resolution (88% vs. 45%; P<0.01), with complications limited to mild periprocedural bleeding, which occurred at equivalent rates between the two groups (32% vs. 20%; P=0.502). More recently, Bakker et al. [19] compared the proinflammatory response, as measured by serum interleukin-6 (IL-6) levels, and clinical outcomes of endoscopic transgastric and surgical necrosectomy in a randomized controlled trial. There was a decreased proinflammatory response following endoscopic necrosectomy, as evidenced by post-procedural IL-6 levels, compared with the response to surgical necrosectomy. In addition, major complications or death occurred less frequently after endoscopic necrosectomy than surgical necrosectomy (20% vs. 80%; P=0.03). Thus, in light of the improved outcomes, minimally invasive interventions to treat WOPN are becoming increasingly popular.

After the initial introduction of endoscopic necrosectomy by Seifert et al. [6], subsequent reports have described successful endoscopic necrosectomy for treating infected pancreatic necrosis, as

Table 7 Previous reports on endoscopic necrosectomy for infected pancreatic necrosis.

First author (year) [Ref]	Study design	n	Successful treatment, %	Morbidity, %	Mortality, %
Seifert (2000) [6]	Retrospective	3	100	0	0
Seewald (2005) [3]	Retrospective	13	69	31	0
Charnley (2006) [8]	Retrospective	13	92[1] (69)	0	15[2]
Papachristou (2007) [10]	Retrospective	53[3]	53	21	0
Voermans (2007) [7]	Retrospective	25	93	7	0
Kang (2008) [11]	Retrospective	1[4]	100	0	0
Mathew (2008) [20]	Retrospective	6	100	0	0
Escourrou (2008) [9]	Retrospective	13	100[5] (85)	46	0
Schrover (2008) [12]	Retrospective	8	75	25	13
Gardner (2009) [18]	Retrospective	25	88	32	0
Seifert (2009) [13]	Retrospective	93	80	26	7.5
Gardner (2011) [14]	Retrospective	104	91	14	5.8
Seewald (2012) [21]	Retrospective	80[6]	83.8	26	0
Bakker (2012) [19]	Prospective[7]	10	80	20	10
Present study	Retrospective	57	75	33	11

[1] After excluding 2 patients with additional percutaneous drainage and a patient with laparoscopic drainage, the success rate decreased to 69%.
[2] Non-related death.
[3] Drainage alone was studied, with endoscopic necrosectomy performed in 22 cases.
[4] Transduodenal approach.
[5] After excluding 2 patients with additional percutaneous drainage, the success rate decreased to 85%.
[6] Drainage alone was studied, with endoscopic necrosectomy performed in 49 cases.
[7] Prospective randomized controlled trial comparing endoscopic necrosectomy with surgical necrosectomy.

shown in **Table 7** [3,7–14,18–21]. The rate of complete resolution of pancreatic necrosis after endoscopic necrosectomy ranged from 53% to 100%. Procedure-related morbidity and mortality was 0%–46% and 0%–13%, respectively. However, most reports were small case series. Recently, multicenter studies enrolling a relatively large number of patients have been reported from Germany [13] and the United States [14]. In the German study, Seifert et al. [13] showed that initial clinical success was obtained in 80% of 93 patients, with a mean hospital stay of 46 days (range 8–170 days), complication rate of 26%, and associated mortality rate of 7.5%. The American study performed by Gardner et al. [14] reported successful resolution in 91% of 104 patients with a mean hospital stay of 12 days (range 9–15 days) after the initial drainage, a morbidity rate of 14%, and a mortality rate of 5.8%. In comparison, in the present study, the successful resolution rate was 75%, with a median hospital stay of 21 days (range 10–101 days) for endoscopic necrosectomy; the morbidity and mortality rates were 33% and 11%, respectively.

The rate of successful resolution in the present study was slightly lower, and the morbidity and mortality may be higher. It was initially hypothesized that these differences might be attributed to the relatively small sample size at each institution, given that the median number of patients enrolled at each institution was 3 (range 1–8) and experience with endoscopic techniques might be insufficient at many institutions. However, the analysis showed that the success rates were not significantly different between the group of institutions with more than two treatment cases and the group of institutions with only one or two treatment cases. Another possible reason is that the study population included several patients with extremely poor medical health. In the 10 patients with extremely poor medical health (ASA grades 4 and 5), the successful resolution rate was 50% and the complication rate was 50%. A subanalysis of factors associated with failed endoscopic necrosectomy also showed that the ratio of patients with poor medical health (ASA grades 3 and more) was significantly higher in the failed endoscopic necrosectomy group than in the successful group (**Table 4**). These results suggest that endoscopic necrosectomy is less favorable for patients in poor medical health. However, it is also true that such patients are also likely to respond poorly to surgical intervention. Indeed, in the present study, 34 of 39 patients with ASA≥3 were initially refused surgical interventions by surgeons. A previous randomized controlled trial also showed that major complications or death occurred more frequently after surgical necrosectomy than after endoscopic necrosectomy (80% vs. 20%; $P=0.03$) [19]. Therefore, we believe that endoscopic necrosectomy, as a less invasive option, is preferable to surgery, especially for patients in poor medical health.

The most common complication associated with endoscopic necrosectomy is bleeding, which may occur during balloon dilation of the transluminal tract or during the removal of necrotic material [22]. In the present study, bleeding arose during balloon dilation in five patients and during the necrosectomy in three. Another four patients developed massive hematemesis between endoscopic necrosectomy sessions. To reduce the risk of bleeding during the necrosectomy, the procedure should be performed under a clear endoscopic view. In this respect, forceful saline lavage was useful and an endoscope with water jet function (GIF-Q260J, Olympus, Tokyo, Japan) was used for many patients (**Table 3**). Although various devices were used to remove the necrotic material, no differences were observed among the devices with respect to bleeding rates. Interestingly, all fatal bleeding episodes occurred between endoscopic necrosectomy sessions. The most common cause was rupture of a pseudoaneurysm, which often forms in response to inflammation, and the subsequent, massive bleeding was difficult to contain using conservative and/or endoscopic treatments. Embolization under interventional radiologic guidance or surgery should be performed in the early stage of this potentially life-threatening complication.

Although air embolism is uncommon, it is one of the most concerning complications. Fatal cases have been reported in both aforementioned multicenter studies [13,14]; the authors recommended using CO_2 gas rather than room air for insufflation. A fatal case of air embolism was also experienced in the current

study; although CO_2 gas was not used in this case, it was used for 68 % of the patients. The use of CO_2 gas is mandatory for preventing air emboli. Moreover, insufflation during the procedure should be reduced to the minimum possible extent, and the procedure should also not be unnecessarily prolonged.

As a comparison, the contemporary number of surgical necrosectomies at the participating institutions was 21, and treatment was successful in 71.4 %, with associated morbidity and mortality rates of 52.3 % and 28.6 %, respectively. The median hospital stay was 140 days (range 30 – 304 days). While endoscopic necrosectomy is clearly much less invasive than surgical necrosectomy, serious complications can nevertheless occur during endoscopic necrosectomy and the procedure can be ineffective. To optimize outcomes and minimize complications, a multidisciplinary approach involving skilled interventional endoscopists, radiologists, and surgeons is necessary to manage the WOPN successfully. Therefore, patients with WOPN should be referred to tertiary care centers where this multidisciplinary approach is available.

In the present study, the timing of stent removal varied according to each case and institution. Stents were removed at the final endoscopic necrosectomy session in 7 patients and electively removed after a median duration of 13 weeks (range 3 weeks – 17 months) in 23 patients. Before stent removal, resolution of the cavity was confirmed on CT imaging in all patients. In nine patients, stents spontaneously dislodged after a median duration of 15 weeks (8 weeks – 9 months), and in 4 patients, the stents were still in situ at the time of the last follow-up (median 22 months; range 11 – 30 months). The timing of stent removal remains controversial, although the stents were typically removed 1 – 3 months after documented resolution of the cavity in previous studies [7, 12 – 14, 18]. Further research is required to examine the optimal time for stent removal.

There are several limitations to the current study. First, due to the retrospective nature, case selection bias cannot be avoided. There are various indications for endoscopic necrosectomy, depending on the institution. In addition, data collection may be imperfect. Inclusion criteria might have been inappropriately applied, and some minor complications might have been missed. Second, each institution only enrolled a small number of patients, which likely affected the treatment outcomes and contributed to increased complication rates.

In conclusion, endoscopic necrosectomy can be an effective treatment for infected WOPN and requires a relatively short treatment period. However, serious complications, including death, can occur. Therefore, patients should be carefully selected, and knowledgeable, skilled, and experienced operators should perform this procedure. Further research into safer technologies is required to reduce the associated morbidity and mortality.

Competing interests: None

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Acknowledgments

This work was supported in part by the Research Committee of Intractable Pancreatic Diseases (principal investigator: Tooru Shimosegawa), Ministry of Health, Labor, and Welfare of Japan.

The authors wish to thank the following colleagues for their helpful advice and encouragement: Shinpei Doi, MD (First Department of Internal Medicine, Gifu University Hospital); Keisuke Yamamoto, MD, PhD, Hirofumi Kogure, MD, PhD, Natsuyo Yamamoto, MD, PhD, and Naoki Sasahira, MD, PhD (Department of Gastroenterology, Graduate School of Medicine, The University of Tokyo).

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