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Evolution of Transluminal Necrosectomy for Acute Pancreatitis to Stent in Stent Therapy: Step-Up Approach Leads to Low Mortality and Morbidity Rates in 302 Consecutive Cases of Acute Pancreatitis

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Abstract

Background: The step-up approach, using either flexible endoscopy or a minimal invasive retroperitoneal access, has reduced mortality and morbidity in patients with acute pancreatitis. The use of fully covered self-expanding metal stents (FCSEMS) or lumen apposing metal stents (LAMS) facilitates endoscopic necrosectomy and drainage of walled-off necrosis (WON). The aim of our analysis was to investigate the 30/90/365-day mortality and morbidity rates of the subtypes of the revised Atlanta classification for acute pancreatitis.
Materials and Methods: We conducted a retrospective analysis of all patients ($n = 302$) treated with acute pancreatitis in our institution from January 2014 to July 2017. Mortality, morbidity, management of fluid collections, interventions, complications, and new onset of diabetes were recorded.
Results: In 30.8% ($n = 93/302$) of patients, pancreatic fluid collection developed. Out of these, 58.1% (54/93) required intervention, consisting of endoscopic treatment in 63% (34/54) or multidisciplinary approach in 37% (20/54). Overall, 90-day mortality rate according to Kaplan–Meier Estimator was 3.7%. Overall, 1-year mortality rate was 6.2%. One-year mortality for uncomplicated acute pancreatic fluid collection, pseudocyst, and WON were 5.4%, 2.6%, and 13.5%, respectively. Hemorrhage in case of metal stent treatment (FCSEMS/LAMS) occurred in 14.3%. If LAMS was combined with double pigtail stent-in-stent, bleeding was seen in 5.3%. No transperitoneal necrosectomy was needed.
Conclusions: Treating acute pancreatitis with a step-up approach, including stent-in-stent procedures, leads to low mortality rates and few stent-associated bleeding complications and minimizes necessity for open transperitoneal surgical necrosectomy.

Keywords: acute pancreatitis, step-up approach, stent-in-stent procedure, low mortality and morbidity, LAMS

Introduction

The heterogeneity of the clinical appearance of acute pancreatitis is overwhelming. On the one hand, there are simple enzyme elevations of serum lipase or amylase without any long-lasting clinical findings, whereas on the other hand, critically ill patients with multiorgan dysfunction are seen. Historically, mortality rates have been reported from 3% of patients with interstitial edematous pancreatitis to 39% in patients who developed pancreatic necrosis.[1,2]

For many years, treatment options were confined to complete abstinence from food and to emergency operations in case of life-threatening intra-abdominal bleeding, intestinal perforation, or organ failure. In case of necrotizing pancreatitis, open surgical necrosectomy was performed at the earliest 12 weeks from onset, comprising multiple procedures with extraordinarily high morbidity and mortality rates.[3] All these led to long hospital stays and poor outcome.

Management of acute pancreatitis has changed significantly over the last decades. In case of mild pancreatitis

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without development of necrosis, early oral feeding does not seem to have any negative effects on the self-limitation of the inflammatory process.[4] The step-up approach, using either flexible endoscopy or a minimal invasive retroperitoneal access, has reduced mortality and morbidity in patients with acute necrotizing pancreatitis.[5–7] For the endoscopic approach, the use of fully covered self-expanding metal stents (FCSEMSs) facilitates necrosectomy and drainage of walled-off necrosis (WON). However, there are reports of higher bleeding rates using fully covered metal stents.[8]

The aim of our analysis was to determine how many of our patients required interventions and the 30/90/365-day mortality and morbidity rates of the subtypes of the 2013 revised Atlanta classification for acute pancreatitis. We specifically wished to find out if stent-related complications as bleeding, migration, and buried stent syndrome might be lowered by performing our evolutionary and meanwhile preferred stent-in-stent method.

Materials and Methods

After the approval of the local Ethics Committee (Ethikkommission der Barmherzigen Schwestern und Barmherzigen Brüder, EKS 47/17, verdict: December 11, 2017), we conducted a retrospective data analysis of all patients ($n = 302$) admitted to our center for acute pancreatitis from January 2014 to July 2017. Overall mortality (30, 90, and 365 days) as well as morbidity, interventions, complications, and new onset of diabetes were recorded.

Statistics

The statistical analyses were carried out with Microsoft Excel 2016 using pivot tables and basic statistics functions as well as R statistical programming language, version 3.3.2, using base functions and survfit from library survival. For mortality analysis, we used the Kaplan–Meier Estimator. It considers the reduction of the sample over time caused by mortality as well as by leaving the study for other reasons. Latter persons are treated as right-censored observations. Therefore, the Kaplan–Meier probabilities on mortality may be slightly different from the conditional proportions. The confidence band of the Kaplan–Meier estimator is based on the so-called Greenwood formula.[9]

General patient management

Every patient admitted to our center for pancreatitis underwent at least ultrasound of the abdomen and blood tests as well as clinical examination. In the case of mild and self-limiting pancreatitis without fluid collection, clinical examination, blood tests, and sonography were revaluated within 6 weeks. In cases where fluid collections were detected by ultrasound, we routinely performed computed tomography (CT) scans to evaluate the development of necrosis. Our step-up approach to patients with fluid collection is displayed in Figure 1.

Medical management

Initially, intravenous fluid hydration was administered, and patients were kept on clear liquids and no solid foods. Pain medication was provided, and if nausea and pain improved, enteral nutrition on a low-fat base was started as soon as possible. In cases of severe acute pancreatitis defined by Acute Physiology and Chronic Health Evaluation (APACHE) II score exceeding a level of 9, patients were monitored and treated in our intensive care unit (ICU).

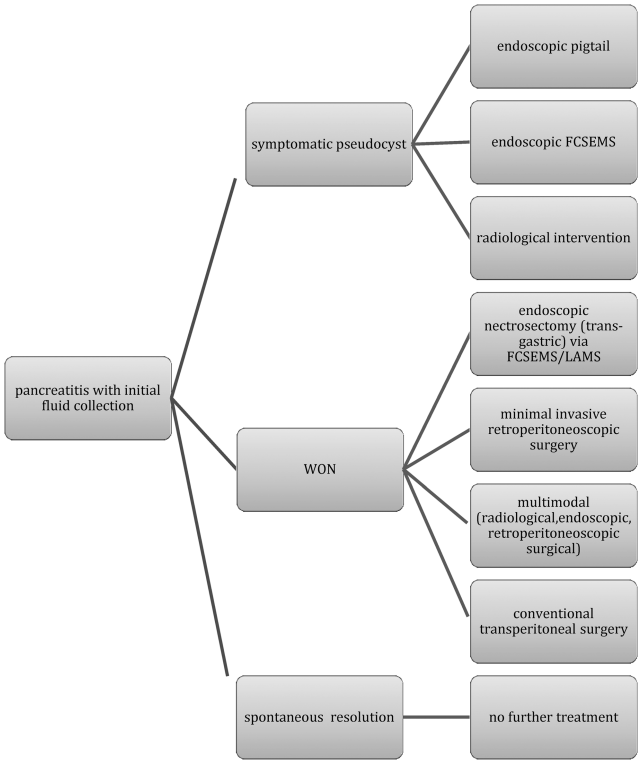

FIG. 1. Step-up approach algorithm.

Endoscopic management

Patients with biliary pancreatitis confirmed by abdominal ultrasound, endoscopic ultrasound (EUS), or magnetic resonance cholangiopancreatography (MRCP) underwent therapeutic endoscopic retrograde cholangiopancreatography (ERCP). If the pancreatic duct was cannulated during ERCP, a temporary pancreatic stent (5 French, 3 cm long; Cook Medical™, Bloomington, IN) was delivered. Biliary stones were removed after papillotomy using balloon catheter or Dormia basket. All EUS-guided procedures were performed by the same endoscopist (G.O.S.).

Drainage of symptomatic pancreatic pseudocysts was performed under EUS guidance using EUS needle, guide wire, needle knife, or cystotome to open up the gastric wall, balloon dilation, and advancement of two double pigtail plastic stents with 3 cm distance between pigtails (7 French or 10 French). If EUS found solid debris in the pseudocyst, FCSEMSs were applied instead of plastic stents. For necrosectomy, FCSEMSs (NAGI™-stent; Taewoong, Seoul, South Korea) or lumen-apposing metal stents (LAMSs) armed with ceramic head and embedded monopolar cutting wire (Hot AXIOS™; Boston Scientific) were used. FCSEMSs and LAMSs reduce pseudocysts and caverns of WON very quickly, if all debris and necrosis are removed. Due to concerns about bleeding, blocking of stents with debris or disconnected pancreatic cauda syndrome, a plastic double pigtail stent within the lumen of FCSEMS or LAMS was placed, as is standard practice in our institution, after one case of bleeding using only FCSEMS

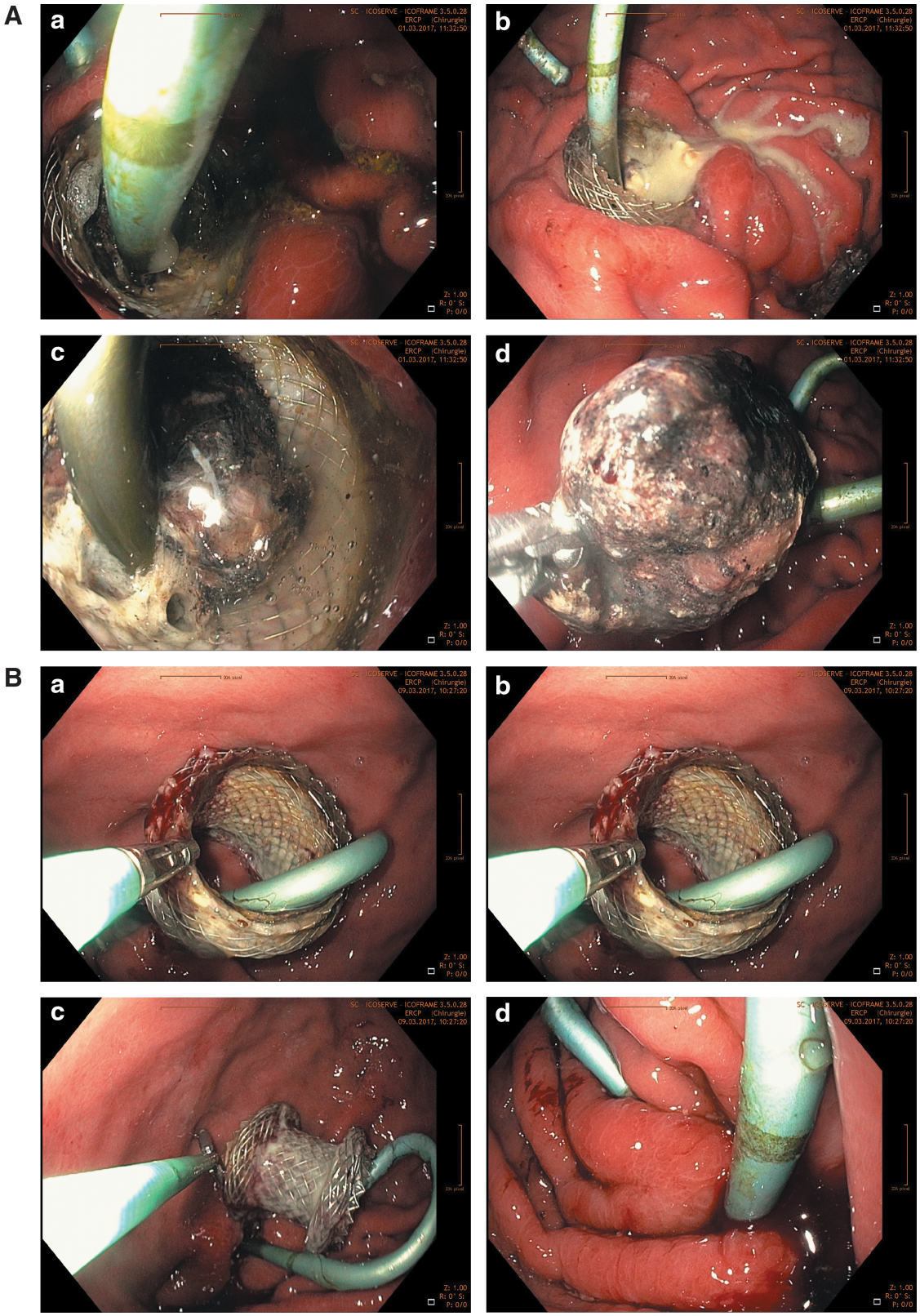

FIG. 2. Series I **(A)** (a–d) endoscopic necrosectomy via LAMS. Series II **(B)** (a–d) removal of the LAMS over the plastic stent. LAMS, lumen apposing metal stent.

Table 1. Demographic Findings and Disease Characteristics

	No fluid collection (n = 209)	*APFC (n = 37)*	*Pseudocysts (n = 38)*	*WON (n = 18)*	*Total (n = 302)*
Age	60.7 ± 19	57.7 ± 16	54.8 ± 15	59.3 ± 11	59.5 ± 18
Gender, %					
Male	54	51	84	89	59
Female	46	49	16	11	41
Duration of stay (days)	8.8 ± 9	15.7 ± 16	12.3 ± 10.5	46.1 ± 53.9	12.3 ± 18.5
ICU necessary, %	7	14	21	78	14
Cause, %					
Toxic	20.6	29.8	57.9	56.6	28.5
Biliary	54.1	45.9	18.4	16.7	46.4
Iatrogenic—ERCP	10.5	2.7	2.6	5.5	8.2
Iatrogenic—surgery	0.5	0	7.9	16.7	2.3
Fat metabolism disorder	0.95	2.7	2.6	0	1.3
Autoimmune	0.95	0	0	0	0.7
Unclear cause	12.4	18.9	10.6	5.5	12.6

APFC, acute pancreatic fluid collection; ERCP, endoscopic retrograde cholangio pancreatography; ICU, intensive care unit; WON, walled-off necrosis.

was observed. After removal of the last necrosis and in case of clean, granulating WON, the LAMS/FCSEMS was removed over the double pigtail. Median time of keeping metal stents *in situ* was 7 weeks, maximum 12 weeks. Endoscopic necrosectomy via LAMS and subsequent removal of the LAMS over the plastic stent is displayed in Figure 2, series I and II. The double pigtail usually remained for 12 months. If MRCP revealed no disruption of the pancreatic duct, plastic stents were removed after this period. When the pancreatic cauda was disconnected, we continued transgastric plastic stenting.

Surgical management

In case of endoscopically inaccessible necrosis, minimal invasive retroperitoneoscopic surgery using standard laparoscopic equipment was conducted. If CT scan showed hardly accessible WONs, especially within the pelvic region, a multidisciplinary approach, including additional radiologically guided percutaneous pig tail drainage, was followed.

Results

A total of 302 patients with acute pancreatitis were treated in our institution during the observation period. Demographic findings, ICU-treatment, cause, and complications of pancreatitis are shown in Tables 1 and 2.

Out of these 302 patients, 30.8% (93 patients) developed pancreatic fluid collection. Of these 41.9% (39/93) resolved spontaneously and 58.1% (54/93) required intervention (Fig. 3).

Endoscopic treatment was conducted in 36.6% (34/93) of patients: 22.6% (21/93) received endoscopic double pigtail drainage, 14% (13/93) were treated with endoscopically placed FCSEMSs (2.2%, 2/93), LAMSs (10.8%, 10/93) and 1 received more than one stent (1.1%, 1/93—3 × FCSEMSs and 1 LAMS). In the case of endoscopic necrosectomy performed via metal stents, the mean number of procedures required to reach clearance of necrosis was 3 (range 2–8 procedures).

On the contrary, 21.5% (20/93) underwent none or at least not exclusively endoscopic treatment as follows: 5.4% (5/93) received minimal invasive retroperitoneal surgical necrosectomy alone and 2.2% (2/93) received only radiological drainage. Furthermore, 14% (13/93) were treated multimodally: radiologically a/o endoscopically a/o surgically. Of this group of patients, 9.7% (9/93) needed radiologic and endoscopic intervention, 5.4% (5/93) also received a LAMS, 2.2% (2/93) received a FCSEMS, and one needed FCSEMS followed by LAMS. In addition, 2.2% (2/93) were treated radiologically and surgically, whereas 2.2% (2/93) received radiologic, endoscopic, and surgical treatment—one of them received a LAMS, and the other one received two LAMSs.

Mortality

Overall, 30-day mortality rate calculated by Kaplan–Meier Estimator was 2%, 90-day mortality rate was 3.7%, and 1-year mortality rate was 6.2%.

Table 2. Complications of Pancreatitis Within the Cohort

	No fluid collection (n = 209), %	*APFC (n = 37), %*	*Pseudocysts (n = 38), %*	*WON (n = 18), %*	*Total (n = 302), %*
Complications					
No	93.3	91.9	73.7	44.4	87.7
Bleeding	2.4	0	7.9	11.1	3.3
Organ failure	1	5.4	2.6	50	4.6
New onset diabetes mellitus	2.5	2.7	7.9	5.6	3.3
DPCS	0	0	5.3	11.1	1.3
Organ complication not due to intervention	1.4	2.7	2.6	5.6	2

APFC, acute pancreatic fluid collection; DPCS, disconnected pancreatic cauda syndrome; WON, walled off-necrosis.

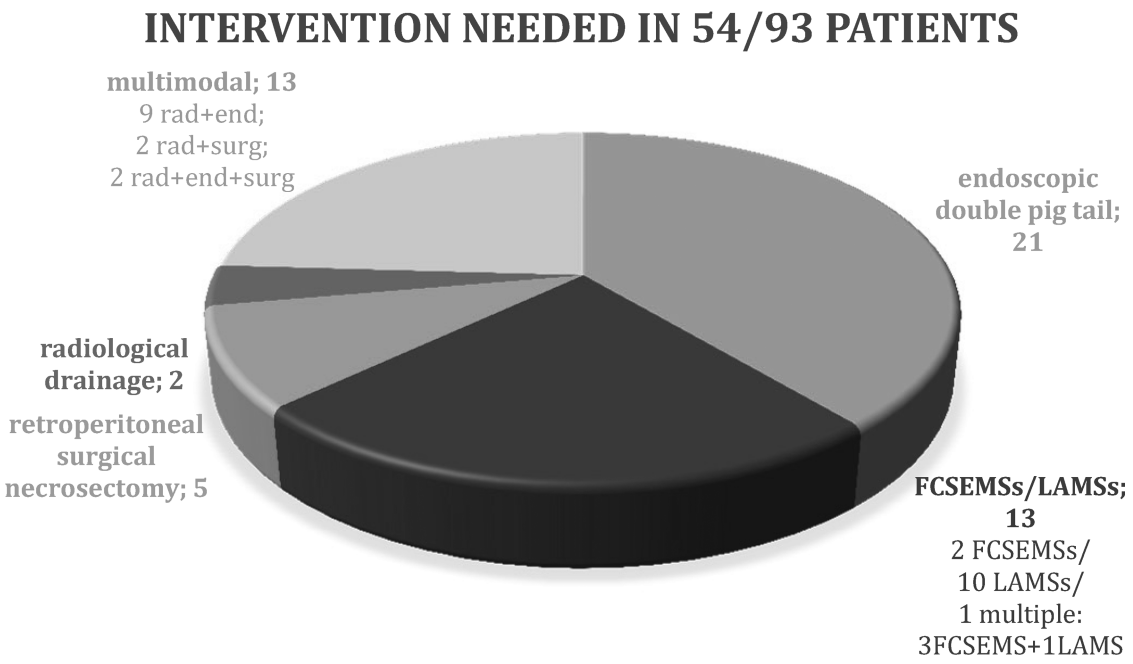

FIG. 3. In 54/93 patients with fluid collection intervention was needed due to pain or infection; in total FCSEMSs/LAMSs (13) consisting of FCSEMSs: 2, LAMSs: 10; multiple: 1 (3 FCSEMSs +1 LAMS); multimodal (13) consisting of 9 radiologic and endoscopic interventions (incl. 5 LAMSs +2 FCSEMSs +1 multiple [FCSEMS+LAMS]); 2 radiologic and surgical interventions; 2 radiologic, endoscopic and surgical treatments (incl. 1 LAMS and 1 multiple [2 LAMSs]). FCSEMS, fully covered self-expanding metal stent; LAMS, lumen apposing metal stent.

Mortality rates depending on characteristics of fluid collection found in our cohort are outlined in Table 3. We distinguished four categories, which are named as No Fluid Collection, acute pancreatic fluid collection, Pseudocysts, and WON.

Figure 4 and Table 3 display mortality rates as Kaplan–Meier probabilities (95% confidence interval).

In our cohort, 30-day mortality rate was 2% (6/302). The specific findings of each fatality are displayed in Table 4.

In five cases, death occurred during day 30 and 90 from admission to hospital. In total, we observed 11 fatalities during the first 90 days (11/302; 3.7%). Detailed findings are outlined in Table 5.

The third group represents fatalities occurring from day 90 to 365 from admission to hospital. None of these six patients died of complications related to pancreatitis. The main cause of death was progressive tumor disease followed by fatal cardiac events. The types of cancer observed were intrahepatic cholangiocarcinoma, T-cell Lymphoma, squamous cell carcinoma of the floor of mouth, and carcinoma of unknown primary. In total, a 1-year mortality rate of 6.2% (17/302) was observed in this study.

Bleeding complications

In this study, we specifically analyzed bleeding complications. In particular, hemorrhage related to endoscopic stentings was evaluated. Bleeding occurred in 10/302 (3.3%) patients and 10/54 (18.5%) were of interventional cases. Bleeding after endoscopic intervention was observed only after metal stent placement. Four cases of bleeding after metal stent treatment for pseudocysts or WON were seen. In total, 28 metal stents (9 FCSEMSs versus 19 LAMSs) were applied, which results in a bleeding rate of 14.3% (4/28) within the metal stent group. Hemorrhage according to type of metal stent was 33.3% (3/9) in the FCSEMS group

Table 3. Death Counts After 30, 90, and 365 Days with Kaplan–Meier Probabilities and 95% Confidence Intervals

	No fluid collection, n = *209*	*APFC,* n = *37*	*Pseudocysts,* n = *38*	*WON,* n = *18*	*Total,* n = *302*
30 Days, 95% CI	1.4% (*n* = 3), 0–3	2.7% (*n* = 1), 0–7.8	2.6% (*n* = 1), 0–7.6	6.2% (*n* = 1), 0–17.4	2% (*n* = 6), 0.4–3.6
90 Days, 95% CI	2.9% (*n* = 6), 0.6–5.2	5.4% (*n* = 2), 0–12.4	2.6% (*n* = 1), 0–7.6	13.5% (*n* = 2), 0–29.3	3.7% (*n* = 11), 1.5–5.9
365 Days, 95% CI	6.4% (*n* = 12), 2.8–9.8	5.4% (*n* = 2), 0–12.4	2.6% (*n* = 1), 0–7.6	13.5% (*n* = 2), 0–29.3	6.2% (*n* = 17), 3.3–9

95% CI, 95% confidence interval; APFC, acute pancreatic fluid collection; WON, walled-off necrosis.

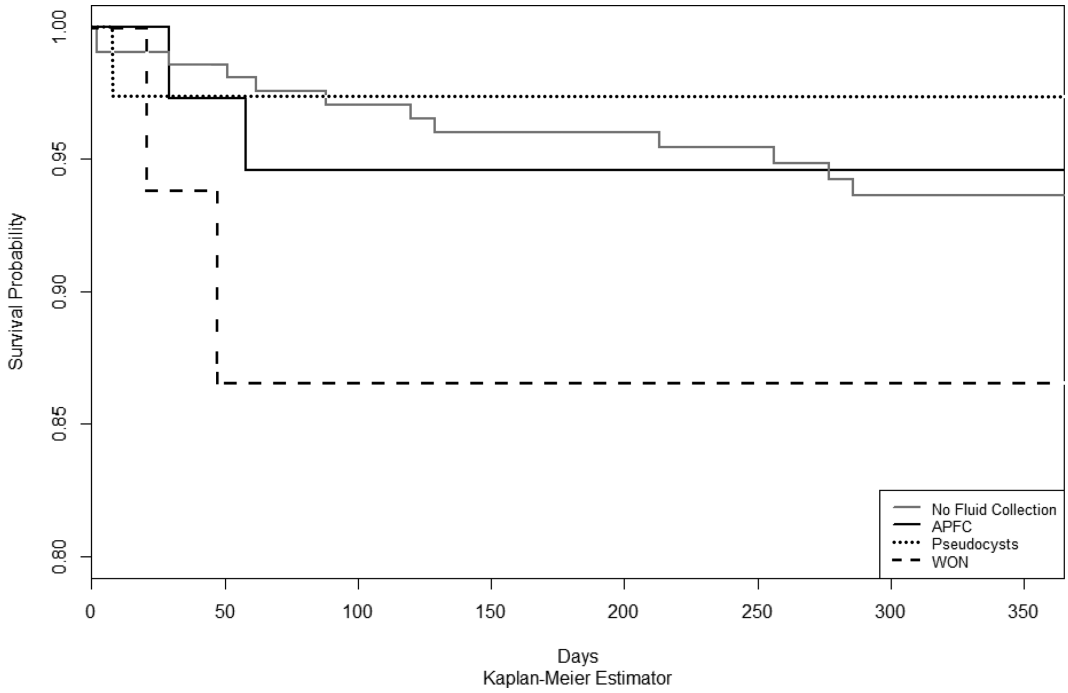

FIG. 4. Kaplan–Meier Estimator for classes of fluid collections.

versus 5.3% (1/19) in the LAMS group. APACHE II score in these patients ranged from 3 to 22. Three cases of hemorrhage occurred in the WON group, one in the pseudocyst group.

In detail, one postinterventional hemorrhage following metal stent application stopped spontaneously, and no banked human blood had to be administered. Another patient, suffering from arterial bleeding from the splenic artery, had to be operated on (splenectomy) as radiologic intervention was not available within a reasonable time slot. Intraoperatively, the bleeding site was found in the peripheral branches of the splenic artery, far away from stent placement. This patient required 2 U of banked human blood. The third patient was referred to our hospital with preexisting severe post-ERCP pancreatitis. Persisting necrotizing pancreatitis was treated with FCSEMS for necrosectomy and additional transluminal double pigtail stents to prevent direct erosion of blood vessels by the metal stent. Nevertheless, this patient suffered from severe life-threatening bleeding originating from branches of the

Table 4. 30-Day Mortality Findings

Age	*Sex*	*Cause of death*	*Days after admission*	*Intervention related*	*History*
94	F	Septic shock	2	Yes	Insufficient initial ERCP
65	M	Ischemic heart failure	21	No	Preexisting severe cardiovascular disease, died of acute myocardial ischemia when recovering from pancreatitis after successful necrosectomy via FCSEMS
81	F	Unknown	29	No	Died 3 weeks after dismission from hospital with the diagnosis serous pancreatitis; no biliary reason for pancreatitis nor was any in-hospital intervention performed
72	F	Cancer related	29	No	Underwent ERCP and received two plastic stents in case of terminal icterus due to metastatic disease in breast cancer; mild self-limiting pancreatitis; death due to progressing metastatic disease
81	M	Septic shock	2	No	Initially operated on because of acute ileus for small bowel adhesions meeting bacterial translocation and sepsis in case of acute pancreatitis
46	M	Ischemic heart failure	8	No	Spontaneous bacterial peritonitis; focus: acute pancreatitis due to chronic alcohol abuse; no intervention performed; autopsy findings: cirrhotic liver disease with peritonitis and acute pancreatitis leading to terminal left heart failure

FCSEMS, fully covered self-expanding metal stent.

Table 5. 90-Day Mortality Findings

Age	*Sex*	*Cause of death*	*Days after admission*	*Intervention related*	*History*
79	M	Thrombosis of the basilaris vein	88	No	In-patient for 5 days only; successful ERCP for biliary pancreatitis; dismission from hospital 83 days before death (readmission at neurologic ICU)
89	F	Pneumonia	58	No	Acute pancreatic fluid collection in case of biliary pancreatitis, spontaneously passing gall stone, no intervention was performed; died of pneumonia 44 days after dismission at retirement home
75	M	Septic multiorgan failure	47	No	Underwent multivisceral resection and additional intraoperative radiotherapy with 12 gray of a leiomyosarcoma of the retroperitoneum spreading to pancreatic tail, spleen, left kidney, adrenal gland, and colon; postoperatively: thrombosis of the vena porta and pancreatitis of the remaining pancreatic head including WON; successfully performed endoscopic transgastric necrosectomy via FCSEMS
82	F	Unknown	51	No	Died 51 days after conservatively treated self-limiting pancreatitis
64	F	Sepsis due to neutropenia in ALL	62	No	Progressive disease of ALL; death from tumor-related neutropenia and sepsis after chemotherapy without causal connection to previous mild medication-associated pancreatitis

ALL, acute lymphatic leukemia; FCSEMS, fully covered self-expanding metal stent; ICU, intensive care unit; WON, walled-off necrosis.

superior mesenteric artery and gastroduodenal artery 5 days after endoscopic necrosectomy. Hemorrhage could be managed by interventional radiology-guided coil embolization. The patient received 7 U of banked human blood in total. No further bleeding events occurred. Patient number four suffered from delayed postinterventional bleeding after LAMS placement without additional plastic stent. Hemorrhage was controlled by coil embolization. Two units of banked human blood were applied.

Buried stent syndrome

Buried stent syndrome occurred in 3.6% (1/28) of metal stents. This was the only case where LAMS 5.3% (1/19) was applied without additional double pigtail stent. Stent removal was easily performed under EUS guidance using a Soehendra Stent Retriever™ (Cook Medical) and grasper.

Stent dislocation

One event of stent dislocation, occurring in the FCSEMS group, when treating a pseudocyst was observed. There was no dislocation in the LAMS group.

Diabetes

New onset diabetes was found in 3.3% (10/302) of patients with acute pancreatitis. In the group of WON patients, the incidence rises to 5.6% (1/18).

Symptomatic disconnected pancreatic cauda syndrome

This very inconvenient syndrome occurred in 4/302 (1.3%) patients of our cohort (2 in the WON group [2/18; 11.1%], 2 in the pseudocyst-group [2/38; 5.3%]). In this situation, double pigtail plastic stents can be left *in situ* for a very long period of time. When a pseudocyst had reoccurred, as was seen in 3 out of 4 of these patients, therapy was simple, since direct access was available. In one case, permanent release of symptoms after directly cannulating the fistula originating from the remaining duct of the pancreatic cauda by guide-wire and plastic stent under EUS view was achieved.

Others

There was no need for even a single transperitoneal necrosectomy within the total group of 302 patients. One laparotomy was performed for acute bleeding from the splenic artery.

Discussion

Acute pancreatitis can have various origins. Most frequently it seems to result from choledocholithiasis or alcohol abuse.[10,11] Regardless of its origin, the disease can manifest in harmless reversible enzyme elevation, as well as in life threatening systemic inflammatory reactions leading to multiorgan failure and death.[12] Specifically, the development of infected necrosis seems to aggravate the clinical state of patients.[13] There is currently no appropriate means to prevent initially serous pancreatitis from manifesting into a necrotizing form.

In many cases, this conversion requires special observation of vital parameters and commonly leads to admission to ICUs, where patients are stabilized until WON is established. After this is achieved, necrosectomy can be performed to eliminate the infectious focus.

In times of conventional transperitoneal surgical necrosectomy, morbidity as well as mortality rates in acute pancreatitis were very high, 34%–95% and 11%–39%, respectively.[14]

In our cohort, we observed a very low mortality rate over 30, 90, and 365 days (Fig. 4 and Table 3).

One of the 2 patients we lost in our WON group suffered from end-stage liver cirrhosis and dilated cardiomyopathy

due to chronic alcohol abuse and therapy was reduced after multidisciplinary ethics conference. The other one suffered from complications after multivisceral resection and additional intraoperative radiotherapy with 12 gray of a recurrent leiomyosarcoma, and therapy was reduced due to infaust prognosis after multidisciplinary ethics conference.

Regarding the 30-day mortality group, we observed a very heterogenous population with a wide range of age. Shared characteristics seem to be the predominant number of comorbidities, whereas the severity of pancreatitis is not the first and foremost reason directly associated with death (Table 4). These findings might support the conclusion that 30-day mortality in acute pancreatitis in our days primarily depends on preexisting comorbidities.

Modern ICU patient management and a step-up approach in interventional treatment seem to transfer most of our patients into a cooled-down status. Only one of the patients had to undergo urgent initial minimal invasive retroperitoneal surgery, lacking enough time to wait for secure cystic wall conditions for endoscopic approach. As far as we know, this way of treatment seems to be equal to the endoscopic step-up approach in terms of mortality rates and major complications.[15] If ever possible, we preferred a primary endoscopic approach to avoid postoperatively persisting retroperitoneocutaneous drainages. Our observation of more mobile patients with shorter hospital stays was confirmed in a recently published multicenter randomized trial performed by van Brunschot et al.[15] This trial moreover showed a lower pancreatic fistula rate in the endoscopy group versus the video-assisted retroperitoneal surgery group.

According to our findings, death occurring beyond a period of 90 days does not seem to be related to pancreatitis. Our cohort did not display any fatalities directly caused by pancreatitis after more than 3 months.

New onset diabetes was rare in our collective (3.3% overall, 5.6% of the WON group) compared to literature.[16,17] However, this long-term complication may require a longer observation period than in this study. We discovered that 11.1% (2/18) of our WON patients suffered from preexisting diabetes. Hence, only 5.6% (1/18) developed new onset diabetes.

Disconnected pancreatic cauda syndrome is another complication commonly seen in cases with prolonged course of necrotizing pancreatitis. Usually, it remains clinically asymptomatic as long as gastrocystic stents are in place. Symptomatic disconnected pancreatic cauda syndrome occurs when gastrocystic stents are removed or lost, and the pancreatic duct is still interrupted. According to our experience, disconnected pancreatic cauda syndrome is best managed by keeping transgastric plastic stents *in situ*, until a rigid draining canal to the stomach has formed. We prefer this method of treatment to external drainages, as they have to stay *in situ* for a long time, which more often leads to persisting pancreatic fistulas.[15] In our series, we did not observe a case of disconnected pancreatic cauda syndrome requiring surgery due to endoscopic failure. Nevertheless, we would consider surgery as treatment option in case of persisting percutaneous fistula, which cannot be transformed to an internal fistula by EUS-guided drainage after more than 1 year.

Treating acute pancreatitis with a step-up approach leads to low mortality rates and less morbidity in comparison to conventional surgery.[2,3,5] Moreover, it helps to minimize the necessity for open transperitoneal surgical necrosectomy. New methods such as stent-in-stent techniques with double pigtail plastic stents within the lumen of self-expanding metal stents could help to reach low morbidity rates, especially concerning bleeding complications, as seen in this study. Patients undergoing outpatient necrosectomy under pure propofol sedation are seen more commonly when using a plastic stent within LAMS.

One must keep in mind that this is a retrospective analysis with all the inhering limitations. Moreover, the number of patients treated with FCSEMSs/LAMSs and additional double pigtail plastic stents is still too low to allow profound statistical analysis. However, there seems to be a benefit regarding stent-related bleeding complications when compared to the literature.[18] We believe that additional plastic stents (at least one per FCSEMS/LAMS) lead to permanent fluid drainage without the risk of stents easily getting clogged by debris, so that they act as a gate keeper for the FCSEMS/LAMS. Moreover, they could serve as smooth spacers to the retroperitoneal blood vessels and seem to prevent sharp ends of FCSEMS/LAMS from injuring arterial vascular walls. More frequent stent migration and higher bleeding rates in LAMSs as described in the literature[8,18] could probably be decreased by anchoring the stent with double pigtail plastic stents. Furthermore, early LAMS removal (immediately after completed necrosectomy) while leaving plastic stents *in situ* (procedure as shown in Fig. 2, series I and II) should allow residual fluids to be drained without apprehension about delayed LAMS-related bleeding complications or buried stent syndrome. To confirm these findings, especially regarding bleeding complications, further randomized controlled trials are required to examine the superiority of stent-in-stent treatment versus FCSEMSs/LAMSs alone.

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Disclosure Statement

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References

1. Singh VK, Bollen TL, Wu BU, Repas K, Maurer R, Yu S, et al. An assessment of the severity of interstitial pancreatitis. Clin Gastroenterol Hepatol 2011;9:1098–1103.
2. van Santvoort HC, Bakker OJ, Bollen TL, Besselink MG, Ahmed Ali U, Schrijver AM, et al. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. Gastroenterology 2011;141:1254–1263.
3. Aparna D, Kumar S, Kamalkumar S. Mortality and morbidity in necrotizing pancreatitis managed on principles of step-up approach: 7 Years experience from a single surgical unit. World J Gastrointest Surg 2017;9:200–208.
4. Vaughn VM, Shuster D, Rogers MAM, Mann J, Conte ML, Saint S, et al. Early versus delayed feeding in patients with acute pancreatitis: A systematic review. Ann Intern Med 2017;166:883–892.

5. van Santvoort HC, Besselink MG, Bakker OJ, Hofker HS, Boermeester MA, Dejong CH, et al. A step-up approach or open necrosectomy for necrotizing pancreatitis. N Engl J Med 2010;362:1491–1502.
6. Nabi Z, Basha J, Reddy DN. Endoscopic management of pancreatic fluid collections-revisited. World J Gastroenterol 2017;23:2660–2672.
7. Bakker OJ, van Santvoort HC, van Brunschot S, Geskus RB, Besselink MG, Bollen TL, et al. Endoscopic transgastric vs surgical necrosectomy for infected necrotizing pancreatitis: A randomized trial. JAMA 2012;307:1053–1061.
8. Bang JY, Hasan M, Navaneethan U, Hawes R, Varadarajulu S. Lumen-apposing metal stents (LAMS) for pancreatic fluid collection (PFC) drainage: May not be business as usual. Gut 2017;66:2054–2056.
9. Klein JP, Moeschberger ML. Survival Analysis—Techniques for Censored and Truncated Data. New York: Springer, 1997.
10. Roberts SE, Akbari A, Thorne K, Atkinson M, Evans PA. The incidence of acute pancreatitis: Impact of social deprivation, alcohol consumption, seasonal and demographic factors. Aliment Pharmacol Ther 2013;38:539–548.
11. Satoh K, Shimosegawa T, Masamune A, Hirota M, Kikuta K, Kihara Y, et al. Nationwide epidemiological survey of acute pancreatitis in Japan. Pancreas 2011;40:503–507.
12. Mofidi R, Duff MD, Wigmore SJ, Madhavan KK, Garden OJ, Parks RW. Association between early systemic inflammatory response, severity of multiorgan dysfunction and death in acute pancreatitis. Br J Surg 2006;93:738–744.
13. Werge M, Novovic S, Schmidt PN, Gluud LL. Infection increases mortality in necrotizing pancreatitis: A systematic review and meta-analysis. Pancreatology 2016;16:698–707.
14. Bugiantella W, Rondelli F, Boni M, Stella P, Polistena A, Sanguinetti A, et al. Necrotizing pancreatitis: A review of the interventions. Int J Surg 2016;28(Suppl 1):S163–S171.
15. van Brunschot S, van Grinsven J, van Santvoort HC, Bakker OJ, Besselink MG, Boermeester MA, et al. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: A multicentre randomised trial. Lancet 2018; 391:51–58.
16. Vipperla K, Papachristou GI, Slivka A, Whitcomb DC, Yadav D. Risk of new-onset diabetes is determined by severity of acute pancreatitis. Pancreas 2016;45:e14–e15.
17. Das SL, Singh PP, Phillips AR, Murphy R, Windsor JA, Petrov MS. Newly diagnosed diabetes mellitus after acute pancreatitis: A systematic review and meta-analysis. Gut 2014;63:818–831.
18. Law ST, De La SernaHiguera C, Simon PG, Perez-MirandaCastillo M. Comparison of clinical efficacies and safeties of lumen-apposing metal stent and conventional-type metal stent-assisted EUS-guided pancreatic wall-off necrosis drainage: A real-life experience in a tertiary hospital. Surg Endosc 2018;32:2448–2453.

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