Details online

Methodological description

Patient inclusion

- Age ≥ 18 years
- Diagnosis of acute cholecystitis according to the Tokyo Guidelines (clinical signs, laboratory findings, and imaging findings)
- High surgical risk, defined as (1) ASA score > III, (2) APACHE II score ≥ 12, (3) onset of symptoms ≥7 days before first presentation, (4) advanced malignancy, and (5) deemed unsuitable for surgery for any other reason based on surgical consultation.
- Written informed consent

Patient exclusion

- Altered anatomy of the upper gastrointestinal tract due to surgery of the oesophagus, stomach or duodenum
- Pancreatitis
- Liver cirrhosis, portal hypertension and/or gastric varices
- Abnormal coagulation (INR >1.5 and not correctable and/or platelets < 50.000/mm^3)
- Previous drainage of the gallbladder
- Pregnancy

IRB/registration

Study protocol was reviewed and approved by the IRB of all participating centers.
Registration at the Dutch Trial Registration (www.trialregister.nl) under number (NTR 3633).

Main outcomes

- Safety, defined as the number of (possible) stent- or procedure-related severe adverse event (SAEs), e.g. bile leakage with development of peritonitis, significant bleeding, or a non-scheduled endoscopic/surgical intervention due to an adverse event.
- A Data Safety Monitoring Board (DSMB) was installed to review all SAEs and to determine whether these were (possibly) associated with the stent or the procedure.
- Technical success of LAMS placement, defined as successful access to the gallbladder followed by adequate transmural LAMS deployment
- Technical success of LAMS removal was defined as successful removal at oesophago-gastroduodenoscopy (EGD) of the LAMS using a polypectomy snare or rat-tooth forceps in a single session.
- Clinical success, defined as resolution of clinical parameters of acute cholecystitis within 96 hours. Clinical parameters assessed were abdominal pain scored by the patients on a 10-point visual analogue scale, body temperature, white blood cell count and serum C-reactive protein concentration.
- Recurrence of cholecystitis, defined as recurrence of acute cholecystitis according to Tokyo Guidelines after complete clinical response, either before or after LAMS removal.

Study approach

- Consecutive patients with acute cholecystitis and an indication for gallbladder drainage at high surgical risk were included in the study.
- Written informed consent was obtained from each enrolled patient before the procedure.
- EUS-guided gallbladder drainage using LAMS

- Daily follow-up until resolution of cholecystitis (pain score, temperature, WBC and C-reactive protein)
- LAMS removal after 3-months
- 3-monthly follow-up, total follow-up one year

Device and technique

- LAMS (Axios; Xlumena, Mountain View, CA); constructed of braided nitinol and fully covered with silicone. Wide flanges on both ends provide anchoring of the gallbladder and gut lumens with an even distribution of pressure on the luminal walls. The diameter of the flanges is approximately twice the diameter of the lumen. Delivery through a 10.5F catheter, which is luer-locked to the endoscope instrumentation channel inlet port to provide controlled deployment of the stent, CE-marked and FDA-approved for drainage of peripancreatic fluid collections.
- Technique:
    - Drainage under conscious sedation (midazolam and fentanyl), monitored anesthesia care (propofol), or endoscopist-administered propofol sedation, depending on institutional standard sedation practices and patient status.
    - All patients were on antibiotics.
    - Visualization of gallbladder and determination of optimal site, stomach or duodenum, for puncture using linear-array EUS.
    - Gallbladder puncture using 19-gauge EUS-FNA needle, passing 0.035-inch guide wire through the needle and coiling in gallbladder.
    - Dilation of fistula tract using a cystostome or balloon dilator.
    - Placement of a delivery catheter over the guidewire, deployment of the distal end of the stent in the gallbladder lumen under fluoroscopic and/or EUS-guidance; deployment of proximal stent end using a combination of fluoroscopic and endoscopic view and EUS guidance, depending on endoscopist preference

Sample size calculation

- Sequential testing safety model was used to calculate the minimum number of patients needed to demonstrate that EUS-guided drainage using a LAMS is not unsafe.(18;19) If the safety boundary in the model (stent- or procedure-related SAEs $\geq$ 25% of patients) was not crossed after inclusion of 14 patients we were allowed to conclude that the procedure is not unsafe, taking into account a risk of 11% of stent- or procedure-related SAEs in patients receiving PTGBD.(3)
- We estimated that a sample size of 23 patients was required to demonstrate a clinically relevant 20% difference in recurrence of cholecystitis during one year of follow-up using a two-sided α of 0.05 with a power of 0.80. We estimated a recurrent cholecytitis rate of 25% after PTGBD based on the literature.(20-27)
- To compensate for a potential loss to follow-up of 10%, we aimed to include 30 patients in the study.

Data analysis

- An interim analysis was performed after each (possibly) stent- or procedure-related SAE and a DSMB meeting was scheduled after every three SAEs.
- SPSS 20.0.0 (SPSS, Inc, Chicago, IL, USA); Continuous variables were reported by using means (standard deviation) and medians (range), as appropriate. Categorical variables were reported in terms of frequency counts and proportions.

Details of results

Patient characteristics

	N=30 (100%)
Mean age, years (range)	85 (68-97)
Male gender (%)	11 (37)
Indication EUS-GBD (%)	
ASA score ≥ 3	13 (44)
APACHE score ≥ 12	3 (10)
Symptoms ≥ 7 days	2 (7)
Advanced malignancy	2 (7)
Combination	5 (16)
Expert opinion	5 (16)
Calculous cholecystitis (%)	22 (87)
Median time since onset symptoms, days (range)	2 (1-28)

Procedural characteristics and clinical outcome of EUS-GBD using a lumen-apposing metal stent (LAMS).

	N=30 (100%)
Technical success	27 (90)
Anaesthesia	
Consious sedation	26 (97)
Monitored anesthesia care	4 (3)
Puncture site	
Stomach	11 (37)
Duodenum	19 (63)
LAMS size	
10 x 10 mm	13 (43)
10 x 15 mm	17 (57)
Median total scope time, min (range)	15 (13-110)
Stent removal	15 (50)
Time to stent removal, days (±SD)	91 (24)
Reason for no stent removal	
Death before scheduled removal	5 (33)
Poor clinical condition	3 (20)
Refusal by the patient	3 (20)
Significant tissue overgrowth	2 (13)
Ongoing cholecystolithiasis	1 (7)
Polypoid lesion in the gallbladder	1 (7)
Stent dwell time for stents left in situ (±SD)	364 67
Clinical success	26/27 (96%)
Recurrent cholecystitis	2/27 (7%)

Overview of all SAEs and review decision of the DSMB

		Outcome	DSMB
1	(Aspiration) pneumonia	Death	**Procedure-related**
2	Pancreatic cancer/infection	Death	**Possible stent-/procedure-related**
3	Urosepsis	Death	Not related
4	Pancreatic cancer	Death	Not related
5	Myocardial infarction	Death	Not related
6	Cholangiosepsis	Death	Not related
7	Colorectal cancer	Death	Not related
8	Melena/ thrombus in gallbladder	Resolved	**Stent-related**
9	Jaundice (hemobilia)	Resolved	**Stent-related**
10	Cholangitis (gallstones)	Resolved	Not related
11	Cholangitis (malignant)	Resolved	Not related
12	Acute (biliary) pancreatitis	Resolved	Not related
13	Ischemic stroke	Sequelae	Not related
14	Pneumonia	Resolved	Not related
15	Hip fracture	Sequelae	Not related