

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No.	Recommendation	Page No.	Relevant text from manuscript
Title and abstract	1	<i>(a)</i> Indicate the study's design with a commonly used term in the title or the abstract	3	A retrospective, observational cohort study comparing effectiveness and safety outcomes of palliative LTAD and regular palliative LVP as a treatment for refractory ascites in consecutive patients with end-stage chronic liver disease followed-up at our UK tertiary centre between 2018 and 2022 was conducted.
		<i>(b)</i> Provide in the abstract an informative and balanced summary of what was done and what was found	3,4	<p>BACKGROUND</p> <p>Long-term abdominal drains (LTAD) are a cost-effective palliative measure to manage malignant ascites in the community, but their use in patients with end-stage chronic liver disease and refractory ascites is not routine practice. The safety and cost-effectiveness of LTAD are currently being studied</p>

in this setting, with preliminary positive results. We hypothesised that palliative LTAD are as effective and safe as repeat palliative large volume paracentesis (LVP) in patients with cirrhosis and refractory ascites and may offer advantages in patients' quality of life.

AIM

To compare the effectiveness and safety of palliative LTAD and LVP in refractory ascites secondary to end-stage chronic liver disease.

METHOD

A retrospective, observational cohort study comparing effectiveness and safety outcomes of palliative LTAD and regular palliative LVP as a treatment for refractory ascites in consecutive patients with end-stage chronic liver disease

followed-up at our UK tertiary centre between 2018 and 2022 was conducted.

Fisher's exact tests and the Mann-Whitney U test were used to compare qualitative and quantitative variables, respectively. Kaplan-Meier survival estimates were generated to stratify time-related outcomes according to the type of drain.

RESULTS

Thirty patients had a total of 35 indwelling abdominal drains and nineteen patients underwent regular LVP. The baseline characteristics were similar between the groups. Prophylactic antibiotics were more frequently prescribed in patients with LTAD ($P = 0.012$), while the incidence of peritonitis did not differ between the two groups ($P = 0.46$). The incidence of acute kidney injury ($P = 0.014$) and ascites/drain-related

hospital admissions ($P = 0.004$) were significantly higher in the LVP group. The overall survival was similar in the two groups (log-rank $P = 0.26$), but the endpoint-free survival was significantly shorter in the LVP group ($P = 0.003$, $P < 0.001$, $P = 0.018$ for first ascites/drain-related admission, acute kidney injury and drain related complications, respectively).

CONCLUSION

The use of LTAD in the management of refractory ascites in palliated end-stage liver disease is effective, safe, and may reduce hospital admissions and utilisation of healthcare resources compared to LVP.

Introduction

Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5,6	In Europe, liver-related mortality has risen from 2.3% of all deaths in 1990 to 3% in 2019 ^[1] . Patients with
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advanced liver disease who are not eligible for transplant frequently need palliative care due to their high risk of death, high burden of symptoms, poor quality of life, and frequent hospitalizations. Early provision of palliative care can lead to improvements in quality of life and reduction of the physical and psychological symptom burden, with the potential for reduced utilisation of healthcare resources and even improved survival for patients with serious illnesses^[2]. Similarly, timely palliative care can improve health-related quality of life and reduce the need for hospitalisation of patients with advanced liver cirrhosis^[3-5]. Ascites remains the most common complication in cirrhosis that necessitates hospitalisation, and progresses to refractory ascites (RA) in up to 30% of cases^[6]. As many as 20% of

patients presenting with ascites die within the first year of diagnosis^[7]. RA is classified as either diuretic resistant or diuretic intractable and, following the onset of RA, patients have a median lifespan of 6–12 months in the absence of liver transplantation^[8]. The current guidelines for the management of RA recommend LVP^[8] with intravenous albumin infusion to decrease the risk of paracentesis-induced circulatory dysfunction^[9]. Although LVP is considered safe, it requires patient-hospital contact as often as weekly and is associated with poor quality of life and malnutrition which, together, increase morbidity and mortality^[8,10,11]. In selected patients with RA, transjugular intrahepatic portosystemic shunt (TIPS) and Automated Low-Flow Ascites Pump System

(alfapump Ò[AP] system) are therapeutic alternatives to repeated LVP^[10,11]. However, TIPS is contraindicated in patients with marked pulmonary arterial hypertension, heart failure, hepatic encephalopathy, coagulopathy, and elevated right or left heart pressures^[12], whereas the alfapump® system is contraindicated in patients with obstructive uropathy, advanced sarcopenia, bed confinement and abdominal skin infections^[13]. Clinical trials are still being conducted to determine the best candidates for the alfapump® device and its cost effectiveness^[14]. Individuals with RA who are not eligible for TIPS or liver transplantation, in particular those with a limited life expectancy, should be considered for palliative care. Repeated LVP is the conventional main treatment in these

cases^[8]. Long-term abdominal drains (LTAD) are tunnelled drains inserted under local anaesthetic, that enable community nurses or trained caregivers to drain small amounts (1-2 L) of ascitic fluid at home, up to three times a week, thus reducing hospital visits and use of healthcare resources^[15,16]. They represent a reliable and cost-effective strategic option in the palliative management of recurrent malignant ascites and are currently being studied as a palliative measure in RA^[16-19].

Absolute contraindications to the insertion of LTAD include loculated or chylous ascites, candidacy for liver transplantation or TIPS, and very short life expectancy, whilst severe renal impairment, previous life-threatening spontaneous bacterial peritonitis and active

infection are considered relative contraindications^[18].

There are currently two types of LTAD available in the UK: PleurXTM, recently rebranded as PeriXTM (UK Medical, Basingstoke, UK) and Rocket[®] (Rocket Medical plc, Watford, UK)^[20].

In 2022, the British Association for the Study of the Liver/British Society of Gastroenterology (BASL/BSG) End of Life Special Interest Group published a consensus to help standardise the use of long-term abdominal drains in cirrhosis, including patient selection and community management^[20]. A recent feasibility trial conducted in the UK compared palliative LTAD with LVP in refractory ascites secondary to advanced liver disease. ^[18] The trial yielded positive results on the efficacy, safety, acceptability, and

				decreased healthcare resource utilisation of LTAD ^[18] . However, pending the results of a national multicentre randomised controlled trial (REDUCe2, ISRCTN26993825), LTAD are currently not used as standard of care in advanced decompensated cirrhosis.
Objectives	3	State specific objectives, including any prespecified hypotheses	6,7	To contribute real-world data to the available scarce evidence, our study aimed to further investigate this subject by retrospectively evaluating the effectiveness and safety of LTAD in comparison with recurrent LVP, which is the current standard of care, in palliated patients with end-stage liver disease and RA followed-up at a UK tertiary centre.
Methods				
Study design	4	Present key elements of study design early in the paper	6,7	Study design This is a retrospective, single centre, observational cohort study aimed at analysing the effectiveness

			and safety of palliative LTAD in comparison with repeat palliative LVP in patients with end-stage liver disease and RA (...)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	(...)Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom, between January 2018 and December 2022.
Participants	6	<p>(a) <i>Cohort study</i>—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up</p> <p><i>Case-control study</i>—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls</p> <p><i>Cross-sectional study</i>—Give the eligibility criteria, and the sources and methods of selection of participants</p>	<p>Patient characteristics</p> <p>All consecutive patients above 18 years of age referred to palliative care owing to end-stage liver disease of any aetiology and RA defined according to the International Ascites Club criteria^[21] (but without loculated, chylous, or malignant ascites), who were not eligible for TIPS and liver transplantation and had undergone palliative treatment of ascites at our centre during the 5-year study period with either repeat LVP or LTAD, were included.</p>
		<p>(b) <i>Cohort study</i>—For matched studies, give matching criteria and number of exposed and unexposed</p> <p><i>Case-control study</i>—For matched studies, give matching criteria and the number of controls per case</p>	

Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	9	<p>Outcomes</p> <p>The primary endpoint was the difference in overall survival between patients with LTAD and patients undergoing repeat LVP. Secondary endpoints were differences in the incidence of drain-related complications in the two groups and endpoint-free survival for first ascites/drain-related hospitalisation, time to AKI (defined as an absolute increase in serum creatinine of at least 26.5micromol/L within 48h or by a >50% increase in serum creatinine from baseline within 7 days, or a urinary output of less than 0.5 ml/kg/hour over >6 hours [23]) and time to drain-related complications between the two groups.</p>
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7	Data was retrospectively collected from electronic patient records to avoid recollection bias, and included: age at diagnosis of RA, aetiology of liver disease, Child-Pugh score

at the time of diagnosis of RA, ascites proteins (as a protein concentration of ≤ 15 g/L in ascitic fluid has been associated with an increased risk of developing spontaneous bacterial peritonitis^[8]), use of diuretics, comorbidities, presence of hepatocellular carcinoma, presence of hepatic encephalopathy, date of LTAD insertion, perioperative complications, baseline creatinine, eGFR and sodium, date of referral to palliative care, use of prophylactic antibiotics, occurrence and date of cellulitis, peritonitis, other localised infections, sepsis, bacteria identified in the case of infection, leakage and bleeding on the site of the abdominal drain, drain displacement, blockage, hypotension, acute kidney injury (AKI), date and reason for hospital admissions, total number of hospital admissions, frequency of ascitic

				drainage per week, litres of ascites drained each time, need for additional LVP, date and cause of death. The presence of shortness of breath, abdominal pain/discomfort, anorexia and poor mobility before and after insertion of LTAD were also evaluated.
Bias	9	Describe any efforts to address potential sources of bias	7	Data was retrospectively collected from electronic patient records to avoid recollection bias
Study size	10	Explain how the study size was arrived at	7	All consecutive patients above 18 years of age referred to palliative care owing to end-stage liver disease of any aetiology and RA defined according to the International Ascites Club criteria ^[21] (but without loculated, chylous, or malignant ascites), who were not eligible for TIPS and liver transplantation and had undergone palliative treatment of ascites at our centre during the 5-year study period with either repeat LVP or LTAD, were included.

Continued on next page

Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9, 10	<p>Kolmogorov-Smirnov and Shapiro-Wilk test of normality were used to assess the distribution of quantitative variables, which were expressed as mean and standard deviation (SD) or median and interquartile range (IQR), as appropriate. Fisher's Exact test and Mann-Whitney U test were used to compare qualitative and quantitative variables, respectively.</p>
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	9, 10	<p><i>Statistical analysis</i></p> <p>Categorical variables were expressed as number and percentage. In the LTAD group, the percentage of patient-related outcomes was calculated using the total number of patients with LTAD as a denominator, whilst the percentage of the drain-related complications was computed using the total number of drains inserted as a denominator. Time 0 of follow-up was considered the time of LTAD insertion (for the LTAD group) or the time of the first LVP since deemed palliative/referred to palliative care (for the LVP group). Data was analysed based on complete case analysis.</p> <p>Kolmogorov-Smirnov and Shapiro-Wilk test of normality were used to assess the distribution of</p>

quantitative variables, which were expressed as mean and standard deviation (SD) or median and interquartile range (IQR), as appropriate. Fisher's Exact test and Mann-Whitney U test were used to compare qualitative and quantitative variables, respectively. Kaplan-Meier survival estimate curves were generated to stratify outcomes according to type of drainage. Patients were censored at death or at the time of last encounter, in case they were alive on 31/12/2022 or lost to follow-up. Statistical analysis was performed using SPSS (v.29.0; IMB® SPSS®, Inc, Chicago, IL). A two-sided *P* value < 0.05 was considered statistically significant.

(b) Describe any methods used to examine subgroups and interactions	10	Kaplan-Meier survival estimate curves were generated to stratify outcomes according to type of drainage.
(c) Explain how missing data were addressed	9	Data was analysed based on complete case analysis.
(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	10	Patients were censored at death or at the time of last encounter, in case they were alive on 31/12/2022 or lost to follow-up.
(e) Describe any sensitivity analyses	N/A	N/A

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, 10	Forty-nine patients met the criteria

		examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed		for this study. Thirty (61%) had LTAD and 19 (39%) were treated with repeated LVP only.
		(b) Give reasons for non-participation at each stage	N/A	N/A
		(c) Consider use of a flow diagram	N/A	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	10, 11, 12	<p><i>LTAD Cohort</i></p> <p>A total of 35 drains were placed in 30 patients. The amount of ascites drained at each home visit was 1-2 litres. The median time with drain in place was 135 (IQR 226) days. This group had a mean age of 71±11 years; 18 (60%) patients were male. The most common aetiology of liver cirrhosis was alcohol (40%), followed by metabolic dysfunction-associated steatotic liver disease (MASLD, 30%). At the time of insertion of the indwelling drains, 9 (30%) patients were classified as Child-Pugh B8, 10 (33%) patients were classified as B9, and 9 (30%) patients were classified as Child-Pugh C.</p> <p><i>LVP Cohort</i></p> <p>The 19 patients in the LVP group had a mean age of 66 ±12 years, and 15 (79%) were male. Alcohol-related liver disease (53%) and MASLD (16%) were again the most common causes of chronic liver disease. Five (26%) patients were classified as</p>

				Child-Pugh B8 and 4 as B7 (21%), while 7 (37%) patients were in Child-Pugh class C. The median drain frequency was 21 (IQR 7) days. The median follow-up time for these patients was 80 days (IQR 239).
		(b) Indicate number of participants with missing data for each variable of interest	N/A	N/A
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	10, 12	The median individual follow-up after decision to provide palliative care was 165 days (IQR 360), for the whole cohort. LTAD Cohort: The median time with drain in place was 135 (IQR 226) days. LVP Cohort: The median follow-up time for these patients was 80 days (IQR 239).
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	10, 11, 12	LTAD Cohort Among the 30 patients in the LTAD group, shortness of breath, abdominal discomfort, anorexia and poor mobility were present in 11 (37%), 21 (70%), 13 (43%), and 24 (80%), respectively. Following LTAD insertion, symptomatic relief of shortness of breath and abdominal pain was seen in 71% and 69% of cases, respectively, while anorexia and poor mobility resolved in 46% and 37% cases, respectively. Data on prophylactic antibiotics

was available for 31 out of the 35 cases of LTAD insertion. Prophylactic antibiotics were prescribed in 25 (81%) cases (Table 1). Ciprofloxacin was the most common choice (88% of cases), while trimethoprim/sulfamethoxazole was prescribed in 2 (12%) cases. One (4%) patient was initially on prophylaxis with ciprofloxacin but was switched to trimethoprim/sulfamethoxazole following development of SBP. Hospital admission due to ascites or drain-related complications occurred in 11 (37%) patients with LTAD. The median time to first admission following insertion of the LTAD was 44 (IQR 93) days. Drain displacement occurred in 4 (11%) cases and prompted drain removal in 3 patients; catheter blockage occurred in 2 (5%) cases, requiring drain removal in 1. Two patients (5%) had self-limiting bleed at the drain site, which did not require hospitalization or removal of the indwelling catheter. Four (11%) patients developed abdominal cellulitis, one of which was also diagnosed with concurrent bacterial peritonitis. Blood and

ascitic cultures yielded multisensitive Gram-positive *S. aureus* for this patient. These infections were treated successfully with antibiotics and resolved without removal of the catheter. Five out of 30 (17%) patients developed bacterial peritonitis (total number of peritonitis episodes 10; 3 patients had a single episode, one patient had 3 episodes and one patient had 4 episodes), despite 2 of them receiving prophylaxis with ciprofloxacin and 1 with trimethoprim/sulfamethoxazole. Among these 5 patients, ascitic fluid cultures detected multisensitive *E. coli*, multisensitive *S. aureus*, multi-resistant coagulase negative staphylococci, *E. cloacae* and *Pseudoglutamicibacter cumminsii*. None of these cases resulted in death.

LVP Cohort

The 19 patients in the LVP group had a mean age of 66 ±12 years, and 15 (79%) were male. Alcohol-related liver disease (53%) and MASLD (16%) were again the most common causes of chronic liver disease. Five (26%) patients were classified as Child-Pugh B8 and 4 as B7 (21%),

while 7 (37%) patients were in Child-Pugh class C. The median drain frequency was 21 (IQR 7) days. The median follow-up time for these patients was 80 days (IQR 239).

Twelve (63%) of the 19 patients in this group were on diuretic treatment, and 8 (42%) were prescribed prophylactic antibiotics (Table 1). In particular, 4 (21%) patients were prescribed ciprofloxacin and 3 (16%) trimethoprim/sulfamethoxazole.

One (5%) patient developed peritonitis whilst on ciprofloxacin and was then switched to trimethoprim/sulfamethoxazole.

Hospital admission due to ascites or drain-related complications occurred in 13 (68%) patients undergoing LVP, with a median time to first admission of 7.5 (IQR 35) days. Two (11%) patients had drain related cellulitis, 1 of which required hospitalization for concurrent confusion. One (5%) LVP was complicated by abdominal wall hematoma requiring interventional radiology-guided embolization of the bleeding vessel. Five (28%) patients developed bacterial peritonitis despite

receiving antibiotic prophylaxis, i.e., 4 patients with ciprofloxacin and 1 with trimethoprim/sulfamethoxazole. In 2 cases, these infections resulted in death. Ascitic cultures identified *E. coli* in one case, while in another case there was no growth despite elevated white cell count on the ascitic fluid and the presence of symptoms compatible with peritonitis. Streptococcus species (*S. orallis*, *S. gordonii* and *S. anginosus*) were isolated in the remaining 3 cases.

Case-control study—Report numbers in each exposure category, or summary measures of exposure

Cross-sectional study—Report numbers of outcome events or summary measures

Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12,13
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Comparison of Outcomes

The comparison of the outcomes of interest in the two cohorts is reported in Table 2. Long-term prophylactic antibiotics were more frequently prescribed in the LTAD group compared to the LVP group (81% vs. 42%; $P = 0.012$). The incidence of peritonitis did not differ between the two groups ($P = 0.46$).

Despite a similar use of diuretics, non-selective beta-blockers, anti-hypertensive, metformin and laxative in the two groups, the

incidence of AKI was significantly lower in patients with LTAD ($P = 0.014$). Furthermore, ascites/drain-related hospital admissions occurred less frequently in the LTAD cohort ($P = 0.004$) (Table 2). Median time to first hospitalisation was also significantly longer in these patients, compared to the LVP cohort (44 vs. 10 days, respectively; $P = 0.002$).

Other clinical endpoints, such as cellulitis, peritonitis, site leakage, bleeding at drain site and hypotension were not significantly different between the groups (Table 2).

The overall survival (since palliation) was not significantly different between the two groups (log-rank $P = 0.26$), Figure 1. Nevertheless, endpoint-free survival was significantly shorter in the LVP group for time to first ascites/drain-related hospitalisation ($P = 0.003$), time to AKI ($P < 0.001$) and time to the development of drain-related complications ($P = 0.018$) (Figure 2).

A “safety” composite endpoint including (1) death secondary to drain-related complications, (2) bleeding at the insertion site, (3)

bacterial peritonitis, and (4) cellulitis was also compared between the two cohorts. Again, this was significantly shorter for the LVP group (log-rank $P = 0.018$) (data not shown).

(b) Report category boundaries when continuous variables were categorized	N/A	N/A
(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A	N/A

Continued on next page

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A	N/A
Discussion				
Key results	18	Summarise key results with reference to study objectives	13	In our single-centre retrospective evaluation of the use of palliative LTAD in comparison with repeat palliative LVP for the management of RA in patients with end-stage liver disease, LTAD was associated with a reduced incidence of AKI, as well as a reduced number of ascites- or drain-related hospital admissions and time to first hospitalisation. Time to the development of AKI and of drain-related complications was also significantly shorter in patients with LTAD.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15, 16	A consensus on the palliative management of patients with decompensated cirrhosis and RA was published only in 2023 ^[24] . Until then, the treatment of these patients exclusively relied upon local standard operating protocols and

the discretion of the individual specialist teams. Accordingly, despite our cohort coming from a single centre, the lack of a unified approach may have resulted in differences in antibiotic prophylaxis, time of referral for LTAD and/or specialist palliative treatment, and management of complications associated with RA. Timing and duration of follow-up might have also led to differences in patients' management, as new technologies and evidence arose between 2018 and 2022. Moreover, the type and dose of diuretics might have changed over time for each individual patient (according to symptoms, creatinine and electrolyte levels), and this may represent a confounding factor. The variable frequency of LVP and amount of ascites removed on each occasion, as well

as the concomitant use of other medications (such as non-selective beta-blockers, metformin, anti-hypertensive and laxatives, although these were not significantly different between the two groups), or possible episodes of hepatic encephalopathy, all of which can favour the occurrence of AKI, are further potential confounding factors. Given the limited sample size, multivariate regression analysis was deemed unsuitable.

The single-centre observational design and the relatively small sample size are limitations of our study that should be taken into consideration in interpreting the results. Larger, more heterogeneous cohorts and randomised controlled trials are needed to validate our findings.

Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14, 15, 16	We found no significant difference in the incidence
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of peritonitis between the 2 groups. All the microorganisms identified were typical for SBP. This is likely the consequence of the more frequent administration of prophylactic antibiotics in patients with indwelling catheters compared to those undergoing LVP (83% vs 42%, $P = 0.012$). In a systematic review from 2019 assessing the use of LTAD in end-stage liver disease^[25], the rates of bacterial peritonitis (BP) varied from 0% to 42% across individual studies, with an overall combined rate of 17%, similarly to our study findings. However, it is unclear whether all reported cases of BP in this systemic review were true BP or there were cases of positive bacterial cultures secondary to colonisation. The more regular follow-up schedule in the setting of a clinical trial and the universal treatment with

prophylactic antibiotics in both groups are likely accountable for the lower rates of peritonitis recorded in the REDUCe study (6% vs 11% in the LTAD vs LVP group, respectively)^[18], compared to real-world data. In the trial, the LTAD group did not show an increased rate of peritonitis compared to the LVP group. The incidence of peritonitis reported in our study may further decrease in the future, as since 2020, antibiotic prophylaxis is prescribed to all palliated patients with RA undergoing LTAD insertion at our centre, as per BSG recommendation^[20]. When comparing the occurrence of complications between the two treatment modalities, there was a significantly lower rate of AKI in the LTAD group ($P = 0.014$) despite similar use of diuretics between the two

cohorts. Previous studies have focused on changes in creatinine over time, which hinders a direct comparison between our findings and other published reports^[25]. Contributing factors to the higher incidence of AKI in the LVP group are likely a higher rate of circulatory dysfunction following drainage of larger quantities of ascites (despite regular administration of intravenous albumin), as well as the higher rate of ascites and drain-related admissions seen in this group, underlining the multifactorial cause of AKI in these patients.

Episodes of leakage and cellulitis were comparable in both groups. These were typically managed with minimal medical intervention and did not require LTAD removal in any of the cases. Though higher rates of site leakage and cellulitis were noted in

the LTAD group in our study (34% and 11%, respectively) compared to the aforementioned systematic review (8% and 6%, respectively)^[25], a comparable incidence of cellulitis/leakage (41% collectively) was observed in the REDUCe study^[18]. There was no significant difference in the overall survival between the LVP and LTAD groups. However, the endpoint-free survival for all other time-related events (time to first ascites/drain-related hospitalisation, time to AKI, and time to drain-related complications) was significantly longer for patients with LTAD. Symptomatic relief of shortness of breath and abdominal discomfort was seen in 70% of cases following LTAD placement, while anorexia resolved in 50% of patients. These findings corroborate the results of

the REDUCe trial, showing that LTAD improves quality of life for patients with RA. Furthermore, the trial has shown that indwelling drains are also cost-effective, as they reduce healthcare resource utilisation and inpatient burden. In fact, median fortnightly total costs were about 15% lower in the LTAD group, as the overall hospital costs were higher in the LVP group^[18]. We did not undertake a cost analysis, as our hospital and community databases are not merged and tariffs for community support workers and community costs were not available. As the REDUCe trial was also undertaken in the UK setting, we would not expect significant differences with regards to costs, in our study.

Generalisability 21 Discuss the generalisability (external validity) of the study results

14, 15, 16

We found no significant difference in the incidence of peritonitis between the 2 groups. All the microorganisms identified

were typical for SBP. This is likely the consequence of the more frequent administration of prophylactic antibiotics in patients with indwelling catheters compared to those undergoing LVP (83% vs 42%, $P = 0.012$). In a systematic review from 2019 assessing the use of LTAD in end-stage liver disease^[25], the rates of bacterial peritonitis (BP) varied from 0% to 42% across individual studies, with an overall combined rate of 17%, similarly to our study findings. However, it is unclear whether all reported cases of BP in this systemic review were true BP or there were cases of positive bacterial cultures secondary to colonisation. The more regular follow-up schedule in the setting of a clinical trial and the universal treatment with prophylactic antibiotics in both groups are likely accountable for the lower

rates of peritonitis recorded in the REDUCe study (6% vs 11% in the LTAD vs LVP group, respectively)^[18], compared to real-world data. In the trial, the LTAD group did not show an increased rate of peritonitis compared to the LVP group. The incidence of peritonitis reported in our study may further decrease in the future, as since 2020, antibiotic prophylaxis is prescribed to all palliated patients with RA undergoing LTAD insertion at our centre, as per BSG recommendation^[20].

When comparing the occurrence of complications between the two treatment modalities, there was a significantly lower rate of AKI in the LTAD group ($P = 0.014$) despite similar use of diuretics between the two cohorts. Previous studies have focused on changes in creatinine over time, which

hinders a direct comparison between our findings and other published reports^[25]. Contributing factors to the higher incidence of AKI in the LVP group are likely a higher rate of circulatory dysfunction following drainage of larger quantities of ascites (despite regular administration of intravenous albumin), as well as the higher rate of ascites and drain-related admissions seen in this group, underlining the multifactorial cause of AKI in these patients. Episodes of leakage and cellulitis were comparable in both groups. These were typically managed with minimal medical intervention and did not require LTAD removal in any of the cases. Though higher rates of site leakage and cellulitis were noted in the LTAD group in our study (34% and 11%, respectively) compared to

the aforementioned systematic review (8% and 6%, respectively)^[25], a comparable incidence of cellulitis/leakage (41% collectively) was observed in the REDUCe study^[18]. There was no significant difference in the overall survival between the LVP and LTAD groups. However, the endpoint-free survival for all other time-related events (time to first ascites/drain-related hospitalisation, time to AKI, and time to drain-related complications) was significantly longer for patients with LTAD. Symptomatic relief of shortness of breath and abdominal discomfort was seen in 70% of cases following LTAD placement, while anorexia resolved in 50% of patients. These findings corroborate the results of the REDUCe trial, showing that LTAD improves quality of life for patients

with RA. Furthermore, the trial has shown that indwelling drains are also cost-effective, as they reduce healthcare resource utilisation and inpatient burden. In fact, median fortnightly total costs were about 15% lower in the LTAD group, as the overall hospital costs were higher in the LVP group^[18]. We did not undertake a cost analysis, as our hospital and community databases are not merged and tariffs for community support workers and community costs were not available. As the REDUCe trial was also undertaken in the UK setting, we would not expect significant differences with regards to costs, in our study.

A consensus on the palliative management of patients with decompensated cirrhosis and RA was published only in 2023^[24]. Until then, the treatment of these patients exclusively relied

upon local standard operating protocols and the discretion of the individual specialist teams. Accordingly, despite our cohort coming from a single centre, the lack of a unified approach may have resulted in differences in antibiotic prophylaxis, time of referral for LTAD and/or specialist palliative treatment, and management of complications associated with RA. Timing and duration of follow-up might have also led to differences in patients' management, as new technologies and evidence arose between 2018 and 2022. Moreover, the type and dose of diuretics might have changed over time for each individual patient (according to symptoms, creatinine and electrolyte levels), and this may represent a confounding factor. The variable frequency of LVP and

amount of ascites removed on each occasion, as well as the concomitant use of other medications (such as non-selective beta-blockers, metformin, anti-hypertensive and laxatives, although these were not significantly different between the two groups), or possible episodes of hepatic encephalopathy, all of which can favour the occurrence of AKI, are further potential confounding factors. Given the limited sample size, multivariate regression analysis was deemed unsuitable.

The single-centre observational design and the relatively small sample size are limitations of our study that should be taken into consideration in interpreting the results. Larger, more heterogeneous cohorts and randomised controlled trials are needed to validate our findings.

Other information

Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1	Funding: Authors have no funding to declare.
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*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.