Endoscopic Transpapillary Stenting or Conservative Treatment for Pancreatic Fistulas in Necrotizing Pancreatitis

Multicenter Series and Literature Review

Olaf J. Bakker, MD, Mark C. van Baal, MD,* Hjalmar C. van Santvoort, MD, PhD,* Marc G. Besselink, MD, PhD,* Jan-Werner Poley, MD,† Joos Heisterkamp, MD, PhD,‡ Thomas L. Bollen, MD,§ Hein G. Gooszen, MD, PhD,¶ and Casper H. van Eijck, MD, PhD;‡ for the Dutch Pancreatitis Study Group*

Objective: Endoscopic transpapillary stenting (ETS) of the pancreatic duct facilitates ductal outflow and may reduce time to pancreatic fistula closure. However, data on the feasibility of ETS in patients with necrotizing pancreatitis are scarce.

Background: Pancreatic fistulas often occur after intervention in necrotizing pancreatitis and frequently close only after months of conservative treatment.

Methods: From a prospective cohort of patients with acute pancreatitis admitted in 15 hospitals (2004–2007), all patients who underwent ETS or conservative treatment for a pancreatic fistula were identified. Safety, feasibility, and outcome of ETS were evaluated. Furthermore, a literature review was performed for similar studies in necrotizing pancreatitis.

Results: Of 731 patients with acute pancreatitis, 19 patients were treated with ETS and 16 patients were treated conservatively for a pancreatic fistula. Fistula closure was achieved in 16 of 19 patients (84%) in the ETS group and in 8 of 12 patients (75%) in the conservative group ($P = 0.175$). The median time to fistula closure after ETS was 71 days (interquartile range [IQR] 34–142) compared with 120 days (IQR 51–175 days) in the conservative group ($P = 0.130$). Complications were observed in 6 patients. A total of 10 studies reporting the results of 281 patients with stent placement for pancreatic fistulas were included in the literature review. Fistula closure was achieved in 200 patients (71%). Stent-related complications were reported in 9% of patients.

Conclusions: ETS seems a feasible and safe alternative to conservative treatment in patients with pancreatic fistulas after intervention for necrotizing pancreatitis.

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From the *Department of Surgery, University Medical Center Utrecht, Utrecht, the Netherlands; †Department of Gastroenterology & Hepatology, Erasmus Medical Center Rotterdam, the Netherlands; ‡Department of Surgery, St. Elisabeth Hospital, Tilburg, the Netherlands; §Department of Radiology, St. Antonius Hospital, Nieuwegein, the Netherlands; ¶Department of OR/Evidence Based Surgery, Radboud University Nijmegen Medical Centre, Nijmegen, the Netherlands and ‡Department of Surgery, Erasmus Medical Center, Rotterdam, the Netherlands.

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None of the authors declare a competing interest.

Reprints: Olaf J. Bakker, Department of Surgery, University Medical Center Utrecht, HP G04.228, P.O. Box 85500, HP G04.228, 3508 GA Utrecht, the Netherlands. E-mail: o.j.bakker@umcutrecht.nl.

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Infection of pancreatic necrosis occurs in around 30% of patients with necrotizing pancreatitis and is considered an indication for intervention.[1] Surgical necrosectomy and percutaneous catheter drainage are the most frequently used techniques to debride and drain the infected collections. The drains are generally kept in place until the spontaneous production decreases or the fluid becomes clear after postprocedural lavage. A subset of patients will, however, have continued spontaneous production of clear fluids from the drain, indicative of a pancreatico-cutaneous fistula.[2–5] The estimated incidence of persisting pancreatic fistulas varies from 17% to 76% after intervention for necrotizing pancreatitis.[6–9] Pancreatic fistulas are associated with considerable morbidity such as metabolic and nutritional disturbances, prolonged hospitalization, and even with mortality.[7]

Pancreatic fistulas most often are treated conservatively, although the time for a pancreatic fistula to resolve spontaneously usually takes more than 3 months and in some cases even over a year.[10] If conservative treatment fails, ultimately, a pancreaticojejunostomy may be indicated.[6,11]

Over the years, several groups of investigators have proposed endoscopic transpapillary stenting (ETS) as an alternative strategy for the management of pancreatic duct (PD) injuries.[12–17] ETS decreases intraductal pressure, which facilitates drainage of pancreatic secretions to the duodenum instead of through the fistula. Most series describe the results of ETS in patients with fistulas after pancreatic surgery for suspected malignancy or for pseudocysts complicating chronic pancreatitis. However, performing an endoscopic intervention in a critically ill patient with necrotizing pancreatitis and concomitant papillary edema, pancreatic ductal or duodenal obstruction by pancreatic collections may be technically challenging and may potentially even worsen clinical outcome.

Only limited data are available on ETS and conservative treatment of fistulas in patients with necrotizing pancreatitis and little is known about the safety of ETS in critically ill patients.[13] We therefore evaluated the feasibility and clinical outcome of ETS and conservative treatment in patients with pancreatic fistulas after intervention for necrotizing pancreatitis from a prospective multicenter database. In addition, we performed a literature review for similar studies reporting the result of ETS and conservative treatment in patients with acute necrotizing pancreatitis.

METHODS

Design

This was a retrospective analysis of a prospective database of 731 patients with a primary episode of acute pancreatitis admitted to the 15 centers of the Dutch Pancreatitis Study Group between March 2004 and March 2007. The ethical review board of each participating hospital approved the protocol for prospective data collection and all patients or their legal representatives gave written informed consent

for inclusion in the database. The baseline characteristics and outcomes of this cohort have previous been reported.[18–20]

Patient Selection

All patients who underwent percutaneous drainage and/or surgical treatment for (suspected) infected necrotizing pancreatitis and subsequently developed a pancreatic fistula were included in this study. Patients were identified by screening all case record forms, endoscopic retrograde pancreaticography (ERP), and other imaging reports of the patients in the database. No strict criteria existed for the indication to perform ERP in patients with a pancreatic fistula in the participating hospitals. The decision to perform ETS depended on hospital policy and endoscopic skills of the gastroenterologist.

A pancreatico-cutaneous fistula was defined as output via an operatively or percutaneously placed catheter (or drainage canal after removal of drains or from a surgical wound) of any measurable volume with an amylase content greater than 3 times the serum amylase activity. A pancreatico-abdominal fistula was defined as the presence of ascites with amylase content greater than 3 times the serum amylase activity. These definitions were adapted from the International Study Group on Pancreatic Fistula criteria.[2]

Technique of Endoscopic Transpapillary Stenting

ERP was performed to locate the site of PD injury or disruption, as demonstrated by contrast leakage from the PD (Fig. 1). In presence of a downstream obstruction or disruption of the PD, a guide wire was inserted and, if possible, a stent was placed. The preferred position was a bridging stent to bypass or cover the PD disruption, and thereby restore the flow of pancreatic secretions. In all patients, bridging of the leakage site was attempted. If bridging was not possible, an internal stent was placed with the proximal tip of the stent in the collection and the distal tip through the papilla (Fig. 2). Finally, if neither a bridging stent nor an internal stent could be placed, a short transpapillary stent was placed to reduce intraductal pressure.

Outcome and Data Collection

Data on patient demographics and clinical outcome were available from the prospective database. The outcomes of the study were procedure-related complications during ETS, any deterioration in clinical condition after ETS or ERCP, and successful fistula treatment after ETS or after conservative treatment. Successful fistula treatment was defined as total resolution of fistula output and absence of large fluid collections on follow-up computed tomography (CT) after removal of all drains without the need for additional interventions.

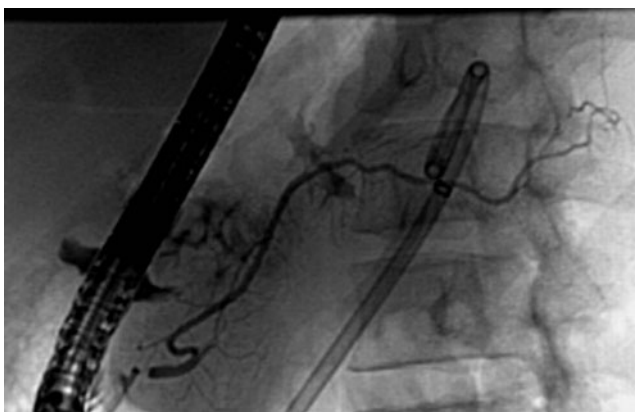

FIGURE 1. Endoscopic retrograde pancreatography (ERP) of a patient with ductal leakage from the head of the pancreas. A percutaneous catheter drain is visible.

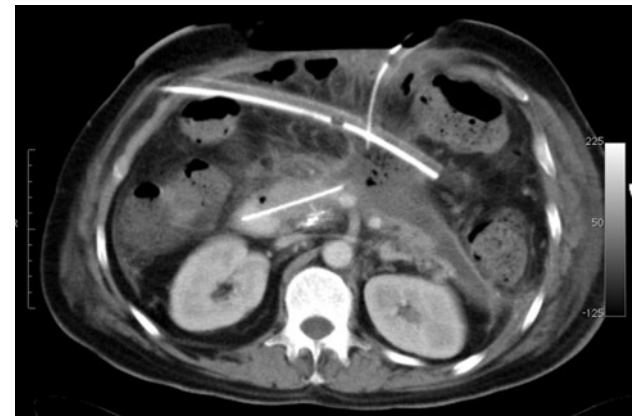

FIGURE 2. Computed tomography (CT) of a patient that underwent surgical necrosectomy with postoperative lavage (2 large bore transabdominal drains visible). An internal stent is visible with the proximal tip of the stent in the collection and the distal tip through the papilla.

Follow-up

Peripancreatic fluid collections can develop, persist, or even return after initial fistula resolution. Therefore, follow-up imaging (US, CT, or MRI) was used for the assessment of long-term outcome of fistula resolution. All available imaging 6 months, 1 year, and 2 years after initial fistula resolution were reviewed by a single experienced radiologist (T.L.B.) for the presence of persistent fluid collections (PFCs).

Literature Review

A MEDLINE search was performed for similar studies reporting the results of endoscopic stenting or conservative treatment for pancreatic fistulas in patients with acute pancreatitis. Search terms were "pancreatic fistula" OR "duct disruption." Cross references were searched in the studies found. Only studies published in the English language were included. Studies reporting the results of surgery for pancreatic fistulas were excluded. All studies reporting the result of transgastric or transduodenal endoscopic treatment for pancreatic pseudocysts or pancreatic fluid collections instead of endoscopic transpapillary treatment for pancreatic fistulas were also excluded.

Statistics

Descriptive statistics were performed and data are presented as numbers with subsequent percentages. Non-normally distributed data are presented as median with interquartile range (IQR).

Univariate logistic regression analysis was performed to assess potential association of each of the variables with the use of ETS or conservative treatment. $P < 0.05$ was considered statistically significant. Significant variables were explored using multivariate regression. For outcome, categorical variables were compared using Fisher's exact test and in case of continuous measures, differences were tested using Mann-Whitney U test. All statistical analyses were performed using SPSS for Windows version 15.0 (SPSS Chicago, Chicago, IL).

RESULTS

Acute Pancreatitis Cohort

Between March 2004 and March 2007, 731 patients with a first episode of acute pancreatitis were included. From 203 patients with severe pancreatitis, 129 patients (64%) suffered from organ failure and 98 patients (48%) developed infected necrosis. In 115 patients (57%), either percutaneous drainage, necrosectomy, or both was performed because of (suspected) infected necrotizing pancreatitis. In 64 patients (56%), percutaneous drainage was performed, 43 of these patients underwent subsequent necrosectomy and 51 patients underwent a primary necrosectomy (without previous drainage).

Pancreatic Fistula Cohort

From these 115 patients, 35 patients (30%) with a pancreatic fistula after radiologic and/or surgical intervention for necrotizing pancreatitis were identified. Nineteen patients were treated with ETS and 16 patients were treated conservatively (see Table 1 for baseline characteristics). An overview of all patients with ETS and conservative treatment are given in Tables 2 and 3. Univariate logistic regression analysis was performed to assess potential association of each of the variables with ETS or conservative treatment. The patients in the conservative group were older with a median age 61 years compared with 46 years in the ETS group ($P = 0.028$). One patient had a pancreatico-abdominal fistula; the remaining 34 patients had a pancreatico-cutaneous fistula. A PD injury or disruption was confirmed by contrast leakage during ERP in 18 of 19 patients treated with ETS (95%). Concomitant obstruction of the PD was observed in 10 of 19 patients (53%). The median fistula output was approximately 150 (IQR 200–300) mL/day for the ETS group and 250 (IQR 75–338) mL/day for the conservative group. These 19 patients were treated in 6 of 15 participating hospitals. Of 19 patients with a pancreatic fistula treated with ETS, 12 patients (63%) had recovered from (multi)organ failure. Three patients were admitted to the intensive care unit (ICU) due to multiorgan failure at the time of ETS. From 16 patients with conservative treatment, 9 patients (56%) suffered from (multi)organ failure at any moment during admission.

In 24 patients, ETS for a pancreatic fistula was attempted and succeeded in 19 patients (79%). The median duration of conservative treatment before ETS was 34 days (IQR 18–92). The remaining 5 patients, in whom ETS was not possible, were treated conservatively. ETS failed in these patients because cannulation of the PD was not possible due to papillary oedema (n = 4) and due to a complete stop of the PD (n = 1). In 13 patients (68%), a PD stent could be placed during the initial procedure (Table 4). In 4 patients (21%), a second procedure was required and 2 patients (11%) required 3 procedures. Bridging of the PD disruption was achieved in only 4 of 19 patients (21%). In the remaining 15 patients, 6 patients received an internal stent and 9 patients a short transpapillary stent.

TABLE 1. Characteristics of Patients with ETS and Conservative Treatment for a Pancreatic Fistula After Intervention for Infected Necrotizing Pancreatitis

Patient Characteristics	ETS (N = 19)	Conservative (N = 16)	*P**
Male gender	11 (37)	8 (50)	0.435
Age (yr)	46 (32–61)	61 (52–70)	0.028
CT severity index	7 (4–9)	8 (6–10)	0.182
Persistent organ failure during admission†	15 (79)	9 (56)	0.156
Pancreatic parenchymal necrosis	14 (74)	15 (94)	0.147
Peripancreatic necrosis/collections only‡	5 (26)	1 (6)	0.147
Infected necrosis	13 (68)	12 (75)	0.668
Time from onset of symptoms to intervention for infected necrosis (d)	26 (11–67)	22 (12–35)	0.227
Type of initial intervention			0.067
Surgical necrosectomy	11 (58)	14 (88)	
Percutaneous catheter drainage	8 (42)	2 (13)	
Octreotide therapy	5 (26)	5 (33)	0.656
Sphincterotomy	8 (42)	5 (31)	0.509
Time from intervention to ERP (d)	34 (18–92)	–	
Type of fistula			1.000
Pancreatico-cutaneous	15 (94)	16 (100)	
Pancreatico-abdominal	1 (6)	0 (0)	
Location of PD disruption			0.178
Head	2 (11)	4 (25)	
Body	7 (37)	4 (25)	
Tail	9 (47)	1 (6)	
Normal pancreatic duct	1 (5)	0 (0)	
Not identified	0 (0)	7 (44)	
Pancreatic duct obstruction	10 (53)	–	
Fistula output (mL/d)	150 (200–300)	250 (75–338)	0.350

*Univariate logistic regression analysis was used to test for differences between groups.
†Organ failure more than 48 hours.
‡No pancreatic parenchymal necrosis.
Data are n (%) or median (interquartile range).

Complications

Complications occurred in 6 patients after stent placement. Migration of the stent occurred in 4 of 19 patients (21%) and clogging in 2 of 19 patients (11%). In 3 of 4 patients with a migrated stent, a new stent was placed. In the fourth patient, the fistula had resolved at the time the stent migration was discovered. The clogged stents were both exchanged during subsequent ERPs. In 1 patient in whom ETS was attempted but failed, a clinical deterioration was observed with an increase in abdominal pain during 1 day and a transient rise in inflammatory markers.

Outcome

Fistula closure (ie, complete resolution of the fistula without need for other interventions) was achieved in 16 of 19 patients (84%) in the ETS group and in 8 of 12 patients (75%) in the conservative group ($P = 0.175$). In the ETS group, 1 patient required a pancreaticojejunostomy for fistula closure 118 days after ETS. Two patients died before fistula closure, 18 and 22 days after stent placement. These were 2 patients suffering from severe multiorgan failure that started before any intervention and persisted throughout the disease course. In the conservatively treated patients, 4 patients (25%) underwent an additional intervention to achieve fistula closure. Pancreaticojejunostomy was performed in 3 patients and 1 patient underwent endoscopic transgastric drainage of the collection. The median time to fistula closure after ETS was 71 days (IQR 34–142) compared with 120 days (IQR 51–175 days) in the conservative group ($P = 0.130$). The association between age, ETS, or conservative treatment and time to fistula resolution was explored using multivariate linear regression. Adjusting for the effect of age did not change outcome of fistula closure or time to fistula resolution.

TABLE 2. Overview of Patients with Necrotizing Pancreatitis Undergoing Endoscopic Transpapillary Treatment for Pancreatic Fistulas

Patient No.	Age	Gender	CTSI	Type of Intervention	Before ETS: Organ Failure	At time of ETS: Organ Failure	At time of ETS: ICU Admission	CRP	Time to ETS (d)	Type of Stent	Time to Fistula Closure (d)	Successful Fistula Closure	Complication
1	27	F	8	PCD	Circ/Resp/Renal	No	No	52	17	Internal	95	Yes	None
2	51	M	4	SN	None	No	No	–	228	Transpapillary	36	Yes + ETD	None
3	68	M	6	SN	Circ/Resp	No	No	92	30	Internal	36	Yes	Migration
4	44	F	4	PCD	Circ/Resp	Yes	Yes	251	34	Transpapillary	–	Deceased	None
5	45	M	10	SN	Circ/Resp/Renal	Yes	Yes	230	39	Internal	365	Yes	None
6	46	M	10	SN	Circ/Resp	No	No	76	19	Transpapillary	38	Yes	None
7	61	M	6	PCD	Circ/Resp/Renal	Yes	Yes	139	1	Internal	–	Deceased	None
8	74	F	4	PCD	Circ/Resp	No	No	97	28	Transpapillary	91	Yes	None
9	16	F	10	PCD	Circ/Resp	No	No	145	34	Bridging	179	Yes	Migration
10	58	M	10	SN	Circ/Resp/Renal	No	No	104	4	Bridging	151	Yes	occlusion
11	28	M	4	SN	None	No	No	74	12	Internal	186	Yes	occlusion
12	31	F	6	SN	Circ/Resp/Renal	No	No	375	40	Transpapillary	28	Yes	None
13	42	F	4	PCD	None	No	No	17	80	Bridging	7	Yes	None
14	48	M	8	SN	Resp	No	No	82	18	Internal	32	Yes	None
15	50	M	8	SN	Resp	No	No	28	92	Transpapillary	71	Yes	None
16	69	M	8	SN	Circ/Resp/Renal	No	No	7	123	Transpapillary	63	Yes	None
17	32	M	8	SN	Circ/Resp/Renal	No	No	42	151	Transpapillary	104	Yes	Migration
18	45	F	6	PCD	Resp/Renal	No	No	53	97	Transpapillary	133	No + PR	Migration
19	75	M	6	PCD	None	No	No	103	26	Bridging	31	Yes	None

CTSI, CT severity index; ETD, endoscopic transgastric drainage; F, female; M, male; PCD, percutaneous drainage; PD, pancreatic duct; PR, pancreatic resection; SN, surgical necrosectomy.

TABLE 3. Overview of Patients with Necrotizing Pancreatitis Undergoing Conservative Treatment for a Pancreatic Fistula

Patient No.	Age	Gender	CTSI	Type of Intervention	Organ Failure	ICU Admission	ETS Attempted	Time to Fistula Closure (d)	Successful Fistula Closure	Complication
1	47	F	8	SN	None	No	Yes	349	No + PR	None
2	61	F	6	SN	Circ/Resp	Yes	Yes	128	No + PR	Deterioration*
3	70	F	6	SN	None	No	Yes	47	No + ETD	None
4	51	F	8	SN	Circ/Resp	Yes	Yes	43	Yes	None
5	39	M	10	SN	None	No	Yes	50	No + PR	None
6	70	M	10	SN	Resp	Yes	No	131	Yes	None
7	52	F	8	SN	Circ/Resp	Yes	No	49	Yes	None
8	53	F	10	SN	Circ/Resp	Yes	No	140	Yes	None
9	61	M	8	SN	Circ/Resp/Renal	Yes	No	212	Yes	None
10	72	M	8	SN	Circ/Resp	Yes	No	170	Yes	None
11	63	M	6	SN	None	No	No	90	Yes	None
12	61	M	8	SN	Resp	Yes	No	92	Yes	None
13	54	M	4	PCD	None	No	No	53	Yes	None
14	53	M	5	SN	None	No	No	177	Yes	None
15	81	F	10	SN	Circ/Resp	Yes	No	182	Yes	None
16	75	F	10	PCD	None	No	No	112	Yes	None

*Clinical deterioration (raise of inflammatory parameters) after unsuccessful stent placement.
CTSI, CT severity index; ETD, endoscopic transgastric drainage; F, female; M, male; PCD, percutaneous drainage; PR, pancreatic resection; SN, surgical necrosectomy.

In the ETS group, the time to fistula closure was not associated with the number of days between intervention for necrotizing pancreatitis and ETS. Neither was it associated with the position of the endoprothesis (transpapillary, bridging, or internal) or the presence of a PD stenosis (data not shown).

Follow-up

The presence of PFCs was investigated in all surviving patients that underwent imaging (US, CT, or MRI) during follow-up. Six months after initial fistula resolution, PFCs were seen at imaging in 6 of 15 patients (40%) after ETS and in 8 of 13 patients (62%) after conservative treatment ($P = 0.449$). After 1 year, 1 patient in the ETS group had died due to metastatic disease. One year and 2 years after fistula resolution, PFCs were noticed in 3 of 14 patients (21%) after ETS and in 7 of 13 patients (54%) after conservative treatment ($P = 0.120$).

Literature Review

After reviewing 58 potential relevant manuscripts, 10 articles with a total of 281 patients (including the present series) with stent placement for pancreatic fistulas were selected.[12–15,17,21–24] An overview is given in Table 5. Only the results for patients with acute pancreatitis are given (as far as these results could be deducted from the articles). Twenty-five complications were reported in the studies,

TABLE 4. Characteristics of Endoscopic Stent Placement (ETS) for Pancreatic Fistulas in Patients with Necrotizing Pancreatitis

ETS Characteristics	N = 19
Number of ETS attempts for stent placement (median)	1 (1–3)
Stent position	
Bridging	4 (21)
Transpapillary	9 (47)
Internal	6 (32)
Diameter stent (Fr)	7 (5–10)
Length stent (cm)	7 (3–15)

Data are n (%) or median (range).

although the pancreatitis severity of most patients was not described in detail. Time to fistula closure ranged from a median of 2 days to 4 months between studies and within the individual studies a wide range of time to closure was observed (similar to our findings). A direct comparison of results between studies is unfortunately seriously hampered due to lack of homogeneity. The study by Boerma and colleagues is most similar to this study. This study, like our study, included only patients with necrotizing pancreatitis and a pancreatic fistula after necrosectomy. In this study, however, only patients with a pancreatic obstruction underwent endoscopic stenting. The overall reported rate of fistula closure after stent placement in the studies retrieved varied between 58% and 100%.

In addition, the literature was searched for studies reporting the result of conservative treatment for pancreatic fistulas in patients with necrotizing pancreatitis. After an extensive MEDLINE and cross-reference search, only a single study was identified.[10] Sikora and colleagues reported on 156 patients with acute severe pancreatitis that underwent percutaneous drainage or surgical intervention. Out of the 81 surviving patients, 43 developed a pancreatic fistula (53%) and were managed conservatively. In 38 patients (88%), fistula closure was achieved after a median of 70 days (28–424 days). However, from these 38 patients with spontaneous closure, 3 patients underwent cystogastrostomy (n = 3) or cystojejunostomy (n = 4) at a later stage for treatment of pseudocysts.

DISCUSSION

This is the largest series on ETS and conservative treatment for pancreatic fistulas after surgical or radiological intervention in patients with necrotizing pancreatitis. Although ETS was performed selectively and not in a prospective manner, our results suggest that ETS is feasible, relatively safe and might form an alternative for conservative treatment in critically ill patients.

Previous studies have described the results of ETS for pancreatic fistulas, as is presented in the literature review. Most studies report a high rate of successful fistula closure after endoscopic stenting. The

TABLE 5. Systematic Literature Review on Endoscopic Treatment of Pancreatic Fistulas

Study	Year	Total No. of Patients	No. of Patients with Endoscopic Treatment*	No. of Patients with Acute Necrotizing Pancreatitis	Position of PD Stent†	Successful Fistula Closure after Stent Placement*	Duration Until Fistula Closure after Stent Placement‡ (d)	Number and Type of Stent-related Complications
Kozarek	1997	9	9 (100)	2 (22)	TP, B	8 (89)	2 (2–7)	1 stent occlusion; 1 infected pseudocyst
Howard	1998	38	7 (18)	10 (26)	TP	7 (100)	NS	NS
Boerma	2000	16	13 (81)	16 (100)	TP, B	13 (100)	10 (2–64)	1 stent occlusion
Costamagna	2001	16	11 (69)	8 (50)	IN, B	10 (91)	9 (2–33)§	NS
Telford	2002	43	43 (100)	NS	TP, IN, B	25 (58)	NS	4 patients with clinical deterioration
Halttunen	2005	50	43 (86)	9 (18)	TP	36 (84)	122 (16–984)	1 patient with fever; 1 patient with mild post-ERCP pancreatitis
Varadarajulu	2005	97	92 (95)	44 (46)	TP, IN, B	52 (55)	NS	1 patient died with multiorgan failure 1 week after ETS; 3 stent occlusions; 2 patients with pus from stent
Brennan	2006	30	30 (100)	7 (23)	TP	21 (70)	NS	1 stent occlusion
Cicek	2006	26	14 (54)	NS	TP, IN, B	12 (86)	7§#	2 stent migrations
Bakker	2009	35	19 (54)	35 (100)	TP, IN, B	16 (84)	71 (34–142)¶	2 stent occlusions; 4 stent migrations; 1 (mild) clinical deterioration
Total		**360**	**281 (81)**	**131 (45)**		**200 (71)**	**2–122 (2–984)**	**26 reported complications in 281 patients (9%)**

*N (percentage).
†TP, transpapillary stent; IN, internal stent; B, bridging stent.
‡Data are median (range).
§Data are mean (range).
¶Median (interquartile range).
#Patients were referred to surgery if drain production did not decrease significantly within 10 days after stent insertion.
NS, not specified.

results, however, are difficult to compare. The studies differ in several aspects. First of all, most studies also included patients with pancreatic fistulas after surgery for pancreatic cancer or chronic pancreatitis. Second, the definition of a pancreatic fistula varied between studies. Third, the timing and indication for endoscopic treatment differed or were not reported. Fourth, the patient characteristics of patients with acute pancreatitis (eg, presence of necrosis or organ failure) are not given. Finally, the position of the stent (transpapillary, internal, or bridging) was not reported in most studies.

Kozarek et al reported in 1997 that transpapillary stenting can effectively close pancreatic fistulas within a week.[12] In 9 retrospectively identified patients with ductal injury after surgery for chronic and acute pancreatitis, 8 fistulas were closed within a week. One stent occlusion and 1 stent migration were described. These promising results unfortunately have not been reproduced by other case series. Howard et al described 7 patients with different types of pancreatic fistulas and treatment with transpapillary stenting.[14] ETS was successful in all patients, although patients with complete ductal disruption were not deemed amenable for ETS and only patients with partial ductal disruption were included. No complications of ETS were reported. Telford et al described results in 43 patients identified with pancreatic ductal disruption of different etiology.[15] Four patients experienced a clinical deterioration after stent placement, although stent occlusion was not documented. The study by Boerma et al is the only study, next to the present series, that solely included patients with necrotizing pancreatitis that had undergone surgical necrosectomy.[13] After ETS, after a median of 10 days, fistula production stopped in all 13 patients. All patients, however, that were treated with endoscopic stenting had a ductal obstruction and all stents were placed through the obstruction. This might have shortened overall time to fistula closure compared with the present series. In the present study, fistula closure was achieved in approximately 80% of patients. The median time to fistula closure, however, was more than 2 months after stent placement. Our results differ from some of the results reported. The observed difference may be explained by the fact that we only included patients that underwent intervention for suspected infected necrosis. In these patients, the ductal anatomy of the pancreas was severely disrupted as is reflected by the high rate of ductal obstruction, ductal disconnection, and the median CT severity index (CTSI). CTSI was 8 or higher in 50% of patients. A CTSI of 8 correlates with at least 30% lack of enhancement of pancreatic parenchyma (along with the presence of 2 or more peripancreatic collections).[25] As a result of the disrupted anatomy, in only 4 patients a bridging stent could be positioned. The transpapillary or internal stent placed in the remaining 15 patients lowers the pancreatic intraductal pressure, but probably does not entirely reduce flow of pancreatic juices into the pancreatic fluid collections. As a consequence, complete closure of the fistula will still take considerable time. A bridging stent has been correlated with a more favorable outcome.[15] In this study, outcome for patients with a bridging stent was similar to results after transpapillary or an internal stent, although patient numbers in this study probably are too small to formally compare the outcome for the different stent positions.

Despite many challenging factors most often encountered in critically ill patients with necrotizing pancreatitis, no complications such as bleeding or perforation directly related to ETS were noted in this study. Several other complications did occur, such as occlusion and migration of stents. Notably, these events did not result in clinical deterioration.

In this study, we used the adapted definition for pancreatic fistula as proposed by the International Study Group on Pancreatic Fistula (ISGPF) that was designed for pancreatic resections.[2] Fistulas after pancreatic resections represent failure of a healing or sealing of a pancreatic-enteric anastomosis. We defined a pancreatic fistula after intervention for necrotizing pancreatitis as output via a percutaneous drain (or drainage canal after removal of drains or from a surgical wound) of any measurable volume of fluid with an amylase content greater than 3 times the serum amylase activity. We feel this definition is more appropriate for patients with necrotizing pancreatitis.

From the number of patients with a pancreatic fistula in the study cohort, the incidence of pancreatic fistulas after intervention for necrotizing pancreatitis cannot accurately be deducted. The physicians decided to perform ETS at their own discretion and the conservatively treated patients were identified from the ERP reports, imaging reports and case record forms. It is possible that some patients with a pancreatic fistula may have gone unnoticed.

This study has several shortcomings. It was a retrospective analysis and ETS was not performed according to a standardized protocol. Conservative treatment before ETS differed among centers. For example, 4 patients received octreotide and 8 patients underwent a biliary sphincterotomy during early ERCP when signs of an impacted stone or significant cholestasis were present. It is unlikely that these differences in conservative treatment strategies may have influenced outcome of ETS because in most patients conservative treatment was attempted for more than 3 weeks. More importantly, selection of patients for ETS and conservative treatment very likely influenced the time to fistula resolution. It is possible that some of the patients undergoing ETS would have had spontaneous closure of their fistula in the same time period with conservative treatment. On the other hand, it is also very much possible that some conservative treated patients would have had earlier resolution if they were treated with ETS. The overall median time to fistula closure did not differ significantly between groups. If ETS really shortens time to fistula closure can only be answered in a comparative, preferably randomized, design. Such a study is needed, but unfortunately difficult to perform.

In conclusion, this study suggests that endoscopic transpapillary treatment in patients with pancreatic fistulas after intervention for infected necrotizing pancreatitis is a feasible and a safe alternative to conservative treatment.

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