Comparison of lumen-apposing metal stents versus double-pigtail plastic stents for infected necrotising pancreatitis

Original research

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ABSTRACT

Objective Lumen-apposing metal stents (LAMS) are believed to clinically improve endoscopic transluminal drainage of infected necrosis when compared with double-pigtail plastic stents. However, comparative data from prospective studies are very limited.

Design Patients with infected necrotising pancreatitis, who underwent an endoscopic step-up approach with LAMS within a multicentre prospective cohort study were compared with the data of 51 patients in the randomised TENSION trial who had been assigned to the endoscopic step-up approach with double-pigtail plastic stents. The clinical study protocol was otherwise identical for both groups. Primary end point was the need for endoscopic transluminal necrosectomy. Secondary end points included mortality, major complications, hospital stay and healthcare costs.

Results A total of 53 patients were treated with LAMS in 16 hospitals during 27 months. The need for endoscopic transluminal necrosectomy was 64% (n=34) and was not different from the previous trial using plastic stents (53%, n=27)), also after correction for baseline characteristics (OR 1.21 (95% CI 0.45 to 3.23)). Secondary end points did not differ between groups either, which also included bleeding requiring intervention—5 patients (9%) after LAMS placement vs 11 patients (22%) after placement of plastic stents (relative risk 0.44; 95% CI 0.16 to 1.17). Total healthcare costs were also comparable (mean difference −€6348, bias-corrected and accelerated 95% CI −€26 386 to €10 121).

Conclusion Our comparison of two patient groups from two multicentre prospective studies with a similar design suggests that LAMS do not reduce the need for endoscopic transluminal necrosectomy when compared with double-

WHAT IS ALREADY KNOWN ON THIS SUBJECT?

⇒ The endoscopic step-up approach is preferred over a surgical step-up approach in eligible patients with infected necrotising pancreatitis.
⇒ The choice of stents is not finally established, while it is believed that the larger lumen diameter of lumen-apposing metal stents (LAMS) facilitates improved drainage of pancreatic and peripancreatic necrosis and may be superior over the current standard, double-pigtail plastic stents.
⇒ The results of the only randomised trial did, however, indicate a higher complication rate, in particular severe bleeding, when LAMS were used.

WHAT ARE THE NEW FINDINGS?

⇒ In our comparative non-randomised study using data from two prospective trials, the need for endoscopic transluminal necrosectomy in patients with infected necrotising pancreatitis treated with LAMS was not lower compared with plastic stents.
⇒ Clinical outcomes, including total number of interventions, length of hospital stay and total healthcare costs, as well as complications (especially bleeding) did not differ either between groups.

HOW MIGHT IT IMPACT ON CLINICAL PRACTICE IN THE FORESEEABLE FUTURE?

⇒ Based on the results of this study, LAMS and plastic stents can both be used for endoscopic transluminal drainage of infected necrosis.

pigtail plastic stents in patients with infected necrotising pancreatitis. Also, the rate of bleeding complications was comparable.

INTRODUCTION

Necrotising pancreatitis is a potentially lethal disease, with a mortality rate up to 30%.[1–4] Minimally invasive step-up intervention is indicated in the majority of patients with infected pancreatic and peripancreatic necrosis.[5 6] The endoscopic step-up approach is favoured over a surgical step-up approach if technically possible, because it leads to shorter hospital stay and fewer pancreaticocutaneous fistulas.[7 8]

Several innovations were developed to improve the endoscopic step-up approach, including lumen-apposing metal stents (LAMS).[9 10] Theoretically, the wider lumen diameter of LAMS offers improved drainage, facilitates endoscopic transluminal necrosectomy and decreases the risk of stent occlusion. LAMS can also be placed via a single-step electrocautery-assisted device, providing an easier and faster drainage procedure when compared with double-pigtail plastic stents. Finally, endoscopic ultrasound (EUS)-guided transluminal drainage using LAMS does not require fluoroscopic guidance, while this is highly preferred when using plastic stents.

International guidelines are not consistent regarding the use of LAMS. While the European Society of Gastrointestinal Endoscopy guideline suggests that both LAMS and plastic stents can be considered, the Asian consensus guideline state that LAMS should not be used outside clinical trials.[5 11] In contrast, the American Gastroenterological Association guideline concludes that LAMS are preferred.[12] The actual benefit of LAMS is, however, uncertain and not yet proven. Additionally, the price of LAMS is substantially higher than plastic stents. To date, the only high level evidence comes from one single-centre randomised trial that found no difference in total number of procedures, length of hospital stay or overall treatment costs.[13] Moreover, an unusual low need for necrosectomy in patients treated with LAMS (13%) as well as with plastic stents (21%) was reported in this trial. In general, necrosectomy is required in at least 50% of patients, and therefore the potential benefit of LAMS could be underestimated.[7 8] Finally, the trial results raised important safety concerns, as LAMS were associated with higher stent-related complications if not removed within 3 weeks.[13 14]

Clear evidence regarding the routine use of LAMS in patients with infected necrotising pancreatitis is lacking. We performed a prospective multicentre study and compared its findings with a previous study with a similar design, to investigate whether the use of LAMS improves endoscopic transluminal drainage and reduces the need for endoscopic transluminal necrosectomy.

METHODS

Study design

The AXIOMA study was an investigator-initiated multicentre prospective cohort study. We prospectively included consecutive patients with infected pancreatic or peripancreatic necrosis (ie, infected necrosis) who could be drained endoscopically with LAMS in 16 hospitals collaborating with the Dutch Pancreatitis Study Group. We compared this cohort to the patients assigned the endoscopic step-up approach with plastic stents in the TENSION trial.[8] The TENSION trial was a multicentre randomised trial in which the endoscopic step-up approach was compared with the surgical step-up approach in patients with infected necrotising pancreatitis.[8] The study protocol of the AXIOMA study, including in- and exclusion criteria, was identical to the TENSION trial, except for the type of transluminal stent.[8]

An independent Data Safety Monitoring Board assessed patient recruitment and evaluated patient safety after consecutive enrolment of 15 patients. Complications were reported by treating clinicians to the coordinating investigator, who reported these events to the Dutch Central Committee for Research involving human subjects. An independent monitor performed clinical trial monitoring. The AXIOMA study was registered in the Netherlands Trial Registry (registry number NL6878). This investigator-initiated study was funded by an unrestricted grant of Boston Scientific Corporation and Amsterdam UMC, Academic Medical Center, Amsterdam, the Netherlands. Patients or the public were not involved in the design, conduct, reporting or dissemination plans of this study. However, the patient association for pancreatic diseases, the 'Alvleesklierevereniging', was actively involved in meetings of the Dutch Pancreatitis Study Group, including regarding the AXIOMA study and TENSION trial. The study is reported in accordance with the Strengthening the Reporting of Observational studies in Epidemiology guidelines.[15]

Study participants

Inclusion criteria were identical to the criteria used in the TENSION trial, in order to create a similar cohort: patients with necrotising pancreatitis, with a strong suspicion or documented evidence of infected necrosis and in whom endoscopic transluminal drainage was deemed indicated and feasible, were eligible for inclusion. Main exclusion criteria were previous invasive intervention for necrotising pancreatitis and chronic pancreatitis according to the M-ANNHEIM criteria (additional criteria provided in online supplemental appendix).[16] We defined infected necrosis as the presence of gas configurations within necrosis on contrast-enhanced CT or a positive culture obtained by fine-needle aspiration. Suspected infected necrosis was defined as clinical signs of persistent sepsis or progressive clinical deterioration despite maximal support on the intensive care unit without any other clear source of infection.

Study procedures

Patients with acute pancreatitis were followed from hospital admission by the study coordinator in the 16 participating centres. Broad-spectrum antibiotics were administered when infected necrosis was suspected or proven. The indication and timing for intervention and eligibility for study inclusion was subsequently evaluated by the nationwide online multidisciplinary expert panel of the Dutch Pancreatitis Study Group.[17] If clinically possible, the intervention was postponed until the stage of walled-off necrosis, when collections were largely or fully encapsulated. After patients provided informed consent, EUS-guided transluminal drainage was performed, similarly to the approach in the TENSION trial, except for the placement of LAMS instead of plastic stents. The LAMS used in this study (Hot AXIOS stent and electrocautery-enhanced delivery system, Boston Scientific) were 15 or 20 mm in diameter and 10 mm in length (online supplemental figure S1). The 20 mm LAMS was preferred when available in the treating hospital. A 7 Fr nasocystic catheter was placed through the LAMS and flushed with 1 L saline/24 hours to keep the fistulous tract open in line with the practice in the TENSION trial. The nasocystic catheter was preferably left in place for irrigation during 1 week. It was allowed to remove the catheter earlier if patients did not tolerate the nasocystic catheter or when the catheter was obstructed. Details

of the study protocol for the plastic stents-group are described in the online supplemental appendix.[8]

If drainage did not lead to clinical improvement after 72 hours, endoscopic transluminal necrosectomy was performed. Clinical improvement was defined as improvement of at least two organ systems (circulatory, pulmonary or renal) or decreased inflammatory markers (C reactive protein (CRP), leucocytes or temperature). Additional percutaneous catheter drainage after endoscopic transluminal drainage was allowed when necrotic collections could not be optimally drained endoscopically. LAMS were removed within 6 weeks. Imaging (preferably magnetic resonance cholangiopancreatography (MRCP)) was conducted to evaluate pancreatic duct integrity prior to stent removal. If the necrotic collection was not fully collapsed or pancreatic duct disruption or disconnection was suspected, the LAMS was, if technically possible, exchanged for plastic stents. In the plastic stents-group, stents were not routinely removed.

Follow-up was completed after 6 months. Outpatient follow-up visits were scheduled at 3 and 6 months after inclusion, to evaluate exocrine and endocrine pancreatic function and to complete two questionnaires (Short-Form-36 (SF-36) and EuroQol Five dimensions (EQ-5D-3L)).[18 19]

End points

The primary end point was the need for endoscopic transluminal necrosectomy. Predefined secondary end points were similar to the TENSION trial and included mortality, new-onset organ failure, bleeding requiring intervention, perforation of a visceral organ and/or enterocutaneous fistula requiring intervention, pancreaticocutaneous fistula, biliary stricture, endocrine and exocrine pancreatic insufficiency, total number of endoscopic, radiological or surgical interventions for infected necrosis (catheter drainage and necrosectomy), total length of intensive care and hospital stay (definitions in online supplemental appendix). Bleeding only requiring blood transfusion (post hoc definition) and bleeding requiring endoscopic, radiological or surgical intervention (similar to the definition in the TENSION trial) are reported separately. LAMS-related complications were post hoc defined as complications that occurred with LAMS in situ. The end points were assessed by an adjudication committee, consisting of five endoscopists and two surgeons. All CT scans and MRIs of the study participants were reviewed and scored by two experienced abdominal radiologists (TLB and MPMK).

Statistical analysis

In the TENSION trial, endoscopic transluminal necrosectomy was performed in 53% of the patients assigned to the endoscopic step-up approach with plastic stents. Based on the findings of another prospective study, we hypothesised that the number of patients needing an endoscopic transluminal necrosectomy procedure could be halved when using LAMS.[20] Assuming a reduction from 53% to 26.5% and using a two-sided significance level of 0.05% and 80% power, we calculated with a χ^2 test that a total of 52 patients needed to be included in the study in addition to the 51 patients assigned to the endoscopic step-up approach with plastic stents from the TENSION trial.

All analyses were done according to the intention-to-treat principle. Patient characteristics are summarised as mean and SD or median and ranges between the 25th and 75th percentile. Results are presented as relative risk (RR) with corresponding CIs or as mean differences with two-sided bias-corrected and accelerated (BCa) 95% CIs calculated by bootstrapping with 5000 samples. Logistic regression analysis was performed to correct for baseline imbalances between groups for the primary end point. An explorative post hoc subgroup analysis was performed to evaluate the primary end point in patients drained with 15 mm vs 20 mm LAMS. There was no missing data for the primary end point, but a few for the secondary end points; all observed data were included in the analysis without imputation. Healthcare costs were calculated from a hospital's perspective, and are presented as mean differences with corresponding two-sided BCa 95% CIs. Unit costs of both groups were price-indexed for the year 2020 and presented in euros. Units and their respective costs are summarised in the online supplemental table S4. All tests were two-sided, with p values <0.05 indicating statistical significance. CIs were not adjusted for multiplicity. Statistical analyses were conducted using R software, V.4.0.3 (R Project for Statistical Computing).

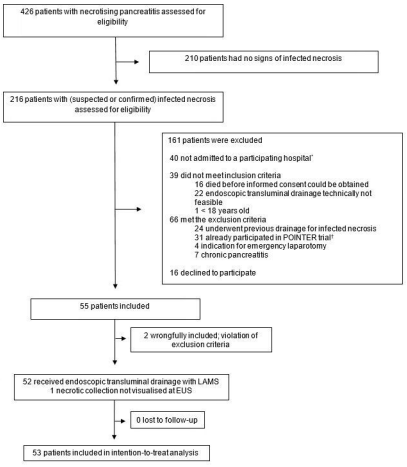

Figure 1 Study enrolment, inclusion and follow-up in LAMS-group. *For clinical and logistical reasons, transfer to a participating hospital participating in AXIOMA study not possible. †Further explained in online supplemental appendix. EUS, endoscopic ultrasound; LAMS, lumen-apposing metal stents.

RESULTS

Study enrolment

From 1 June 2018 to 4 March 2020, a total of 426 patients with necrotising pancreatitis were screened for eligibility. Fifty-three patients were prospectively included in the study (figure 1). Two patients were incorrectly included because percutaneous catheter drainage was preceded prior to study enrolment. Both patients were, after approval of the ethical committee and prior to analysis, replaced with new study participants. The number of included patients finally exceeded the original study sample size, because the last two patients simultaneously consented to enrolment in two different study centres.

One of the 53 enrolled patients did not underwent EUS-guided transluminal drainage with LAMS, because the necrotic collection could not be visualised by EUS. This patient was treated with antibiotics and percutaneous catheter drainage. According to the intention-to-treat principle, outcomes of this patient were included in analysis of the LAMS-group. The remaining 52 patients underwent EUS-guided transluminal drainage with LAMS. Clinical outcomes of the patients in the 53 patients LAMS-group were compared with 51 patients in the plastic stents-group.

Table 1 Baseline characteristics

Characteristics	LAMS (n=53)	Plastic stents* (n=51)
Age—mean±SD	59±13	63±14
Male sex—no. (%)	33 (62)	34 (67)
Body mass index—mean±SD	29±5	30±8
CT severity index† —mean±SD	7±2	7±2
Extent of pancreatic necrosis—no. (%)		
<30%	23 (43)	26 (51)
30%–50%	18 (34)	15 (29)
>50%	12 (23)	10 (20)
Encapsulation—no. (%)		
Medium encapsulated	6 (11)	1 (2)
Largely encapsulated	15 (28)	14 (27)
Fully encapsulated	32 (60)	36 (71)
Necrosis extending >5 cm down the retrocolic gutters—no. (%)	20 (38)	20 (39)
Gas configurations—no. (%)	19 (36)	23 (45)
Disease severity‡		
Admitted to ICU—no. (%)	14 (26)	21 (41)
SIRS§—no. (%)	47 (89)	33 (65)
C reactive protein¶ (mg/L)—median (p25–p75)	248 (144–325)	168 (106–256)
White cell count (10^{-9}/L)**—median (p25–p75)	15 (11–22)	14 (9–17)
Organ failure—no. (%)	12 (23)	13 (25)
Multiple organ failure—no. (%)	7 (13)	9 (18)
Time from onset of symptoms to ETD (days)—median (p25–p75)	36 (26–62)	43 (30–58)

Additional baseline variables are provided in online supplemental table S1.
*Data from plastic stent-group are derived from the multicentre randomised TENSION trial.
†Based on the CT before inclusion; score ranges from 0 to 10, higher scores indicate more extensive pancreatic and peripancreatic necrosis.
‡Data were based on maximum values during the 24 hours before inclusion.
§P=0.005.
¶P=0.017; missing in six patients.
**Missing in two patients.
ETD, endoscopic transluminal drainage; ICU, intensive care unit; LAMS, lumen-apposing metal stents.

Table 2 Primary and secondary end points

Outcome	LAMS (n=53)	Plastic stents* (n=51)	Relative risk (95% CI)	P value
Primary end point				
Need for endoscopic transluminal necrosectomy—no. (%)	34 (64)	27 (53)	1.21 (0.87 to 1.68)	0.320
Secondary end points				
Death—no. (%)	6 (11)	9 (18)	0.64 (0.25 to 1.67)	
New-onset organ failure—no. (%)	9 (17)	7 (14)	1.24 (0.50 to 3.07)	
Pulmonary	7 (13)	4 (8)	1.68 (0.52 to 5.41)	
Cardiovascular	7 (13)	3 (6)	2.25 (0.61 to 8.21)	
Renal	4 (8)	2 (4)	1.92 (0.37 to 10.05)	
New-onset multiple organ failure†—no. (%)	6 (11)	2 (4)	2.89 (0.61 to 13.65)	
Bleeding—no. (%)	9 (17)	11 (22)	0.79 (0.36 to 1.74)	
Bleeding only requiring blood transfusion—no. (%)	4 (8)	0 (0)	–	
Bleeding requiring intervention—no. (%)	5 (9)	11 (22)	0.44 (0.16 to 1.17)	
Perforation of a visceral organ or enterocutaneous fistula—no. (%)	1 (2)	4 (8)	0.24 (0.03 to 2.08)	
Pancreaticocutaneous fistula—no. (%)	3 (6)	2 (4)	1.44 (0.25 to 8.28)	
Biliary stricture—no. (%)	1 (2)	3 (6)	0.32 (0.03 to 2.98)	
Exocrine insufficiency				
Use of enzymes—no. (%)	19 (36)	17 (34)	1.05 (0.62 to 1.79)	
Faecal elastase <200 mg/g—no. (%)‡	23 (48)	23 (52)	0.92 (0.61 to 1.38)	
Endocrine insufficiency—no. (%)	11 (21)	10 (20)	1.06 (0.49 to 2.28)	

Data are n (%).
*Data from the plastic stents-group are derived from the multicentre randomised TENSION trial.
†New-onset organ failure was defined as organ failure not present at randomisation.
‡Missing in five patients in LAMS-group and seven patients in the plastic stents-group
LAMS, lumen-apposing metal stents.

Outcomes

Baseline characteristics

Baseline characteristics were mostly equally distributed between patients treated with LAMS and plastic stents (table 1 and online supplemental table S1). More patients in the LAMS-group met the systemic inflammatory response syndrome (SIRS) criteria (89% vs 65%, p=0.005) and had higher CRP levels at inclusion (median 245 (p25–p75 114–325) vs median 168 (p25–p75 106–256), p=0.017) when compared with the plastic stents-group. Twenty-five patients (47%) were drained with 15 mm LAMS and 27 patients (51%) with 20 mm LAMS.

Primary and secondary end points

The primary end point did not differ between groups: 34 patients (64%) in the LAMS-group vs 27 patients (53%) in the plastic stents-group needed an endoscopic transluminal necrosectomy (RR 1.21; 95% CI 0.87 to 1.68, p=0.320) (table 2). After correction for baseline characteristics (age, sex, timing of drainage, extent of necrosis and necrosis extending >5 cm down the retrocolic gutters) and baseline imbalances (SIRS and CRP), the OR for need for endoscopic transluminal necrosectomy in the LAMS-group versus plastic stents-group was 1.21 (95% CI 0.45 to 3.23).

No difference was found in mortality rate: six patients (11%) died in the LAMS-group vs nine patients (18%) in the plastic stents-group (RR 0.64; 95% CI 0.25 to 1.67). Nine patients (17%) developed new-onset organ failure in the LAMS-group vs seven patients (14%) in the plastic stents-group (RR 1.24; 95% CI 0.50 to 3.07).

Bleeding occurred in 9 patients (17%) in the LAMS-group vs 11 patients in the plastic stents-group (22%) (RR 0.79; 95% CI 0.36 to 1.74). Four patients (8%) developed a bleeding requiring only a blood transfusion in the LAMS-group versus none of the patients in the plastic stents-group (online supplemental figure S2). The remaining 5 patients (9%) in the LAMS-group required an (endoscopic, radiological or surgical) intervention to manage the bleeding vs 11 patients (22%) in the plastic stents-group (RR 0.44; 95% CI 0.16 to 1.17), after a mean of 26 days (median 20 days; p25–p75 14–26) and 37 days (median 26 days; p25–p75 18–55) postdrainage (mean difference −11 days; 95% CI −34 to 18), respectively. Six of 9 patients (67%) had indwelling LAMS and 9 of 11 patients (82%) indwelling plastic stents at the time of the bleeding. Pseudoaneurysms were present in 5 of 9 patients (56%) in the LAMS-group and 10 of 11 patients (91%) in the plastic stents-group. Additional predefined major complications did not differ between groups (table 2).

Other LAMS-related complications were reported in four patients (8%): stent migration occurred in two patients (4%), who were both treated conservatively. Perforation with LAMS in situ did not occur. The LAMS was found buried under overgrowing gastric mucosa in two patients (4%), but could be removed successfully. Complications other than the predefined

Table 3 Secondary end points related to healthcare utilisation

Outcome	LAMS (n=53)	Plastic stents* (n=51)	Relative risk/Mean difference (95% CI)
Interventions for infected necrosis			
Total number interventions (catheter drainage and necrosectomy)—mean (BCa 95% CI)	4.9 (3.8 to 6.4)	4.3 (3.4 to 5.6)	0.6 (–1.1 to 2.3)
Total number of drainage procedures—mean (BCa 95% CI)	2.5 (1.9 to 3.6)	2.5 (2.0 to 3.6)	0 (–1.0 to 1.1)
ETD procedures—mean (BCa 95% CI)	1.1 (1.0 to 1.3)	1.3 (1.1 to 1.7)	–0.2 (–0.6 to 0.0)
Total number of necrosectomies—mean (BCa 95% CI)	2.4 (1.7 to 3.4)	1.8 (1.2 to 2.6)	0.6 (–0.5 to 1.6)
ETN procedures—mean (BCa 95% CI)	2.3 (1.7 to 3.3)	1.8 (1.2 to 2.6)	0.6 (–0.4 to 1.7)
Need for additional PCD—no. (%)	17 (32)	14 (27)	1.17 (0.65 to 2.12)
Need for VARD—no. (%)	2 (4)	2 (4)	0.96 (0.14 to 6.58)
Hospital admission			
Length of ICU admission (days)—mean (BCa 95% CI)	8 (4 to 14)	13 (7 to 26)	– 6 (–17 to 2)
Length of hospital stay (days)—mean (BCa 95% CI)	43 (34 to 55)	53 (42 to 68)	–10 (–27 to 5)
Healthcare costs			
Initial endoscopic drainage procedure—mean (BCa 95% CI)	€5056 (€4479 to €5153)	€2813 (€2490 to 2934)	€2244 (€1941 to €2491)
Total healthcare costs—mean (BCa 95% CI)	€46 860 (€37 991 to €59 680)	€53 208 (€41 479 to €72 123)	-€6348 (-€26 386 to €10 121)

Data are n (%) or mean (BCa 95% CI).
*Data from the plastic stent-group are derived from the multicentre randomised TENSION trial.
BCa, bias-corrected and accelerated CI; ETD, endoscopic transluminal drainage; ICU, intensive care unit; LAMS, lumen-apposing metal stents; PCD, percutaneous catheter drainage; VARD, video-assisted retroperitoneal debridement.

primary and secondary end points are summarised in online supplemental table S2.

Length of intensive care stay (mean 8 days vs 13 days; mean difference −6 (95% CI −17 to 2)) and hospital stay (mean 43 days vs mean 53 days; mean difference −10 (95% CI −27 to 5)) did not differ between groups. The mean number of endoscopic, radiological or surgical interventions for infected necrosis (catheter drainage and necrosectomy) was 4.9 (95% CI 3.8 to 6.4) in the LAMS-group vs 4.3 (95% CI 3.4 to 5.6) in the plastic stents-group (table 3). Seventeen patients (32%) needed percutaneous catheter drainage in the LAMS-group vs 14 patients (27%) in the plastic stents-group-group.

The LAMS was removed after a mean of 47 days (median 41 days; p25–p75 34–50). In 27 patients (51%), the LAMS was exchanged for plastic stents (online supplemental figure S3). During follow-up, two patients (4%) in the LAMS-group versus none in the plastic stents-group developed a symptomatic recurrence of pancreatic fluid collections that required intervention. Both patients had a disrupted or disconnected pancreatic duct on MRCP. The LAMS was previously successfully replaced with plastic stents in one of the patients who developed a recurrence, while this was not possible in the other patient.

At 6 months follow-up, there were no differences in the development of endocrine and exocrine pancreatic insufficiency between groups. The results of the SF-36 and EQ-5D-3L questionnaires and the post hoc analysis are summarised in online supplemental tables S3 and S6.

Costs

The mean costs for the initial endoscopic transluminal drainage procedure were higher for the LAMS-group, with a statistically significant mean difference of €2244 (BCa 95% CI €1941 to €2491) (table 3 and online supplemental table S5). Total healthcare costs were €46 860 (BCa 95% CI €37 991 to €59 680) for the LAMS-group and €53 208 (BCa 95% CI €41 479 to €72 123) for the plastic stents-group (mean difference −€6348, BCa 95% CI −€26 386 to €10 121).

DISCUSSION

This study compared clinical outcome after endoscopic transluminal drainage with LAMS with plastic stents in patients with infected necrotising pancreatitis. The results suggests that LAMS do not reduce the need for endoscopic transluminal necrosectomy as compared with plastic stents. Complication rates, including the risk of bleeding, were comparable between groups. While the initial drainage procedure was more expensive when using LAMS, we found no difference in total healthcare costs.

Our results partly confirm, and contradict the findings of the only single-centre randomised trial that has been performed so far on this topic.[13 14] First, our results confirm that drainage with LAMS did not have the expected clinical advantages in terms of lowering the requirement for endoscopic transluminal necrosectomy. Furthermore, our results support the findings that overall treatment costs are similar, even though the LAMS device is more expensive. In fact, the higher costs of LAMS are probably a minor component of the total treatment costs for patients with necrotising pancreatitis.

Nevertheless, our results contradict the trial's previous findings which demonstrated a higher rate of complications when using LAMS. Our findings indicate similar outcomes for LAMS and plastic stents, without an apparent higher risk of complications or severe bleeding, when the LAMS was removed within 6 weeks. Bleeding is the most feared complication associated with LAMS. It is believed that, as soon as the necrotic collection has collapsed, the opposite cavity wall is exposed to the distal end of the LAMS, which could cause tissue and vascular injury.[13 14] Noteworthy, our results demonstrated that only 67% of patients with indwelling LAMS developed a bleeding; a causal relationship was therefore not evident in our study. LAMS should be removed as early as possible when no longer needed; the authors of the aforementioned randomised trial confirmed in another prospective study that delayed removal was associated with more complications.[21] Based on our study, the 6 weeks interval seems safe. A longer period is usually not required, because exchange for plastic stents is possible when the necrotic collection is not

fully resolved. In conclusion, we confirm the results of a recent systematic review of mainly retrospective studies, reporting that there is no increased bleeding risk when using LAMS.[22] The results of two ongoing randomised trials will provide more information on LAMS safety.[23 24]

However, one important difference between the currently available randomised trial and our study must be taken into consideration. In our study, nasocystic catheters were placed through the LAMS for irrigation, similar to the practice in the plastic stents-group.[8] We choose this approach to strengthen our methodology and minimise differences between groups. However, there is currently no high-level evidence on the advantages of irrigation with a nasocystic catheter on clinical outcome, nor on the most optimal duration, type and volume of irrigation fluids. Moreover, it is currently unclear whether nasocystic irrigation offers any advantages when combined with a LAMS. Similarly, the placement of plastic stents within the LAMS has recently been suggested to improve drainage and prevent damaging the opposite cavity wall.[25 26] Nonetheless, high quality evidence to support this practice is currently lacking.

Necrosis of the pancreatic parenchyma frequently leads to loss of pancreatic duct integrity and is associated with recurrence of pancreatic fluid collections.[27 28] In line with the current guidelines, we therefore choose to exchange LAMS for plastic stents in case of a persistent collection or a proven disrupted duct, to maintain a permanent fistula between the pancreatic duct and the GI tract.[5] Given the low recurrence rate in our study and the inability to replace the LAMS with plastic stents in some patients, the exchange seems not necessary in all patients. Another recent retrospective study including 274 patients also challenged this practice: while approximately 75% of patients had a disrupted or disconnected pancreatic duct following acute necrotising pancreatitis, LAMS were not exchanged for plastic stents.[29] Recurrence of pancreatic fluid collections was, however, noticed in 13% of patients, with only 7% requiring further intervention.

We acknowledge several limitations of this study, despite its multicentre and prospective design. First, our study design, including the use of a historic control group, limits the interpretation of the results. As a consequence, we had to control for some baseline differences. Possible presence of confounding effects despite the similar study designs cannot be ruled out. We also acknowledge that the study was not powered to detect a difference in complications.

Second, we acknowledge that the use of a nasocystic catheter can be seen as a technical variant, which limits the external validity of our results. The LAMS used in this study might be designed to be used without a nasocystic catheter, especially because it was expected that the larger lumen of the LAMS would facilitate drainage, making additional flushing unnecessary. Because the nasocystic catheter was only in situ for 1 week, we do not expect that our study results would have changed without the placement of a nasocystic catheter.

Third, we used both the 15 and 20 mm LAMS in the study, which potentially could have affected clinical outcome. During the course of the study, not all hospitals in the Netherlands had immediate access to the 20 mm LAMS. In view of insufficient evidence about the advantages of the larger lumen, we decided to continue with both stents, reflecting routine clinical practice in the Netherlands. Moreover, outcome did not differ between stent size (online supplemental table S6).

Last, we did not measure the duration of the endoscopic transluminal drainage procedure, which could be a potential important advantage. However, significant reduction of procedural time in favour of LAMS was already proven in the only randomised trial and confirmed in daily clinical practice.[13]

In summary, our study suggests that the use of LAMS does not substantially reduce the need for endoscopic transluminal necrosectomy and leads to similar patient outcomes, complications and healthcare costs when compared with double-pigtail plastic stents in patients with infected necrotising pancreatitis.

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Contributors This study was primarily designed by LB, RCV, MGB, JEvH, J-WP, FPV, MBo, PF and RPV, and was subsequently discussed in research meetings with

all authors. The study was conducted by LB, RCV, MGB, MAB, TLB, SAWB, VCC, WC, CHD, SMvD, HMvD, CvE, E-JvG, MH, WLH, PH, JEvH, MAJMJ, JECK, MPMK, EK, SK, ML, VBN, LP, J-WP, RQ, RJdR, HCvS, CJSW, MS, HCT, BW, DSU, NGV, FV, RLJvW, MBr, PF and RPV. The data were collected and analysed by LB who also drafted the manuscript under supervision of RPV. All authors contributed to the interpretation of the data and to the draft of the manuscript. All authors have approved of the final manuscript. The guarantor of the article is RPV.

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