In severe acute pancreatitis, necrosis of pancreatic parenchymal and ductal epithelial cells may lead to pancreatic duct disruption, leakage of pancreatic juice, and development of amylase-rich peripancreatic fluid collections, whereas in mild disease the pancreatic duct remains intact [1, 2]. In a retrospective series, Lau et al. reported that the presence of a demonstrable pancreatic duct leak is associated with pancreatic necrosis and prolonged length of hospital stay, and suggested endoscopic retrograde pancreatography (ERP) be performed when conservative therapy fails [1].

Several studies demonstrate a benefit of endoscopic transpapillary stenting in patients with pancreatic fistulae of heterogeneous etiologies, including acute and chronic pancreatitis, trauma, and postoperative complications [1 – 6]. However, only a few studies have focused on pancreatic fistulae exclusively after ANP [1, 7], despite the reported incidence of pancreatic fistulae after ANP being as high as 78 % [8] and up to 100 % after open surgical necrosectomy [3].
Studies investigating the efficacy of pancreatic stent placement therapy for peripancreatic fluid collection have shown that pancreatic ductal anatomy determines the major complications resulting from pancreatitis [4, 5]. In cases of partial ductal disruption, bridging stent placement is associated with successful outcomes [4, 9]. Theoretically, early prophylactic placement of a bridging pancreatic stent in cases of necrotizing pancreatitis could help maintain pancreatic duct continuity and decrease the pressure gradient of pancreatic juice towards the duodenal lumen, preventing peripancreatic fluid leakage and the evolution of disconnected duct syndrome with its associated complications. To the best of our knowledge, this kind of prophylactic treatment has not been studied previously. Therefore, we designed a multicenter, prospective, randomized clinical trial to test the impact of early prophylactic pancreatic duct stenting (PPDS) in ANP on the need for surgical, endoscopic, or percutaneous interventions, length of hospital stay, and admission to the intensive care unit compared with traditional treatment.

**Methods**

**Design**

This trial was a two-center, randomized, superiority clinical trial designed to test the hypothesis that early PPDS in ANP will decrease local complications and subsequent endoscopic, surgical, and radiological interventions associated with pancreatic duct disruption, and to compare PPDS with conservative treatment. The trial was conducted at Oulu University Hospital (Finland) and Copenhagen University Hospital Hvidovre (Denmark). The study was developed and decided upon by the Nordic countries’ Allied Network for Development and Research in Endoscopy (ANDRE) group. The trial is reported according to the Consolidated Standards of Reporting Trials (CONSORT; see Supplementary material).

**Participants**

Patients between 18 and 75 years of age admitted to participating hospitals with contrast-enhanced computed tomography (CECT)-diagnosed necrotizing pancreatitis were evaluated for the study. CECT findings included an area of nonenhancing pancreatic parenchyma that was thought to represent necrosis. If no necrosis was observed upon initial CECT in suspected cases, CECT was repeated after 1 week. If CECT revealed pancreatic necrosis affecting > 30% of the head, neck, or body of the pancreas or 20%–30% parenchymal necrosis affecting the main pancreatic duct, the patient was enrolled in the study.

The exclusion criteria were: isolated necrosis of the pancreatic tail, as bridging PPDS is impossible in these cases; pregnancy; age < 18 years or > 75 years; suspicion of abdominal tumor on CECT or magnetic resonance imaging; inability to give informed consent; or insufficient fitness to tolerate endoscopy. Patients were also excluded if advanced therapeutic pancreaticobiliary endoscopists were not available. An experienced endoscopic retrograde cholangiopancreatography (ERC) endoscopist should have at least 10 years of experience with 300 ERCPs annually, with approximately 30%–40% including pancreatic stent placement.

**Randomization**

For each participating center, a computer-generated randomization list was created by the statistician at Oulu University Hospital, who was not involved with patient care. Randomization was performed in blocks, with the block size varying randomly between 4, 6, and 8. The results were sealed in numbered, opaque envelopes by a biostatistician, who was not involved in patient care. After confirming the patient’s eligibility, the research surgeon opened an envelope in numerical order to randomize the patient to either PPDS or conservative treatment.

**Ethical aspects**

The study was approved by the ethics committees of both hospitals and conducted in accordance with the Declaration of Helsinki and the principles of the International Conference on Harmonization Good Clinical Practice guidelines. The trial was also performed according to local legal and regulatory requirements. The trial was registered at ClinicalTrials.gov (NCT01767233). Informed consent was obtained from all participants prior to randomization in both oral and written forms. A detailed explanation on the nature, aims, and consequences of the study was given to all patients by the participating physician prior to consenting.

**Intervention**

**PPDS group**

For patients randomized to the PPDS group, ERP was scheduled as soon as possible, preferably before the end of the first week after symptom onset and before potential ductal disruption. All patients were prepared and sedated prior to ERP, as is standard practice at both participating centers. During ERP, the pancreatic duct was cannulated and opacified. Regardless of whether leakage was observed, a pancreatic stent (5–10 Fr) that was long enough to bridge the area of necrosis was inserted with or without pancreatic sphincterotomy. Endoscopic papilotomy was performed, if needed. If the first ERP procedure was unsuccessful, a second attempt was planned for within 1 week. Patients in the PPDS group returned for stent removal or replacement 8 weeks after the primary ERP, or sooner if needed. If no leakage was observed at the second ERP, the stent was removed. In cases of persistent leakage, a new stent was placed and ERP was repeated at 8-week intervals until the cessation of leakage without ductal stricturing. The rest of the treatment was identical to the conservative group.

**Conservative group**

Patients randomized to the conservative group were treated according to international guidelines [10].
Data collection

Patient characteristics were recorded at the initial visit, including age, sex, pancreatitis etiology, clinical, radiological, and laboratory findings, and the time from symptom onset to randomization. In the PPDS group, we recorded the ERP findings, including pancreatic duct diameter, partial or complete ductal disruption, and stricture development, as well as the technical success or failure of PPDS, and early and late ERP-related complications.

At 12 months after randomization, we analyzed surgical, endoscopic, and radiological procedures and findings (primary outcome) in both patient groups, as well as mortality, length of hospital stay, admission to the intensive care unit, and hospital readmissions. We also recorded fluid collections larger than 3 cm in diameter, and the development of exocrine (fetal elastase I) and endocrine pancreatic insufficiency.

Primary and secondary outcomes

The primary end point for the study was the rate of percutaneous, endoscopic, laparoscopic, or open surgical drainage and/or debridement 1 year after randomization. We assumed that by this method, we could test the feasibility and safety of PPDS, as reflected by the local complication rate associated with necrotizing pancreatitis. The indications for intervention were: infection in necrosis, gastrointestinal or bile obstruction, pain caused by pancreatic or peripancreatic collection, and leakage of pancreatic juice (i.e. ascites or pleural fluid with an amylase content >3-times the serum amylase activity). In both groups, infection was defined as positive fine-needle aspiration or drainage culture from the pancreatic necrosis. If patients presented with pyrexia, elevated infection parameters (C-reactive protein and leukocytosis), and suspicion of infected necrosis on CECT (gas shown in the necrosis), infection was diagnosed without culture.

The predefined secondary end points included length of hospital stay, new onset endocrine or exocrine insufficiency and persistent fluid collection, mortality, and other local complications 1 year after the randomization.

Sample size

The sample size calculation was performed against the secondary outcome (survivors’ length of hospital stay during the 1-year follow-up) because we did not have exact data on all endoscopic, radiological, or surgical procedures performed 1 year after the onset of the disease (primary outcome). We assumed that length of hospital stay was a good reflection of the primary outcome. From the data collected at Oulu University Hospital during the period 2000 –2006, we calculated that the average length of hospital stay for treatment of severe pancreatitis was 59.6 days. The sample size calculations indicated that we needed 36 patients per group to show a decrease in the length of hospital stay from 59.6 days to 40.0 days (standard deviation [SD] 29.2 days; two-tailed α = 0.05; power = 0.80). We anticipated a 10% drop-out rate; therefore, we aimed to have a group size of 40 and a total of 80 patients.

Statistical methods

Summary statistics are presented as mean and SD unless otherwise stated. Analyses were performed primarily using the intent-to-treat principal, and secondarily using the per-protocol principal. Group comparisons were performed using the Student’s t test (continuous data) or Fisher’s exact test (categorical data). Two-tailed P values are presented, with P<0.05 considered significant. The P values should be treated with caution because of the multiple dependent comparisons. Differences between means and proportions with 95% confidential intervals (CIs) were used to estimate effect sizes and their precision. This was a two-center study, but the impact of the center could not be counted owing to the small sample size.

Analyses were performed using SPSS for Windows (Released 2016, Version 24.0; IBM Corp., Armonk, New York, USA).

Results

During the study, suspicion arose of an increased rate of complications in the stent group. Interim analysis led to premature trial termination based on ethical concerns regarding a significantly higher rate of infected necrosis in the PPDS group.

A total of 25 patients with ANP were enrolled in the study between February 2011 and July 2015. The inclusion flow chart is presented in Fig. 1. According to hospital discharge registry diagnosis codes, a total of 155 patients were treated for necrotizing pancreatitis during the study period, and 25 (23.4%) of these patients were evaluated for the study: 12 were randomized to the PPDS group and 13 to the conservative treatment group. One patient in the PPDS group was excluded due to misdiagnosed pancreatic necrosis upon the initial CECT. Baseline characteristics were similar between the PPDS and conservative treatment groups (Table 1).

Primary end points

According to the intent-to-treat analysis, 7/11 patients (63.6%) in the PPDS group had infected pancreatic necrosis compared with 3/13 (23.1%) in the control group (difference between infection rate 40.6 percentage points, 95% CI 1.4% to 66.5%; P = 0.095). Infected pancreatic necrosis developed in all five patients with successful PPDS. Per-protocol analysis revealed significantly more frequent development of infected necrosis among patients with successful PPDS (5/5, 100%) than among patients in the conservative treatment group (3/13, 23.1%; difference between rates 76.9 percentage points, 95% CI 25.7% to 91.8%; P = 0.01).

The composite primary end point of surgical, endoscopic, or radiological intervention occurred in 8 of the 11 patients (72.7%) in the PPDS group during the 1-year follow-up, compared with 4 out of 13 patients (30.8%) in the conservative treatment group (Table 2). The difference between intervention rates for the PPDS and conservative groups was 42.0 percentage points (95% CI 2.2 to 67.1%; P = 0.10).

In the PPDS group, the indication for intervention was infected pancreatic necrosis (5 positive aspiration samples and 3 clinically suspected) in 8 of the 11 patients. One of three pa-
tients with clinically suspected infection died 3 days after necrosectomy, but in the post-mortem examination the bacterial culture was negative. Four patients underwent necrosectomy (two open, two endoscopic transgastric), and four patients underwent percutaneous drainage (including two with simultaneous endoscopic transgastric necrosectomy). Two patients were treated by transpapillary drainage; one of these patients developed infected necrosis 2.5 months after successful bridging PPDS, and pancreatic stent exchange with antibiotic treatment led to successful recovery. The other patient developed infected walled-off necrosis 4 months after a failed PPDS attempt, and recovered after repeated and successful endoscopic pancreatic stenting and antibiotic treatment.

In the control group, the indication for intervention was infected necrosis in three cases, and they were treated with endoscopic transgastric drainage (two of them with percutaneous drainage). One patient underwent endoscopic transgastric drainage (without percutaneous drainage) for a sterile collection causing pain.

All patients with infected pancreatic necrosis and bacterial culture are shown in ▶ Table 3. In the PPDS group, positive culture contamination was monoclonal in three cases, and in two cases the contamination had multibacterial etiology. In the control group, positive culture was monoclonal in both cases. None of the patients had positive blood culture. Among the five patients with successful PPDS, the mean time between PPDS and proven infection was 24 days (range 5–76 days). Patients with infection without successful pancreatic stent placement (three in the conservative group and three patients with failed PPDS) developed infection in a mean 47.5 days (range 18–120 days) after randomization.

Secondary end points

The total length of hospital stay during the 1-year follow-up was 39.3 days in the PPDS group and 31.3 days in the conservative treatment group (difference between means 8.0 days, 95%CI –15.5 to 31.7 days; P = 0.49). Throughout the 1-year follow-up, 7 (63.6%) of the 11 patients in the PPDS group required readmission to the hospital, compared with 2 (15.4%) of the 13 patients in the conservative treatment group. The mean number of readmissions was 2.9 (range 1–6) in the PPDS group.

After 1 year, 4 of the 11 patients in the PPDS group still had a pancreatic stent because of a persistent fistula or collection (>3 cm), including three patients who underwent successful PPDS. Five of the 13 patients in the conservative treatment group had walled-off necrosis, but none required pancreatic surgery.

CT-confirmed necrotizing pancreatitis assessed for eligibility (n = 155)

Excluded (n = 130)
- Not meeting inclusion criteria (n = 115)
- Necrosis in the tail of pancreas (n = 37)
- Necrosis less than 30% (n = 35)
- Not fit for endoscopy (n = 16)
- Age over 75 (n = 16)
- Not able to consent (n = 5)
- Experienced endoscopist not available (n = 5)
- Malignant tumor in CT (n = 1)
- Declined to participate (n = 15)

Randomized (n = 25)

PPDS (n = 12)

Conservative treatment (n = 13)

Discontinued (n = 1)
- Wrong diagnosis

Follow-up at 1 year

Analyzed (n = 11)

Analyzed (n = 13)

▶ Fig. 1 Flow chart of participant inclusion in the trial. PPDS, prophylactic pancreatic ductal stenting.
stents or other treatment. The two groups did not differ in the incidence of new onset diabetes or pancreatic exocrine insufficiency.

One patient in the PPDS group died 34 days after admission as a result of biliary pancreatitis after failed PPDS. Open necrosectomy was performed with suspicion of infected necrosis, but post-mortem revealed that the cause of death was severe pancreatitis and Stevens-Johnson syndrome, not infected necrosis. In the conservative group, one patient experienced portal and superior vein thrombosis without infection and had a good recovery.

Endoscopic findings and procedures

In the PPDS group, the mean time from symptom onset to planned PPDS was 4.6 days (range 2–9 days). Pancreatic duct cannulation and opacification was successful in 7 of the 11 patients (63.6%). Partial pancreatic duct leakage was observed in three patients, and no patients had complete disruptions. PPDS was achieved in 5 (45.5%) of the 11 patients. A long bridging stent (5–7 Fr × 12–15 cm) was successfully placed in two cases (▶Fig. 2a; see also Table 1 in the online-only Supplementary material). In the other three cases, only a short nonbridging stent could be placed owing to a stenotic pancreatic duct. Two patients were cannulated successfully but exhibited a stenotic pancreatic duct that precluded any stenting, even with a 5-Fr stent (▶Fig. 2b).

Among the seven patients with successful cannulation, the average pancreatic duct diameter was 2.0 mm (SD 3.0–1.6 mm) in the head, 1.6 mm (2.0–1.3 mm) in the body, and 1.1 mm (1.3–1.0 mm) in the tail (Table 1). In the four cases of cannulation failure, pronounced duodenal edema prevented major papilla visualization in three patients and prevented access to the second part of the duodenum in one patient. In three of these cases, an additional attempt also failed. No pancreatic sphincterotomies were performed. No immediate ERP- or anesthesia-related complications were recorded in the PPDS group.

Discussion

The main result of this study was that PPDS in necrotizing pancreatitis is harmful. All patients with successful PPDS experienced infected necrosis. In addition, successful early bridging stenting was achieved in only one-fifth of the patients, mainly due to pancreatic duct stenosis and duodenal edema.

During their disease course, the majority of patients with necrotizing pancreatitis will experience leakage from the disrupted or disconnected pancreatic duct, resulting in intrapancreatic and/or peripancreatic fluid collections [1, 11–13]. Thus, it was reasonable to hypothesize that PPDS placement may decrease later morbidity by limiting enzyme exposure to the necrotic area and the healthy tissue surrounding it [14]. Although

Karjula Heikki et al. Prophylactic pancreatic duct stenting in severe acute necrotizing pancreatitis ... Endoscopy 2019; 51: 1027–1034
endoscopically placed pancreatic duct stents are widely accepted for use in pancreatic fistulae of varying etiologies, only limited data are available concerning fistulae in ANP. Previous studies have mainly described endoscopic treatment performed later in the evolution of severe pancreatitis after failure of conservative treatment [3, 12, 15–17]. According to a recent literature review of PPDS treatment for pancreatic fistulae caused by acute pancreatitis, the median time from symptom onset to endotherapy is 42 days (range 21–154 days) [18]. The corresponding time in our present study was 4.6 days (range 2–9 days). To the best of our knowledge, this was the first study to explore the potential role of early PPDS in ANP.

Prior to initiating the present study, concerns were raised that ERP and insertion of a pancreatic duct stent through a sterile necrosis area may carry a risk of introducing infection into an otherwise sterile environment [19]. However, we did not find any data from previous studies confirming this risk [1, 8]. The interim analysis in our present study revealed that infected necrosis developed in 7 (63.6%) of the 11 patients in the PPDS group, including all patients with successful prophylactic stent placement.

In the natural course of ANP, there is a 30%–70% risk of developing infected necrosis. However, we prematurely terminated our study for ethical reasons because the infection rate observed in the conservative treatment group was much lower than that in the PPDS group. Thus, the significantly increased risk of infectious complications related to PPDS is the main finding of our study. A previous study included 70 consecutive patients who underwent ERCP for necrotizing biliary pancreatitis within the first week following admission, without pancreatic stenting [11]; the authors reported a 21.4% rate of infected pancreatic necrosis, which is comparable to the 23.1% infection rate in the conservative treatment group of the present study. In addition, patients with successful PPDS seem to develop infection much earlier (mean 24.0 days) than patients with infected walled-off necrosis without a stent (mean 47.5 days). This suggests that the much higher infection rate in the PPDS group was most likely caused by stent insertion.

Several randomized trials have shown that placement of a small-caliber pancreatic stent in patients at high risk for post-ERCP pancreatitis (PEP) is effective by reducing the risk and severity of PEP [20, 21]. In their series of 3216 ERCPs, Kerdsirichairat et al. reported that 64 patients (2.0%) developed PEP [22], 14 of whom were considered to have moderately severe pancreatitis; urgent salvage ERCP and pancreatic stenting was performed within 2–48 hours, with rapid resolution of clinical pancreatitis without any necrotizing pancreatitis or late complications. Madácsy et al. also demonstrated efficiency of rescue ERCP and placement of a small-caliber pancreatic duct stent during the early course of PEP [23]. However, PEP tended to have a milder course and the incidence of severe PEP was low [24]. Nonetheless, temporary small-caliber pancreatic duct stent placement may offer sufficient drainage to reverse the process of acute PEP [20, 21, 22, 23]. Our results indicate that when necrosis is proven in CECT, we are beyond this particular

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Prophylactic stenting</th>
<th>Conservative treatment</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>11</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Major complication or death, n (%)</td>
<td>8 (72.7)</td>
<td>4 (30.8)</td>
<td>0.10</td>
</tr>
<tr>
<td>Death</td>
<td>1 (9.1)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Infection of necrosis</td>
<td>7 (63.6)</td>
<td>3 (23.1)</td>
<td>0.10</td>
</tr>
<tr>
<td>Patients requiring intervention, n (%)</td>
<td>8 (72.7)</td>
<td>4 (30.8)</td>
<td>0.1</td>
</tr>
<tr>
<td>Necrosectomies (laparotomy/mini-invasive)</td>
<td>3 (27.3)</td>
<td>4 (30.8)</td>
<td>&gt;0.90</td>
</tr>
<tr>
<td>Drainage procedures</td>
<td>4 (36.4)</td>
<td>2 (15.4)</td>
<td>0.36</td>
</tr>
<tr>
<td>Other*</td>
<td>2 (18.2)</td>
<td>0</td>
<td>0.08</td>
</tr>
<tr>
<td>Length of hospital stay</td>
<td>39.3 (9–81)</td>
<td>31.3 (6–95)</td>
<td>0.49</td>
</tr>
<tr>
<td>ICU admissions, n (%)</td>
<td>3 (27.3)</td>
<td>4 (30.8)</td>
<td>&gt;0.90</td>
</tr>
<tr>
<td>Readmissions, n (%)</td>
<td>7 (63.6)</td>
<td>2 (15.4)</td>
<td>0.10</td>
</tr>
<tr>
<td>Others after 1 year, n</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fistula/collection</td>
<td>4</td>
<td>3</td>
<td>&gt;0.90</td>
</tr>
<tr>
<td>Stent in the pancreas</td>
<td>4</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4</td>
<td>4</td>
<td>0.68</td>
</tr>
<tr>
<td>Use of pancreatic enzymes</td>
<td>4</td>
<td>3</td>
<td>0.65</td>
</tr>
</tbody>
</table>

ICU, intensive care unit.
* Additional endoscopic transpapillary stenting.
In the PPDS group, we unexpectedly encountered substantial difficulties during the ERP, with a cannulation success rate of 63.6%, a stenting success rate of 45.5%, and only an 18.2% success rate for placement of a bridging stent. This was surprising considering the high personal experience of the three endoscopists, who had performed up to 7000 previous ERCP procedures. The main obstacle to cannulation was extreme duodenal edema, which prevented access to the second part of the duodenum in one case and visualization of the major papilla in three cases. Later in the disease course, edema had disappeared and all pancreatic cannulations were successful. However, at this point, ERP revealed ductal stenosis, with an average duct diameter of 2.0–1.1 mm from the pancreatic head to the tail, which prevented the placement of a bridging stent in three patients. The observed duct diameter was approximately half of the previously reported normal pancreatic duct diameter of 4.6–3.1 mm [25]. Of the four pancreatographies performed 7–9 days after symptom onset, 3 (75.0%) revealed partial pancreatic ductal disruption. This parallels previous reports indicating that ductal leaks are found only after 4 days of disease evolution [2]. We found no cases of total pancreatic disruption, which was expected because disconnected duct syndrome occurs later in the disease process [13].

During our 1-year follow-up, the patients in the PPDS group fared worse than those in the conservative treatment group (Table 3), showing an increased length of hospital stay, including readmissions. Moreover, a significant portion of the pa-

---

**Table 3** Details of patients with infected pancreatic necrosis.

<table>
<thead>
<tr>
<th>Patient and study group</th>
<th>PPDS achieved</th>
<th>Method of diagnosis</th>
<th>Culture</th>
<th>Infection diagnosis from randomization, days</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1 PPDS</td>
<td>Yes</td>
<td>Positive culture</td>
<td>Staphylococcus epidermidis</td>
<td>6</td>
<td>Percutaneous drainage</td>
</tr>
<tr>
<td>Patient 3 PPDS</td>
<td>Yes</td>
<td>Positive culture</td>
<td>Escherichia coli</td>
<td>15</td>
<td>Percutaneous drainage</td>
</tr>
<tr>
<td>Patient 6 PPDS</td>
<td>No</td>
<td>Clinical</td>
<td>Negative</td>
<td>33</td>
<td>Open necrosectomy</td>
</tr>
<tr>
<td>Patient 7 PPDS</td>
<td>Yes</td>
<td>Positive culture</td>
<td>Streptococcus anginosus, Candida albicans, Pediococcus pentosaceus</td>
<td>18</td>
<td>Open necrosectomy</td>
</tr>
<tr>
<td>Patient 8 PPDS</td>
<td>No</td>
<td>Clinical</td>
<td></td>
<td>120</td>
<td>ETS</td>
</tr>
<tr>
<td>Patient 9 PPDS</td>
<td>Yes</td>
<td>Clinical</td>
<td></td>
<td>76</td>
<td>Repeated ETS</td>
</tr>
<tr>
<td>Patient 10 PPDS</td>
<td>Yes</td>
<td>Positive culture</td>
<td>Enterobacter species</td>
<td>5</td>
<td>Endoscopic transgastric necrosectomy + percutaneous drainage</td>
</tr>
<tr>
<td>Patient 11 PPDS</td>
<td>No</td>
<td>Positive culture</td>
<td>E. coli, Enterobacter cloacae, Klebsiella oxytoga</td>
<td>66</td>
<td>Endoscopic transgastric necrosectomy + percutaneous drainage</td>
</tr>
<tr>
<td>Patient 20 Conservative</td>
<td>N/A</td>
<td>Positive culture</td>
<td>E. coli</td>
<td>23</td>
<td>Endoscopic transgastric necrosectomy + percutaneous drainage</td>
</tr>
<tr>
<td>Patient 23 Conservative</td>
<td>N/A</td>
<td>Clinical</td>
<td></td>
<td>25</td>
<td>Endoscopic transgastric necrosectomy + percutaneous drainage</td>
</tr>
<tr>
<td>Patient 24 Conservative</td>
<td>N/A</td>
<td>Positive culture</td>
<td>Enterococcus faecium</td>
<td>18</td>
<td>Endoscopic transgastric necrosectomy</td>
</tr>
</tbody>
</table>

ETS, endoscopic transpapillary stenting; PPDS, prophylactic pancreatic ductal stenting; N/A, not applicable.

---

**Fig. 2** Endoscopic retrograde pancreatography (ERP) findings in a patient with acute necrotizing pancreatitis (ANP). **a** ERP demonstrated a narrow pancreatic duct in the pancreas corpus and tail. **b** ERP showed a very narrow pancreatic duct with partial disruption in the pancreas corpus. Prophylactic pancreatic duct stenting was not possible due to the stenotic pancreatic duct.

therapeutic window and, at this stage, PPDS is no longer beneficial.

In the PPDS group, we unexpectedly encountered substantial difficulties during the ERP, with a cannulation success rate of 63.6%, a stenting success rate of 45.5%, and only an 18.2% success rate for placement of a bridging stent. This was surprising considering the high personal experience of the three endoscopists, who had performed up to 7000 previous ERCP procedures. The main obstacle to cannulation was extreme duodenal edema, which prevented access to the second part of the duodenum in one case and visualization of the major papilla in three cases. Later in the disease course, edema had disappeared and all pancreatic cannulations were successful. However, at this point, ERP revealed ductal stenosis, with an average duct diameter of 2.0 – 1.1 mm from the pancreatic head to the tail, which prevented the placement of a bridging stent in three patients. The observed duct diameter was approximately half of the previously reported normal pancreatic duct diameter of 4.6 – 3.1 mm [25]. Of the four pancreatographies performed 7 – 9 days after symptom onset, 3 (75.0%) revealed partial pancreatic ductal disruption. This parallels previous reports indicating that ductal leaks are found only after 4 days of disease evolution [2]. We found no cases of total pancreatic disruption, which was expected because disconnected duct syndrome occurs later in the disease process [13].

During our 1-year follow-up, the patients in the PPDS group fared worse than those in the conservative treatment group (Table 3), showing an increased length of hospital stay, including readmissions. Moreover, a significant portion of the pa-
tients in the PPDS group still had a pancreatic stent after 1 year of follow-up (4/11, 36.4%) compared with none in the conservative treatment group. This result is most likely related to the significantly higher rate of pancreatic necrosis infection in the PPDS group. Despite these differences, the 1-year mortality rate within the PPDS group was only 9.1% (1/11), which compares favorably to the 16%–60% mortality rates in previous reports [11,13,18,26]. No deaths occurred in the conservative treatment group.

In conclusion, the present study failed to show superiority of early PPDS over conservative treatment in patients with ANP. Instead, the result was the opposite: the rates of endoscopic, surgical, and radiological interventions were greater in the PPDS group owing to a high infection rate. The present study indicates that PPDS in ANP seems to increase the complication rate and is perhaps harmful for the patients.

Competing interests
None

References


Karjula Heikki et al. Prophylactic pancreatic duct stenting in severe acute necrotizing pancreatitis... Endoscopy 2019; 51: 1027–1034