NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of tunnelled peritoneal drainage catheter insertion of refractory ascites in cirrhosis

Long-term liver scarring (cirrhosis) can cause fluid to build up (ascites) in the abdomen, causing difficulty in breathing, nausea, bloating, acid reflux, abdominal pain, poor appetite and infection. The fluid can be drained in hospital (peritoneal drainage) with a temporary drainage tube (catheter) to help relieve the symptoms but the fluid recurs (refractory). So, drainage needs to be repeated every 1 to 2 weeks. This may cause pain and infection.

In this procedure, with a local anaesthetic (or occasionally under sedation or a general anaesthetic) a catheter is inserted (tunnelled) under the skin into the abdomen. Excess fluid can then be drained when needed, at home or in community care into a bottle or a bag. In between times, the catheter is capped and covered with a clean dressing. The aim is to reduce the need for hospital admissions and improve quality of life.

Contents

Abbreviations

Word or phrase	Abbreviation
Acute kidney injury	AKI
Cirrhosis-Associated ascites Symptom	CAS
Chronic liver disease	CLD
Child-Pugh Score	CPS
End-stage liver disease	ESLD
European quality of life	EuroQol
EQ-5 dimension 5-point scale questionnaire	EQ-5D-5L
EQ-5 dimension visual analogue scale	EQ-5D-VAS
Interquartile range	IQR
Long-term ascitic drainage	LTAD
Large-volume paracentesis	LVP
Model of End Stage Liver Disease	MELD
Not reported	NR
Integrated Palliative Outcome Scale	IPOS
Permanent indwelling peritoneal catheters	PIPC
Quality of life	QOL
Refractory ascites	RA
Randomised controlled trial	RCT
Short Form Liver Disease Quality of Life	SFLDQoL
Spontaneous bacterial peritonitis	SBP
Transjugular intrahepatic portosystemic stent shunt	TIPSS
Zarit Burden Interview - carer reported	ZBI-12

Introduction

The National Institute for Health and Care Excellence (NICE) prepared this interventional procedure overview to help members of the interventional

procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and professional opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in January 2022.

Procedure name

- Long-term tunnelled peritoneal drainage catheter insertion for palliation of refractory ascites in cirrhosis

Professional societies

- British Society for Interventional Radiology (BSIR)
- British Society of Gastroenterology (BSG)
- Association of Upper Gastrointestinal Surgeons (AUGIS)
- British Association for the Study of the Liver (BASL)
- Association for Palliative Medicine of Great Britain and Ireland.

Description of the procedure

Indications and current treatment

Refractory ascites is a common complication of cirrhosis of the liver. Build-up of fluid causes difficulty in breathing, fatigue, nausea, poor appetite, acid reflux, abdominal pain and infection. Mortality at 2 years in people with refractory ascites is 50% or more, and 5-year survival is normally less than 20%.

Treatment options for symptomatic relief include dietary sodium and fluid restriction, diuretics, large-volume paracentesis (a temporary drain inserted into the abdomen to drain the ascitic fluid) with albumin infusion or insertion of a TIPSS. If the cause of liver failure and ascites cannot be treated or treatment fails, liver transplantation may be used in some people. If TIPSS or liver

transplantation is not suitable, LTAD peritoneal catheters are used as a palliative treatment option.

What the procedure involves

The procedure is usually done as a day case with local anaesthesia, with or without sedation. Ultrasound, fluoroscopy or both are used to guide catheter insertion and placement. A guidewire introducer needle is inserted percutaneously into the peritoneal cavity and ascitic fluid is aspirated. A guidewire is then inserted through the introducer and into the peritoneal cavity. A fenestrated drainage catheter is tunnelled subcutaneously from a second incision 5 cm away from the guidewire insertion site. It is then inserted over the guidewire into the peritoneal cavity using a dilator and peel-away sheath. A polystyrene cuff on the catheter is positioned inside the tunnel. The dilator and guidewire are removed and the catheter-insertion site and exit sites are sutured. Antibiotics may be offered during and after the procedure.

A lockable drainage line is connected to a valve at the outer end of the catheter to allow the ascitic fluid to be drained into a vacuum bottle or a drainage bag. Before hospital discharge, the ascites is normally drained to dryness and albumin replacement is given. After this procedure, ascites drainage is done in the community or at home without giving replacement albumin. This is typically supervised by district nurses.

People can drain small amounts of ascitic fluid repeatedly from their peritoneal cavity into vacuum bottles. The volume of fluid drained and how often it is done can be adjusted according to their needs.

Efficacy summary

Technical success

In a systematic review of LTAD peritoneal catheters for refractory ascites in ESLD (n=18 studies), technical insertion of the catheter was successful in 100% of patients (Macken 2019).

Place of ascites management (subsequent drainage)

In the systematic review of LTAD peritoneal catheters, 9 studies reported ascites management at home, either by community nurses, patients themselves or caregivers. Three studies reported management in either a hospice or the patient’s home and 2 reported management either in a hospital outpatient setting or the patient’s home. Four studies did not state the place of ascites management (Macken 2019).

In a feasibility RCT of 36 patients with RA caused by ESLD comparing 17 patients with LTAD peritoneal catheters (and fortnightly home visits) and 19 patients with LVP, ascites drainage at home by nurses and carers was reported in 67% (10/15) patients in the LTAD peritoneal-catheter group. The median number of visits per week for drainage was 1.9 (IQR 0.6 to 2.5) in this group (Macken 2021).

In an RCT of 13 patients with RA caused by ESLD comparing 6 patients with LTAD peritoneal catheters and 7 patients with LVP, drainage at home was reported in 6 patients. Vacuum bottles were used in amounts of 2 litres per drainage, with a median interval of 2 to 5 days. One patient needed LVP after 56 days because of clotting in the catheter (Kimer 2020).

Further hospital admissions needing ascites drainage

In the systematic review of LTAD peritoneal catheters, no further hospital admissions were needed in 14 studies that reported drainage following LTAD peritoneal-catheter insertion. Hospital admission for full drainage with intravenous albumin was needed for 2 patients in 1 study and for 3 patients in another study (for unrelated conditions; Macken 2019).

In the feasibility RCT of 36 patients, further drainage at hospital was needed in 5 patients each in the LTAD peritoneal-catheter (n=17) and LVP (n=19) groups. However, this was mainly for non-ascites related problems (Macken 2021).

Median number of hospital ascitic-drainage catheters

In the feasibility RCT of 36 patients, the median number of hospital ascitic-drainage catheters was 5 before randomisation in both groups. This reduced to 0 (IQR 0,1) in the LTAD peritoneal-catheter group and 4 (IQR 3,7) in LVP group at 12-week follow up. (Macken 2021).

Specialist palliative care support

In the systematic review of 18 studies, 12 studies reported that LTAD peritoneal-catheter insertion was done as a palliative procedure. Five studies used LTAD peritoneal catheters in patients having long-term and non-long-term care. Three studies took input from specialist palliative care (Macken 2019).

Duration LTAD peritoneal catheter remained in place

In the systematic review of 18 studies, how long LTAD peritoneal catheters remained in place varied across studies. Median LTAD peritoneal-catheter duration reported in 9 studies ranged between 6 weeks to 8 months (Macken 2019).

Patient survival after LTAD peritoneal-catheter insertion

In the systematic review of 18 studies, median patient survival varied across studies. In 6 studies it ranged between 29 days to 6 months (Macken 2019).

In the feasibility RCT of 36 patients, median survival at 12 weeks was 53% (9/17) in the LTAD peritoneal-catheter group and 63% (12/19) in the LVP group. Median survival in patients who died was 53 days in LTAD peritoneal-catheter group and 61 days in LVP group (Macken 2021).

Biochemical outcomes

In the feasibility RCT of 36 patients, serum albumin (g/litre) decreased from baseline to 12 weeks in both the groups (from median of 33 g/litre to 29 g/litre in the LTAD peritoneal-catheter group compared with 31 g/litre to 30 g/litre in the LVP group). Patients in the LTAD peritoneal-catheter group did not routinely have human albumin solution. Serum creatinine (micromol/litre) decreased from 109.5 micromol/litre to 104.5 micromol/litre in the LTAD peritoneal-catheter group but increased from 113.5 micromol/litre to 127 micromol/litre in the LVP group (Macken 2021).

In the RCT of 13 patients, a moderate fall in plasma albumin levels was seen in the LTAD peritoneal-catheter group compared with the LVP group (p=0.07, median decrease in albumin in LTAD peritoneal catheter group was 4 g/litre). Intravenous albumin had no clear influence on the albumin levels. No statistically significant changes in plasma sodium (p=0.14) or creatinine levels (p=0.67) were seen in the groups (Kimer 2020).

Symptom control (questionnaire assessment)

In the feasibility RCT of 36 patients, median physical symptoms, emotional symptoms, communication scores and total IPOS scores (assessed using the IPOS questionnaire with 17 items and scores ranging from 0 to 68) remained consistent in both the LTAD peritoneal-catheter and LVP groups during 12 weeks of follow up (Macken 2021).

QOL

In the systematic review of 18 studies, 1 study assessed QOL (using a questionnaire similar to the Chronic Liver Disease Questionnaire) after LTAD peritoneal-catheter insertion. All patients reported improvements in mobility and daily activities. Nursing staff also stated that it ‘benefited and supported earlier placement’ (Macken 2019).

In the feasibility RCT of 36 patients, generic health-related quality of life measured on the EQ-5D-5L VAS (range 0 [worst] to 100 [best]) showed a trend towards improvement in the LTAD peritoneal-catheter group (from baseline 57.6 to 66.3 at 12 weeks). The EQ-5D-5L index (5 dimensions scored on a 5-point scale; -0.59 [worst] to 1 [best]) worsened in the LTAD peritoneal-catheter group (from baseline 0.65 to 0.59 at 12 weeks)but there was some improvement in the LVP group (from baseline 0.52 to 0.57 at 12 weeks). Liver-specific health-related QOL, using the SFLDQoL questionnaire (was better in the LTAD peritoneal-catheter group than the LVP group at baseline in all domains except hopelessness. During follow up at 12 weeks, scores decreased in the LTAD peritoneal-catheter group but increased in most domains in the LVP group.

Caregiver burden assessed using ZBI-12 scores (0 [never best] to 48 [nearly worst]) remained stable in the LTAD peritoneal-catheter group. There was an increasing trend (that is, worsening carer burden) in the LVP group (from baseline 14.6 to 20 at 12 weeks). Macken 2021).

In the RCT of 13 patients, the median CAS score indicated that QOL was poor at baseline (LTAD peritoneal catheter 19 points and LVP 21 points) and there was no statistically significant difference between the groups during the course of the trial (Kimer 2020).

Acceptability

In the feasibility RCT of 36 patients, 6 of the nurses and 14 of the patients (6 in LTAD peritoneal-catheter and 8 in LVP group) interviewed showed that LTAD peritoneal catheters transformed the care pathway and improved symptom control (Macken 2021).

Safety summary

Death

Deaths (mainly liver related) were reported in 41% (7/17) of patients in the LTAD peritoneal-catheter group and 26% (5/19) of patients in the LVP group in the feasibility RCT of 36 patients. Five of these (3 in LTAD peritoneal-catheter and 2 in LVP group) happened within 4 weeks, and 4 deaths in each group happened outside the hospital (Macken 2021).

Infections

Bacterial peritonitis was reported in 17% (29/166) of patients in 16 studies, in the systematic review of 18 studies. Rates varied from 0% to 42% in individual studies. Excluding 1 outlier study (14 patients with catheter related organisms),

the rate was 11% (15/133). Four of these patients had LTAD peritoneal catheters removed and had antibiotics. Eight patients had long-term prophylactic antibiotics and 1 had palliative care. The authors stated that the infections were no higher than what would be expected in people with ESLD. (Macken 2019).

SBP was reported in 1 patient in the LTAD peritoneal-catheter group (n=17) and 2 patients in the LVP group (n=19) in the feasibility RCT of 36 patients. Treatment details were not reported (Macken 2021).

In the RCT of 13 patients, all patients in the LTAD peritoneal-catheter group (n=6) developed colonisation of the catheter within 1 to 4 months but only 33% (2/6) of patients developed bacterial peritonitis. These patients withdrew from the study but had antibiotics and had intravenous albumin as part of treatment. In the LVP group (n=7), bacterial peritonitis was reported in 1 patient after rupture of an umbilical hernia and development of hepatorenal syndrome. The patient withdrew from the study. Infection of unknown origin was also reported in 1 patient in the same group (Kimer 2020).

SBP after LTAD peritoneal-catheter insertion at a median 60 days (IQR 20 to 45 days) was reported in 63% (14/24) or patients in a retrospective review of 24 patients. These patients had antibiotics but 5 of them died (Elnagar 2020).

Cellulitis

Cellulitis at the catheter-insertion site was reported in 6% (9/147) patients with LTAD peritoneal catheters in the systematic review of 18 studies (Macken 2019).

The rate of self-limiting cellulitis or leakage (that did not result in hospital admission) was higher in the LTAD peritoneal-catheter group compared with LVP group in the feasibility RCT of 36 patients (41% [7/17] compared with 11% [2/19]; Macken 2021).

Non-infectious complications

In the systematic review of 18 studies, non-infectious complications were reported in few studies and none were life threatening. These included:

- minor transient hyponatraemia in 11% (16/142)
- rise in creatinine in 8% (12/142)
- leakage of ascites at access port-insertion sites in 8% (12/142)
- catheter occlusion in 6% (8/142)

- elevated serum urea (managed by reducing drainage episode frequency) in 2% (3/142)
- accidental catheter displacement in 1% (2/142)
- other events (AKI in 1, hematoma in 1, hepatic encephalopathy in 1, blood stained ascites post insertion in 1, bleeding that was self-resolved in 2) in 4% (6/142).

Worsening renal function

Worsening renal function happened in 35% (6/17) of patients in the LTAD peritoneal-catheter group and 37% (7/19) of patients in the LVP group in the feasibility RCT of 36 patients (Macken 2021).

Accidental dislodgement of the catheter

The catheter was accidentally pulled out (24 hours after insertion) in 1 patient in the LTAD peritoneal-catheter group in the feasibility RCT of 36 patients. The patient declined catheter reinsertion (Macken 2021).

Detachment of the catheter from the subcutis (at 56 days) was reported in 1 patient in the LTAD peritoneal-catheter group (n=6) in the RCT of 13 patients. The patient withdrew from the study (Kimer 2020).

Intestinal perforation

Perforation of the ascending colon during implantation of an indwelling peritoneal catheter (and confirmed on CT) was reported in a case report of 1 patient with refractory ascites due to liver cirrhosis. The catheter was inserted to reduce intra-abdominal pressure and allow appropriate ventilation. An emergency laparotomy was done, the catheter was removed and perforation sites were sutured and closed. The patient died after 2 months because an irreversible malnutrition state resulted in a chronic respiratory failure (Paparoupa 2020).

LTAD peritoneal-catheter removal

LTAD peritoneal catheters were removed for various reasons in the retrospective review of 24 patients. In 67% (10/15) patients who developed SBP, catheters were removed at a median 10 days of antibiotics use. Other reasons for removal included leakage of the catheter in 8% (2/24) patients and blockage in another 8% (2/24) patients (Elnagar 2020).

LTAD peritoneal-catheter replacement

LTAD peritoneal catheters were replaced in 27% (4/15) of patients who developed SBP in the retrospective review of 24 patients. 3 of these patients developed recurrent SBP despite prophylaxis treatment (Elnagar 2020).

Anecdotal and theoretical adverse events

In addition to safety outcomes reported in the literature, professional experts are asked about anecdotal adverse events (events that they have heard about) and about theoretical adverse events (events that they think might possibly occur, even if they have never happened).

For this procedure, professional experts listed the following anecdotal adverse event: tunnel catheter being pulled out and causing strain to the tissue. They considered that the following were theoretical adverse events: injury to subcutaneous arteries leading to haemorrhage, leakage around the entry causing excoriation to skin.

The evidence assessed

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to long-term tunnelled peritoneal drainage catheter insertion for palliation of refractory ascites in cirrhosis. The following databases were searched, covering the period from their start to 20-08-2021: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the internet were also searched. No language restriction was applied to the searches (see the literature search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The inclusion criteria were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with refractory ascites in cirrhosis.
Intervention/test	Long-term tunnelled peritoneal drainage catheter insertion for palliation.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety, efficacy or both.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 250 patients from 1 systematic review, 2 RCTs (1 of which was a feasibility RCT that was described in 2 reports), 1 case report and 1 conference abstract.

Other studies that were considered to be relevant to the procedure but were not included in the main summary of the key evidence are listed in the appendix.

Summary of key evidence on Long term tunnelled peritoneal drainage catheter insertion for palliation of refractory ascites in cirrhosis

Study 1 Macken L (2019)

Study details

Study type	Systematic review
Country	UK
Search details	Search from inception to 2018; databases searched: MEDLINE, EMBASE, CINAHL, Google Scholar and Cochrane Database of Systematic Reviews. Hand searching of journals, reference lists and conference abstracts was also done.
Study population and number	n=18 studies (176 patients) with PIPC in refractory abdominal ascites due to ESLD (or cirrhosis) (12 full papers and 6 conference abstracts included) 3 prospective, 7 retrospective cohort studies; 1 retrospective cohort study with matched controls; 5 case series, 1 case report and 1 RCT protocol (PIPC versus LVP). Indications: RA due to CLD (n=10 studies, 2 included both ascites and hepatic hydrothoracies), ascites due to cirrhosis, malignancy and other aetiologies (n=8 studies).
Age and sex	NR
Study selection criteria	Inclusion criteria: studies in English, all types of study designs, adult patients (>18 years) who had PIPC for recurrent drainage of RA due to ESLD in palliative management. Studies including both CLD and non-CLD aetiologies for ascites. Exclusion criteria: studies with paediatric patients, with only hepatic hydrothoracies, patients without CLD, animal studies, shunting devices (including peritoneovenous, TIPSS) and ALFApump, papers reporting solely on malignant ascites and/or patients having chemotherapy, duplicate publications.
Technique	PIPCs used: 1. permanent indwelling (tunnelled) peritoneal catheters in 12 studies (9 PleurX™, 1 Rocket® and 2 unspecified catheters) 2. permanent subcutaneous port with intra-abdominal catheter in 3 studies (Celsite Drainport in 1, port-a-cath peritoneal implantable system in 1 and unspecified catheter in 1) and 3. permanent tunnelled peritoneal dialysis catheters in 3 studies (1 Tenckhoff catheter and 2 unspecified catheters). Insertion method: 10 were done under ultrasound guidance; 1 under ultrasound and fluoroscopic guidance, 1 using X-ray guidance and 1 was inserted surgically (Tenckhoff catheter). 2 studies did not report insertion methods. Procedure was performed by interventional radiologists (8 studies), interventional nephrologists (2 studies) and consultant physicians/gastroenterologists (2 studies), and trained physicians (1).

Follow up	NR
Conflict of interest/source of funding	None to declare. Authors received funding from National Institute for Health Research (NIHR) under its research for patient benefit Programme, Kent Surrey and Sussex Deanery, Dunhill Medical Trust, and Gilead Medical Sciences.

Analysis

Study design issues: systematic review conducted as per PRISMA guidelines (Preferred Reporting Items for Systematic reviews and Meta-Analyses). Comprehensive search method and strategy was used, 2 authors screened and selected studies and extracted data, the quality of non-randomised studies was assessed using the Newcastle-Ottawa Scale (NOS). Studies were small of low quality with different study designs, indications and groups, and reported on different indwelling catheters. Cases of hepatic hydrothoracies were excluded from the analysis.
Data on the severity of liver disease (Child-Pugh and/or MELD scores were reported in only 10 studies), patient and catheter related survival and prior history of SBP were limited and in- consistent. There was significant heterogeneity in prophylactic antibiotic regimens and use. QOL was assessed but pre-intervention questionnaire was not available for comparison.

Study population issues: studies reported between 1 to 33 patients.

Key efficacy findings

Number of patients analysed: 176 patients (18 studies)

Technical insertion success: 100%

Use of prophylactic antibiotics: 9 studies reported the use of peri-procedural antibiotics (2 of the studies used in limited cases during insertion procedure), 3 of these studies and another 2 studies reported use of long term prophylactic antibiotics. 7 studies reported that no prophylactic antibiotics were used.

Place of subsequent drainage/ascites management: 9 studies reported ascites management at home either by community nurses, patients themselves or care givers; 3 reported in either a hospice or patient's home and 2 reported either in a hospital outpatient setting, or the patients' home. 4 studies did not state the place of ascites management. Hospital admission for full drainage with intravenous albumin cover was needed for 2 patients in 1 study and 3 patients in another study (for unrelated conditions).

Specialist palliative care support 12 studies reported that PIPC was performed as a palliative procedure. 5 studies used PIPC in patients on long term care and non-long term care. 3 studies took input from specialist palliative care.

Patient survival after PIPC insertion and duration PIPC remained in situ

Study	N	Patient survival post insertion	Duration PIPC remained in situ
Ahmed 2018 (RCT protocol)	1	6 months	NR
Corrigan 2018 (conference abstract, published and in appendix)	24	6 months (50%) 12 months (25%)	NR

Hingwala 2017 (cohort study)	8	NR	Median 146 days (IQR 33.5-1039 days)
Imler 2018 (conference poster)	16	3 months (60.2%) 6 months (38.5%)	NR
Knight 2017 (cohort study)	3	Median 85 days	NR
Kriese 2013 (conference poster)	4	NR	Median 30 days (IQR 20-50)
Kundu 2012 (conference poster)	12	NR	Median 2 months
Lungren 2013 (cohort study)	7	NR	Mean 60 days (IQR 0-796 days)
Macken 2016 (case series)	7	Median 29 days (IQR 8-219)	NR
Monsky 2009 (cohort study)	2	NR	NR
Po 1996 (conference poster)	1	Mean 6 months	NR
Reinglas 2016 (cohort study)	33	NR	Median 117.5 days
Reisfield 2003 (case report)	5	6 weeks/until death	Mean 6 weeks
Riedel 2018 (cohort study with controls)	7	Mean 200 days	NR
Rosenblum 2001 (case series)	9	NR	Mean 255 days
Savin 2005 (cohort study)	4	NR	1810 days
Semadeni 2015 (conference poster)	9	Mean 192 days	Mean 111 days
Solbach 2017 (cohort study)	24	NR	Mean 83.2 days

Duration PIPC remained in situ duration of PIPC in situ varied across studies. Median PIPC duration reported in 9 studies ranged between 6 weeks to 8 months.

Median patient survival also varied across studies. In 6 studies it ranged between 29 days to 6 months.

QOL 1 study assessed QOL (using a questionnaire similar to the Chronic Liver Disease Questionnaire) after PIPC insertion. All patients reported improvements in mobility and daily activities. Nursing staff also stated that it 'benefited and supported earlier placement'.

Key safety findings

Adverse events and complications (n=16 studies)

Infections	**% (n)**
Bacterial peritonitis	17 (29/166)* IQR 0-42%
Bacterial peritonitis (excluding 1 study as an outlier)	11 (15/133)**
Cellulitis at catheter insertion site^	6 (9/147)
Other complications in patients with ESLD	
Minor transient hyponatraemia	11 (16/142)
Rise in creatinine	8 (12/142)
Leakage of ascites at insertion sites (access port site)	8 (12/142)
Catheter occlusion	6 (8/142)
Elevated serum urea (managed by reducing drainage episode frequency)	2 (3/142)
Accidental catheter displacement	1 (2/142)
Others (AKI, haematoma, hepatic encephalopathy of unknown cause, blood stained ascites post insertion) 2 bleeding complications were self-resolved.	3 (1/142)
Complications in studies with mixed RA aetiology	
“catheter malfunction” unspecified	n=5
ascites leakage at incisional site (requiring suture placement)	n=5
temporary occlusions (patency restored using tPA infusion)	n=3
self-limiting ecchymosis	n=3
Complications without RA aetiology	
ascites leakage at catheter insertion site	n=13
unspecified catheter malfunctions	n=5
occluded catheters (3 peritoneal ports with patency restored after administration of tissue plasminogen activator (tPA)	n=5
accidental catheter displacements	n=4
Groin pain	n=2
Abdominal pain	n=1
undiagnosed loculated ascites (due to port failure)	n=1

*14 of these patients in 1 study had catheter related organisms in routine cultures and of uncertain clinical significance.

**4 had PIPC removed and had antibiotics; 8 had antibiotics with PIPC left in situ; 1 was palliated as was end of life, in 2 no subsequent management was described.

^4 mixed cohort studies reported 11 patients with either cellulitis or “local infection”; but underlying aetiology was not reported, therefore they were not included in analysis.

There were no device related deaths.

Study 2 Macken L (2021), Cooper M (2021)

Study details

Study type	Feasibility RCT (REDUCe study ISRCTN30697116)
Country	UK
Recruitment period	2015-2018
Study population and number	36 patients with refractory ascites due to ESLD 17 with long-term abdominal drains (LTAD) versus 19 with LVP.
Age	Mean 66.3 years in LTAD group versus mean 67.9 years in LVP group. LTAD 76% (13/17) male versus LVP 74% (14/19) male
Patient selection criteria	Inclusion criteria: ascites that recurred rapidly after LVP (a minimum of 2 LVPs), requiring 1 or more LVPs/month, age > 18 years, CPS > 9 (unless felt to be palliative despite lower CPS) and capacity to give informed consent. Exclusion criteria: loculated or chylous ascites, > grade 1 hepatic encephalopathy, active infection (SBP) and eligible for liver transplantation.
Technique	LTAD insertion was done in hospital as a day procedure under local anaesthesia and ultrasound guidance. Patients, caregivers, community nursing teams, and primary care physicians were provided guidance on LTAD use. The community nurses did home visits 2-3 times/week, draining 1-2 litres of ascitic fluid at each visit. No human albumin solution was administered. LVP was done in day units or hospital (as per local practice). A peritoneal drain was inserted for up to 6 hours for ascites drainage and intravenous human albumin solution administered (8g -10g per litre of ascitic fluid removed). Antibiotic prophylaxis (ciprofloxacin 500 mg once a day) was offered to all LTAD and LVP patients for the study duration.
Follow up	12 weeks; median 82 versus 86 days
Conflict of interest/source of funding	Study funded by National Institute for Health Research. Rocket Medical provided the LTAD free of cost for the trial but were not involved in the study design.

Analysis

Follow-up issues: high attrition rate, 42% (15/36) patients were lost to follow-up (3 withdrew from study, 12 died outside hospital within 4 weeks [7 in the LTAD group and 5 in the LVP group]). Overall, 9 patients in LTAD group and 12 patients in LVP group completed the study.

Study design issues: feasibility non-blinded RCT across 5 centres (50% patients from 1 centre) with small target sample size. Patients were identified at day-case units or at hospital admissions; randomised to intervention or standard of care using a web based system and allocations were shown after registering a patient. Study success criteria were attrition not >50%, < 50% ascites-related study time in hospital versus LVP group and 80% completion of questionnaire/interviews, <10% LTAD removal because of complications.

Clinical/questionnaire-based assessments were done fortnightly during home visits by research team and recorded electronically. Symptoms were assessed using the IPOS questionnaire, and QOL was assessed

using the SFLDQoL questionnaire, the EuroQol 5 dimensions instrument and carer-reported Zarit 12 questionnaire. For qualitative study, telephone interviews were conducted, data recorded, transcribed verbatim, and analysed using thematic analysis.

Study population issues: The prevalence of hepatic encephalopathy, alcohol aetiology for ESLD and BMI were higher in the LTAD group. Serious comorbidities (n=25, 69%), prior hepatic encephalopathy (n=9, 26%), Child-Pugh C disease (n=7, 20%), hepatocellular cancer (n=6, 18%) and serum creatinine >1.5ULN (n=6, 17%) were reported in some patients.

Key efficacy findings

- Number of patients analysed: 17 LTAD versus 19 LVP
- All LTADs were inserted successfully.

Ascites drainage

	LTAD (n=17)	**LVP (n=19)**
Median amount of ascitic fluid drained/week (litres)	3.85 (IQR 2.85 to 4.51)	4.42 (IQR 3.00 to 6.09)
Median number of visits per week for drainage	1.9 (IQR 0.6 to 2.5)	0.33 (IQR 0.17 to 0.5)
Ascites drainage outside hospital /at home (by nurses/carers)	67% (10/15)	
Further drains at hospital /day unit	33% (5/15) 13 drains (5 non-ascites related, 8 in day unit)	69 drains (64 in day unit, 5 in hospital but 4 were non-ascites related)
Median number of ascitic drains	Before randomisation 5 (IQR 3 -8)	Before randomisation 5 (4, 7)
	After randomisation 0 (0,1)	After randomisation 4 (3, 7)

Biochemical outcomes

	LTAD (n=17)	**LVP (n=19)**
Serum albumin (g/litre), median (IQR)		
Baseline	33(33, 36)	31 (29, 34)
Week 12	29 (26.5, 32.5)	30 (25, 35)
Serum creatinine (micromol/litre) (median, IQR)		
Baseline	109 (79. 141)	113.5 (89, 134)
Week 12	104.5 (81, 115.5)	127 (63, 158)
Serum bilirubin (micromol/litre)		
Baseline	22 (15, 37)	23 (17, 48)
Week 12	17	26

Median survival

	LTAD (n=17)	LVP (n=19)
Median survival at 12 weeks (% (n)	53% (9/17)	63% (12/19)
Median survival in those who died (days)	53 (range 27 to 70)	61%(range 26 to 61)

Patient reported outcomes (questionnaire based assessment)

	n/N	LTAD (mean±SD)	n	LVP (mean±SD)	Mean difference (95% CI)
EQ 5D-5L index					
Baseline	17	0.65±0.30	18/19	0.52±0.28	
12 weeks	8/9	0.59±0.15	12/12	0.57±0.24	0.02 (-0.18, 0.22)
EQ-5D-5L VAS					
Baseline	17	57.6 ±26.7	18/18	54.1± 23.4	
12 weeks	8/9	66.3 28.1	12/12	55.7± 20.8	10.6 (-0.9.2, 30.4)
Zarit Burden Interview 12					
Baseline	9	17.9± 9.4	8	14.6± 8.4	
12 weeks	3	18.0± 11.5	5	20.0± 3.7	-2.0 (-15.1, 11.1)
IPOS -physical					
Baseline	17	10.6± 7.2	18/19	15.6± 5.8	
12 weeks	8/9	14± 6.4	12/12	15.3± 7.6	-1.3 (-8.1, 5.6)
IPOS-emotional					
Baseline	16/17	6.9± 3.2	18/19	6.6± 3.4	
12 weeks	8/9	6.5± 5.1	12/12	4.5± 2	1.6 (-1.4, 5.4)
IPOS-communication					
Baseline	17	2.4±2.9	18/19	2.4±2.6	
12 weeks	8/9	2.4±2.4	12/12	1.8±2.1	0.6 (-1.5, 2.7)
IPOS -patient (total)					
Baseline	16/17	19.2±8.9	18/19	24.5±9.8	
12 weeks	8/9	22.9±10.8	12/12	21.5±8.9	-2.7 (-8.6, 3.1)
SFLDQoL (range 0 to 100; higher scores better)					
Symptoms					
Baseline	17	64.5± 19.8	18/19	49.8± 23.1	
12 weeks	8/9	54.6± 21.2	10/12	53.3± 20.7	1.3 (-19.7, 22.2)
Effect					
Baseline	15/17	58.9± 23.5	17/19	50.5± 24.2	
12 weeks	8/9	61.5± 27.8	10/12	60.4± 26.7	1.0 (-26.3, 28.4)

Memory					
Baseline	17	74.6± 23.3	18/19	67.0± 27.9	
12 weeks	8/9	64.8± 28.7	10/12	74.4± 19.9	-9.5 (-33.8, 14.7)
Distress					
Baseline	17	47.1± 39.7	18/19	37.5± 30.0	
12 weeks	8/9	35.9± 39.8	10/12	58.8± 32.8	-22.8 (-59.0, 13.4)
Sleep					
Baseline	17	57.4± 22.2	18/19	36.0± 21.9	
12 weeks	8/9	45.0± 14.1	10/12	41.5± 15.1	3.5 (-11.3, 18.3)
Loneliness					
Baseline	17	67.1± 19.3	18/19	72.8± 31.5	
12 weeks	8/9	51.9± 30.1	10/12	89.0± 15.6	-37.1 (-60.4, -13.9)
Hopelessness					
Baseline	17	50.0± 26.5	18/19	43.1± 24.6	
12 weeks	8/9	29.2± 27.1	10/12	48.3± 17.9	-19.2 (-41.7, 3.4)
Stigma					
Baseline	17	66.4± 28.7	18/19	61.8± 24.2	
12 weeks	8/9	60.9± 28.1	10/12	64.4± 24.3	-3.4 (- 29.6, 22.7)
Sexual function					
Baseline	17	Not available	19	Not available	
8 weeks	2/13	4.4± 0.1	3/14	2.4± 1.7	

n/N number of patients completing questionnaires /number alive at each visit.

Increasing EQ-5D-5L scores indicate better health outcome.

Increasing IPOS and ZB1-12 scores indicate higher symptom and carer burden respectively.

Increasing SFLDQoL scores indicate better QoL.

Acceptability of LTAD (qualitative study)

14 patients (6 in LTAD and 8 in LVP group) and nurses (n=6) interviewed indicated that LTADs can transform the care pathway for ESLD as a palliative option by enabling care at home, improved symptom control of ascites, personalised care and regular support from community nurses. 5 out of 8 patients in the LVP arm expressed disappointment in not being randomised to the LTAD arm. Nurses expressed the need for additional support if this becomes standard of care (Cooper M 2021).

Key safety findings

	LTAD, n	LVP, n
Serious adverse events		
Death	7	5
Stroke	1	
Fall	1	

Hospital acquired pneumonia	1	1
Hepatic hydrothorax	1	1
SBP	1	2
Worsening renal function	2	1
Hyperkalaemia	1	1
Worsening HE	1	
Acute gastroenteritis	1	
Umbilical hernial leakage	1	
Abdominal pain		1
Hospital admission after LVP		1
Leg fracture		1
Variceal bleed		2
Adverse event (minor, self-limiting, none needing hospitalisation)		
Abdominal pan	5	4
Nausea, vomiting, diarrhoea, and constipation	7	8
Urinary tract infection	2	1
Sacral/vaginal/penis pain/ skin laceration	6	9
Lower respiratory tract/chest infection	3	1
Falls	6	4
Hoarse voice	1	
Oesophageal candida	1	
Pruritis	1	1
Hypotension	1	1
Anaemia/GI bleed	2	4
Hyperkalaemia/ hyponatremia	3	2
Worsening renal function	4	6
Cellulitis /leakage at drainage site	7	
Hepatic encephalopathy	3	
Worsening oedema /breathlessness	2	
Drain accidentally pulled out (24hrs after insertion, declined reinsertion)	1	
Mouth ulcers		2
Epistaxis		2
Increased ferritin		1
Cough/reflex		3
Positive blood culture		1
Bleeding leakage after LVP		2
Increasing bilirubin		1
Fever		1

Hospice admission		1
Hypoglycaemia		2
Umbilical hernia blister		1

Study 3 Kimer N (2020)

Study details

Study type	RCT (NCT03027635 PETRA)
Country	Denmark
Recruitment period	2017-2018
Study population and number	N= 13 patients with cirrhosis and ascites 6 with PIPC versus 7 with LVP and albumin infusion.
Age	Median 68 years (IQR 48 to 77 years); 54% (7/13) male.
Patient selection criteria	Inclusion criteria: adults with cirrhosis and non-malignant recurrent ascites (refractory to medical treatment and with complications) and expected survival of more than 3 months. Exclusion criteria: eligible for TIPS insertion, hepatic encephalopathy or variceal bleeding within 2 weeks, ongoing infection, intraabdominal surgery within 4 months, an increased risk of complications as judged by the healthcare provider.
Technique	PIPC : PleurX (BD Carefusion, UK) tunnelled peritoneal catheter is inserted in 6 patients to allow drainage of ascites < 2 litre per day) in the patients' own home using vacuum containers by home nurses. LVP and albumin infusion done as per clinical guidelines in 7 patients. paracentesis was performed whenever needed throughout the study period, with intervals between 5 and 14 days. Procedures were done under local anaesthesia and x ray/ultrasound guidance by hepatologists. All patients had antibiotics daily. An additional puncture next to the catheter was performed when bacterial colonization was suspected.
Follow up	6 months (median 181 days in LVP group versus 127 days in PleurX group)
Conflict of interest/source of funding	BD Carefusion supported this trial with PleurX bottles and catheters. Study was funded by a grant from Amager-Hvidovre Hospital and from Copenhagen University International Fund. Authors declared that they either received funding for research, lecture fees from companies or served as member of advisory board.

Analysis

Follow-up issues: high attrition rate (1 patient in the PleurX group developed complications before the procedure, 1 patient in each group died, 2 patients in each group withdrew from study because of serious adverse events). Overall, 8/13 patients completed the study.

Study design issues: very limited number of patients were included; randomisation was computer generated and allocation was concealed by using opaque sealed envelopes. Primary outcome was paracentesis free survival. QOL was assessed at baseline and monthly using the CAS score (a 14-item scale assessing ascites related symptoms, with score ranges from 14 to 40, and the higher the score, the worse the burden of symptoms). Patients were monitored for infections and all culture positive samples were repeated after 14 days for verification.

Study population issues: 11 patients had recurrent ascites despite diuretic treatment. At baseline, all patients needed LVP with 6–14 days intervals.

Other issues: the study intended to recruit more patients but was terminated early because of slow recruitment in patients with end stage liver disease and other comorbidities. Many patients did not meet inclusion criteria.

Key efficacy findings

- Number of patients analysed: 6 LTAD versus 7 LVP

Paracentesis free survival

4 patients in each group completed the trial at a median follow-up of 181 days in LVP group and 127 days in LTAD group.

Changes in biochemical outcomes

A moderate fall in plasma albumin levels was observed in the LTAD group compared to the LVP group (median decrease in albumin in LTAD group was 4 g/litre, p=0.07). Intravenous albumin had no clear influence on the albumin levels. No significant changes in plasma sodium (p=0.14) or creatinine levels (p=0.67) were observed during the study period.

Number of paracentesis

Paracentesis In the LVP group: first paracentesis was at 6 to 20 days. During follow-up, patients needed LVP with a median interval of 13 days (range 8–16). The median number of LVPs ranged from 4 to 35 and the median dose of albumin administered at each LVP was 2 portions of 20 g (range 0–4 portions of 20 g).

Paracentesis In the LTAD group: 1 patient needed LVP after 56 days because of clotting of the catheter. The remaining patients had drainage at home using vacuum bottles in amounts not exceeding 2 litre per drainage, with a median interval of 2-5 days. 5 patients in the LTAD group had intravenous albumin for hypotension in 2 patients, hyponatremia in 1 patient and as part of the treatment of SBP in 2 patients. The total median dose of albumin administered was 2 portions of 20 g (range 2–4 portions of 20 g).

QOL

The median CAS score indicated that QOL was poor at baseline (LTAD 19 points and LVP 21 points) and there was no significant difference between the groups during the study period.

Key safety findings

	LTAD group (n=6)	LVP (n=7)
Procedure related complications	**0**	**0**
Mortality		
Terminal liver failure	1	
Head trauma injury		1
Adverse events		
Variceal bleeding		1

Sepsis (patient in LTAD group withdrew before catheter insertion)	1^	2
Hyponatremia (due to frequent use of catheter in 1)	2	
Bacterial peritonitis (infections occurred within 1-4 months and had antibiotics)**	2	1*
Infection of unknown origin		1
Hepatic encephalopathy	1	2*
Hepatorenal syndrome (in the patient with sepsis in LTAD group)	1	2*
Hypokalaemia	1	
Detachment of the catheter from the subcutis (at 56 days, patient withdrew from study)	1^	
Erysipelas		1

^in the LTAD group, 2 patients withdrew from study (1 patient with sepsis and hepatorenal syndrome before catheter insertion and 1 after catheter detachment at 2 months).

*In the LVP group, 2 patients withdrew from study (1 patient with prolonged admission for hepatorenal syndrome and hepatic encephalopathy, 1 patient with bacterial peritonitis after rupture of umbilical hernia).

**In the LTAD group, all patients colonised the catheter but 2 developed bacterial peritonitis. The most common bacterial colonisation was Staphylococcus Epidermidis (n = 4/6).

Study 4 Paparoupa M (2020)

Study details

Study type	Case report
Country	Germany
Recruitment period	NR
Study population and number	N=1 patient with refractory ascites due to cirrhosis of the liver admitted to the intensive care unit because of severe community-acquired pneumonia and implanted with a tunnelled peritoneal drainage catheter.
Age	68 year old male
Patient selection criteria	
Technique	Permanently-tunnelled catheter was placed percutaneously (ASEPT® Peritoneal Drainage System, 15.5 F 5.2 mm×71 cm). The procedure was done under ultrasonographic guidance.
Follow up	12 weeks median 82 versus 86 days
Conflict of interest/source of funding	Authors declare they have no competing interests.

Key safety findings

Ascending colon perforation during implantation of a tunnelled peritoneal drainage catheter

After permanent catheter implantation clear ascites was drained initially but a few hours later, peritoneal fluid could not be removed and bowel content was detected. An abdominal CT confirmed perforation of the ascending colon and the catheter has been passed through the bowel wall and re-entered the peritoneal cavity. No peritonitis or pneumoperitoneum occurred. An emergency laparotomy was performed, catheter was removed and perforation sites were sutured and closed. Patient also had a TIPSS, to manage portal hypertension. However, a relaparotomy with right hemicolectomy was done on the second day, as an insufficiency of the previously sutured perforation sites occurred. The patient died after 2 months in intensive care, as an irreversible malnutrition state resulted in chronic respiratory failure.

Study 5 Elnagar M (2020)

Study details

Study type	Conference abstract (retrospective review)
Country	UK
Recruitment period	2009-2019
Study population and number	N=24 patients had LTAD for refractory ascites. Ascites was secondary to liver cirrhosis in 22 patients and heart failure/cardiac cirrhosis in 2 patients. Median MELD score was 14(range 6–32). Median number of LVP in 6 months before LTAD insertion was 5 (range 0–15), with median interval of 2 weeks. SBP before LTAD treated in 7 patients, 6 remained on prophylaxis.
Age	17/24 male
Patient selection criteria	NR
Technique	LTAD (Rocket catheter) inserted under ultrasound guidance by experienced interventional radiologists.
Follow up	6 months
Conflict of interest/source of funding	Not declared

Key safety findings

Complications following LTAD insertion

Complications	**% (n=24)**
SBP after LTAD insertion (at median 60 days [range 20-45 days]). Treated with antibiotics	62.5% (15/24) (5 of these died)
LTAD removal	
SBP (after median 10 days of antibiotics)	**67% (10/15)**
LTAD replacement and prophylaxis	27% (4/15)
Recurrent SBP	3/4
Leakage	**8% (2/24)**
Blockage	**8% (2/24)**

Validity and generalisability of the studies

- Very limited evidence from small case series and 2 small feasibility RCTs.
- Long-term peritoneal catheter drainage was used for palliative care of patients with focus on symptomatic relief.
- A variety of different indwelling catheters were used.
- Limited data on severity of liver disease, QOL, duration of catheter in situ and patient survival reported in studies.

Existing assessments of this procedure

The British Society of Gastroenterology in collaboration with British Association for the Study of the Liver (Aithal 2020) guideline on the management of ascites in cirrhosis recommends that:

5. Large volume paracentesis (LVP)

5.1. Patients should give informed consent for a therapeutic or diagnostic paracentesis. (Quality of evidence: low; Recommendation: strong)

5.2. Ultrasound guidance should be considered when available during LVP to reduce the risk of adverse events (Quality of evidence: low; Recommendation: weak)

5.3. Routine measurement of the prothrombin time and platelet count before therapeutic or diagnostic paracentesis and infusion of blood products are not recommended. (Quality of evidence: moderate ; Recommendation: strong)

6. Use of human albumin solution (HAS)

6.1. Albumin (as 20% or 25% solution) should be infused after paracentesis of >5 litre is completed at a dose of 8 g albumin/litre of ascites removed. (Quality of evidence: high; Recommendation: strong)

6.2. Albumin (as 20% or 25% solution) can be considered after paracentesis of within 6 hours of diagnosis, followed by 1 g/kg on day 3, is recommended. (Quality of evidence: low; Recommendation: weak)

7. Transjugular intrahepatic portosystemic shunt (TIPSS)

7.1. TIPSS should be considered in patients with refractory ascites. (Quality of evidence: high; Recommendation: strong)

7.2. Caution is required if considering TIPSS in patients with age >70 years, serum bilirubin >50 micromol/litre, platelet count < 75×109 /litre, model for end-stage liver disease (MELD) score ≥18, current hepatic encephalopathy, active infection or hepatorenal syndrome. (Quality of evidence: moderate; Recommendation: strong).

12. Palliative care

12.1. Patients with refractory ascites who are not having evaluation for liver transplant should be offered a palliative care referral. Besides repeated LVP, alternative palliative interventions for refractory ascites should also be considered. (Quality of evidence: weak; Recommendation: strong)

Research recommendation

13.8. Effectiveness and safety of long-term abdominal drains should be assessed in RCTs for the palliative care of patients with cirrhosis and refractory ascites (Aithal GP 2020).

The American Association for the Study of Liver Diseases (AASLD, Biggins 2021) guidance on the diagnosis, evaluation, and management of ascites and hepato-renal syndrome (HRS) in patients with chronic liver disease recommends the following treatment options.

Medical treatment options for refractory ascites

Guidance Statements

•Continued dietary sodium restriction (<2 g/day) is required in patients with RA to reduce the rate of ascites accumulation.

•Fluid restriction is ineffective for the management of RA, but restricting fluid intake to less than 1,000 ml/day is recommended for treatment of hyponatremia (e.g., <125 mEq/litre).

•In the management of RA, there are insufficient data to recommend the long-term use of albumin infusions outside the setting of large- volume paracenteses.

LVP

Guidance Statements

•LVP is the first- line treatment for RA.

•Albumin infusion at the time of LVP of >5 litre is recommended to mitigate the risk of PPCD. The risk of PPCD may increase with >8 litre of fluid evacuated in one single session.

•The recommended dose of albumin replacement, based on expert opinion, is 6-8 g for every litre of ascites removed.

TIPS and Liver Transplantation

Guidance Statements

•Careful patient selection is the key to the success of TIPS in the management of RA.

•A small- diameter coated stent of less than 10 mm is preferred to reduce the likelihood of post-TIPS complications, including hepatic encephalopathy.

•If ascites recurs after initial clearance, a TIPS venogram should be considered, and TIPS revision should be performed if stenosis is identified. In those patients, periodic Doppler ultrasound surveillance should be considered.

•Liver Transplantation should be considered in patients with RA

The European Association for the Study of the Liver clinical practice guidelines (Angeli 2018) for the management of patients with decompensated cirrhosis states that:

Repeated LVP plus albumin (8 g/ of ascites removed) are recommended as first line treatment for refractory ascites (I;1).

Diuretics should be discontinued in patients with refractory ascites who do not excrete >30 mmol/day of sodium under diuretic treatment (III;1).

Patients with refractory or recurrent ascites (I;1), or those for whom paracentesis is ineffective (for example, because of the presence of loculated ascites) should be evaluated for TIPS insertion (III;1).

TIPS insertion is recommended in patients with recurrent ascites (I;1) as it improves survival (I;1) and in patients with refractory ascites as it improve the control of ascites (I;1).

Related NICE guidance

Below is a list of NICE guidance related to this procedure.

IP overview: Long term tunnelled peritoneal drainage catheter insertion for palliation of refractory ascites in cirrhosis

Interventional procedures

- Subcutaneous automated low-flow pump implantation for refractory and recurrent ascites caused by cirrhosis. NICE Interventional procedures guidance 631 (2018). Available from https://www.nice.org.uk/guidance/IPG631

Medical technologies

- PleurX peritoneal catheter drainage system for vacuum assisted drainage of treatment resistant recurrent malignant ascites. NICE Medical technologies guidance MTG9 (2012). Available from https://www.nice.org.uk/guidance/MTG9

NICE guidelines

- Cirrhosis in over 16s: assessment and management. NICE guideline NG50 (2016) Available from https://www.nice.org.uk/guidance/NG50
- Alcohol dependence and harmful alcohol use. NICE clinical guideline 115 (2011). Available from https://www.nice.org.uk/guidance/CG115
- Alcohol use disorders: physical complications. NICE clinical guideline 100 (2010). Available from https://www.nice.org.uk/guidance/CG100

Additional information considered by IPAC

Professional experts' opinions

Expert advice was sought from consultants who have been nominated or ratified by their professional Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by professional experts, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. 3 professional expert questionnaires for long term tunnelled peritoneal drainage

catheter insertion for palliation of refractory ascites in cirrhosis were submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme will send questionnaires to NHS trusts for distribution to patients who had the procedure (or their carers). When NICE has received the completed questionnaires, these will be discussed by the committee.

Company engagement

A structured information request was sent to 6 companies who manufacture a potentially relevant device for use in this procedure. NICE received 2 completed submissions. These was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

- long term ascitic drains (LTAD) also being used in patients with refractory malignant ascites is out of the scope of this review.

- Studies where indwelling catheters were inserted for a short period (2-5 days) were not included in the overview.

Ongoing studies

NIHR133889: Palliative long-term abdominal drains versus repeated drainage in untreatable ascites due to advanced cirrhosis: a randomised controlled trial (REDUCe 2 Study). Location University of Sussex UK (study funded by NIHR HTA)

NCT04569565: Prospective evaluation of PleurX drain for treatment of cirrhotic refractory ascites; interventional study, single group assignment, n=12; indication: cirrhotic refractory or resistant ascites; device used: PleurX catheter; primary outcome: ascites symptom inventory score (ASI-7) [change from baseline to 6 months; study completion date: March 2019; location: Canada; status: completed.

NCT02975726: Peritoneal dialysis catheters for the treatment of refractory ascites management: a randomized un-blinded pilot study; n=2, peritoneal dialysis catheter versus LVP; primary outcome: change in the physical

component of QOL 2 months post intervention; location Canada; study completion date: February 2019; status: completed.

References

1. Macken L, Hashim A, Mason L et al. (2019) Permanent indwelling peritoneal catheters for palliation of refractory ascites in end-stage liver disease: A systematic review. Liver International; 39:1594–1607.
2. Macken L, Stephen B, Heather G et al. Randomised clinical trial: palliative long-term abdominal drains versus large-volume paracentesis in refractory ascites due to cirrhosis. REDUCe study. Alimentary Pharmacology and Therapeutics, 52 (1). pp. 107-122.

   Cooper M, Pollard A, Pandey A et al. (2021) Palliative long-term abdominal drains versus large volume paracentesis in refractory ascites due to cirrhosis (REDUCe Study): Qualitative Outcomes. Journal of Pain and Symptom Management. 62 (2), 321-
3. Kimer N, Riedel AN, Hobolth L et al. (2020) Tunneled Peritoneal Catheter for Refractory Ascites in Cirrhosis: A Randomized Case-Series. Medicina 2020, 56, 565; doi:10.3390/medicina56110565
4. Paparoupa M, Wege H, Creutzfeldt A et al. (2020) Perforation of the ascending colon during implantation of an indwelling peritoneal catheter: a case report. BMC Gastroenterology. 20:345
5. Elnagar M, Lawson A, Taylor N et al. (2020) Long term abdominal drain for refractory ascites: royal derby hospital experience. Gut ;69 (Suppl 1):A1–A51
6. Aithal GP, Palaniyappan N, China L, et al. (2020) Guidelines on the management of ascites in cirrhosis. BMJ Gut, 1-21 Epub ahead of print: doi:10.1136/gutjnl-2020-321790 https://gut.bmj.com/content/gutjnl/early/2020/10/15/gutjnl-2020-321790.full.pdf?with-ds=yes
7. Biggins SW, Angeli P, Gracia-Taso G et al. (2021) Diagnosis, evaluation, and management of ascites, spontaneous bacterial peritonitis and hepatorenal syndrome: Practice Guidance by the American Association for the Study of Liver Diseases Hepatology, Vol. 74, No. 2, 1014-1048
8. Angeli P, Bernardi M, Villanueva C et al. (2018) The European Association for the Study of the Liver. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. J Hepatol, https://doi.org/10.1016/j.jhep.2018.03.024

Literature search strategy

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	20/08/2021	Issue 8 August 2021
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	20/08/2021	Issue 8 August 2021
International HTA database	20/08/2021	n/a
MEDLINE (Ovid)	20/08/2021	1946 to August 19
MEDLINE In-Process (Ovid) &	20/08/2021	1946 to August 19
MEDLINE ePubs ahead of print (Ovid)	20/08/2021	August 19 2021
EMBASE (Ovid)	20/08/2021	1974 to 2021 August 19

Trial sources searched

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1 exp Catheters/32375
2 ((catheter* or drain* or tube* or cannula*) adj4 ("long term" or long-term or permanent or indwell* or tunnel* or abdom*)).tw. 20844
3 (PIPC or LTAD).tw. 332
4 or/1-3 48560
5 exp Ascites/ 16939
6 ascit*.tw. 43470
7 5 or 6 47466
8 4 and 7 540

9	exp Liver Cirrhosis/	93679
10	(Cirrhot* or Cirrhos* or (liver adj4 fibrosis)).tw.	105796
11	exp End Stage Liver Disease/	3476
12	((liver adj4 (disease or failure)) or ESLD).tw.	99183
13	or/9-12	201161
14	8 and 13	100
15	(PleurX or Tenckhoff or Celsite or drainaport*).tw.	678
16	7 and 15	40
17	14 or 16	135
18	Animals/ not Humans/	4842959
19	17 not 18	133

Appendix

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the summary of the key evidence. It is by no means an exhaustive list of potentially relevant studies.

Additional papers identified

Article	Number of patients/follow up	Direction of conclusions	Reasons for non-inclusion in summary of key evidence section
Corrigan M, Thomas R, McDonagh J et al. (2021) Tunnelled peritoneal drainage catheter placement for the palliative management of refractory ascites in patients with liver cirrhosis. Frontline Gastroenterology;12:108–112.	Retrospective cohort study N=25 Cirrhosis, peritoneal, pleural Unspecified indwelling peritoneal catheter.	All procedures were technically successful. 6 patients were readmitted for abdominal pain and suspected infected ascites. There were 3 cases of abdominal wall cellulitis and 3 of leakage around the tunnel site; all managed conservatively.	Included in systematic review added to summary of evidence.
Fukui H, Kawaratani H, Kaji K et al. (2018) Management of refractory cirrhotic ascites: challenges and solutions. Hepatic Medicine: Evidence and Research. 10 55–71	Review	This review briefly summarizes the changing landscape of variable treatment modalities for cirrhotic patients with refractory ascites, aiming at clarifying their possibilities and limitations.	Review
Lungren MP, Kim CY, Stewart JK et al. (2013) Tunneled peritoneal drainage catheter placement for refractory	Retrospective cohort study N=7 ESLD Mixed peritoneal	Mean catheter survival 60 days. Patient survival not reported. Cellulitis reported	Included in systematic review added to summary of evidence.

ascites: Single-center experience in 188 patients. J Vasc Interv Radiol; 24:1303-1308	pleurX inserted under ultrasound guidance. Ascites managed at home.	in 3 with mixed aetiology. "catheter malfunction" in 5, 4 ascites leakage at incisional site (requiring suture placement).	
Macken L, Mason L, Evans C et al. (2018) Palliative long-term abdominal drains versus repeated drainage in individuals with untreatable ascites due to advanced cirrhosis: study protocol for a feasibility randomised controlled trial. Trials 19:401	Study protocol for a feasibility RCT.	plan to recruit 48 patients with refractory ascites and randomise them (1:1) to either (1) LTAD or (2) current standard of care (LVP) for 12 weeks. Outcomes of interest include acceptability of the LTAD to patients, carers and healthcare professionals as well as recruitment and retention rates.	Study protocol.
Macken L, Joshi D, Messenger J, et al. Palliative long-term abdominal drains in refractory ascites due to end-stage liver disease: a case series. Palliat Med. 2017;31(7):671-675.	Retrospective case series N=7 Cirrhosis, peritoneal Rocket IPC inserted managed at home.	Following LTAD, mean hospital attendances reduced to 1 (0-4) from 9 (4-21); with none for ascites management. Median survival after LTAD insertion was 29 days (8- 219). The complication rate was low and non-life-threatening.	Included in systematic review added to summary of evidence.
Ngu NL, Anderson P, Hunter J et al (2021) Short-term intraperitoneal catheters: An ambulatory care intervention for	Case series N=12 patients with cirrhosis and refractory ascites had frequent low-	Median IPC duration was 65-days (IQR: 16.5–93). There were no IPC-related	Larger studies included.

refractory ascites secondary to cirrhosis during COVID-19. JGH Open. 2021 Sep 1;5(10):1154-1159. doi: 10.1002/jgh3.12641. PMID: 34622001; PMCID: PMC8485402.	volume ascitic drainage through a tunneled, Rocket IPC. with 1–2 litre of ascitic fluid drained over 1–3 sessions per week either at the patients' homes or at the hospital day ward over 12-week multidisciplinary ambulatory care program.	deaths. Early removal was necessitated in 3 patients because of leakage, non-adherence, and bacteraemia. On day 30, the median self-reported health score increased from 50 (IQR: 50–70) to 78 (IQR: 50–85), attributable to a reduction in symptom burden.	
Olson JC (2020). Palliative interventions in patients with cirrhosis with refractory ascites and hepatic hydrothorax: who, what, and when? Clinical Liver Disease, 16 (2), 63-65.	Review	This review analyses more recent publications that evaluate the safety and feasibility of certain palliative procedures for management of refractory ascites and HH in selected patients with cirrhosis.	Review
Po C, Bloom E, Mischler L, Raja R. Home ascites drainage using a permanent Tenckhoff catheter. Adv Perit Dial. 1996;12:235-236.	Prospective case series N=1 mixed peritoneal. Peritoneal dialysis catheter inserted surgically. Managed at home by patient.	Median duration of survival 6 months.	Included in systematic review added to summary of evidence.
Reinglas J, Amjadi K, Petrcich B, Momoli F, Shaw-Stiffel T. The palliative management of refractory cirrhotic ascites using the PleurX catheter. Can J Gastroenterol	Retrospective cohort study N=33 patients with refractory ascites (cirrhosis, peritoneal)	Technical success 100%. The median duration catheter in situ was 117.5 days. Drain patency was	Included in systematic review added to summary of evidence.

Hepatol. 2016;2016:4680543.	pleurX inserted under ultrasound guidance. Home care by nurses.	maintained in 90% of patients. s SBP in 38% of patients. The median time to infection was 105 days. All patients had antibiotics.	
Reisfield G, Wilson G. Management of intractable, cirrhotic ascites with an indwelling drainage catheter. J Palliat Med. 2003;6:787-791.	Case report N=5 patients with refractory ascites as a result of liver disease Cirrhosis, peritoneal pleurX tunnelled indwelling peritoneal catheter.	Mean duration of catheter in situ 6 weeks. no evidence of bleeding or peritonitis	Included in systematic review added to summary of evidence.
Riedel AN, Kimer N, Hobolth L, Gluud LL. Prognosis of patients with ascites after PleurX insertion: an observational study. Scand J Gastroenterol. 2018;53(3):340-344	Retrospective cohort study N=7 cirrhotic patients with refractory ascites Mixed peritoneal pleurX tunnelled indwelling peritoneal catheter follow-up 480 days.	Mean survival 200 days.	Included in systematic review added to summary of evidence.
Solbach P, Höner zu Siederdissen C, Taubert R, et al. Home-based drainage of refractory ascites by a permanent-tunneled peritoneal catheter can safely replace large-volume paracentesis. Eur J Gastroenterol Hepatol. 2017;29(5):539-546.	Prospective cohort study N=24 patients with refractory ascites in end-stage liver disease	Placement was successful in all. The number of paracentesis decreased from 2.2 to 0/week, the volume of daily ascites removal remained stable. kidney function, serum sodium, and serum albumin remained stable. Seven adverse events	Included in systematic review added to summary of evidence.

		occurred in six (25%) patients.	