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Systematic Review

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Long-Term Abdominal Drains as a Therapeutic Option in Refractory Ascites – A Systematic Review

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Keywords
Refractory ascites · End-stage liver disease · Indwelling abdominal drains

Abstract

Introduction: Refractory ascites (RA) is the most common complication of end-stage liver disease (ESLD) with a significant burden in terms of symptoms and overall quality of life (QoL). There are limited therapeutic options available for this population and most ultimately undergo serial large-volume paracentesis (LVP). Long-term abdominal drains (LTAD) are commonly used for malignant ascites drainage but not for ascites related to ESLD, due to concerns about kidney injury and infection. ***Objectives:*** This review aims to describe the safety, effectiveness, and impact on the QoL of LTAD in ESLD-related ascites. ***Methods:*** Using systematic review methodology, PubMed-MEDLINE, Embase, and Google Scholar databases were searched for studies published between January 1, 2001, to June 1, 2024, combining medical subject headings (MeSH) ([cirrhosis OR chronic liver disease] AND refractory ascites AND [permanent-tunneled peritoneal catheter OR tunneled catheter OR indwelling catheter OR long-term abdominal drains]). Inclusion and exclusion criteria were applied to the results. ***Results:*** One hundred thirty-nine studies were identified, with 16 deemed eligible for final analysis, including three randomized clinical trials. The studies varied in design, included different types of LTAD, and were generally of low quality, with many lacking statistical power due to small sample sizes. In terms of effectiveness, technical success was 100%, and as long as LTAD remains in situ, no need for additional LVP is required. Overall, the catheters remained in situ for periods ranging from 3 to 436 days. In terms of safety, kidney injury occurred in 17–50% of patients, but only if >1.5 L/day were drained. Infections, including cellulitis and peritonitis, occurred in 7–58% of patients and were generally resolved with antibiotic therapy and/or device removal. LTAD do not appear to have a negative impact on mortality. Regarding QoL, the data are contradictory with most studies reporting an overall neutral effect. ***Conclusion:*** LTAD should be considered as an option in RA from ESLD in the future but more quality studies are needed to confirm their safety and benefits in controlling symptoms. This could be an important step in terms of improving the palliative needs of this population.

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Drenos abdominais de longa duração como uma opção terapêutica na ascite refratária – uma revisão sistemática

Palavras Chave
Ascite refratária · Doença hepática terminal · Drenos abdominais permanentes

Resumo

Introdução: A ascite refratária é a complicação mais comum da doença hepática terminal condicionando elevada morbilidade e impacto na qualidade de vida. Tendo em conta as opções terapêuticas limitadas, a maioria dos doentes acaba por realizar apenas paracenteses seriadas de grande volume. Utilizados na drenagem da ascite maligna, os drenos abdominais de longa duração, não são tradicionalmente utlizados na ascite relacionada com a doença hepática, devido a preocupações com a lesão renal e infeção. ***Objetivos:*** Esta revisão tem como objetivo descrever a segurança, efetividade e o impacto na qualidade de vida dos drenos abdominais de longa duração na ascite refratária da doença hepática terminal. ***Métodos:*** Usando uma metodologia de revisão sistemática, foi realizada uma pesquisa nos motores de pesquisa PubMed-MEDLINE, Embase e Google Scholar para estudos publicados entre 1 de janeiro de 2001 e 1 de junho de 2024, que combinassem os seguintes termos médicos ([cirrhosis OR chronic liver disease] AND refractory ascites AND [permanent-tunneled peritoneal catheter OR tunneled catheter OR indwelling catheter OR long-term abdominal drains]). Aos resultados foram aplicados os critérios de inclusão e exclusão. ***Resultados:*** Foram identificados 139 estudos, dos quais apenas 16 foram elegíveis para análise final, incluindo três ensaios clínicos randomizados. Os estudos apresentaram uma heterogeneidade significativa entre si e baixo poder estatístico, com diferentes tipos de drenos utilizados e amostras relativamente pequenas. Em termos de efetividade, o sucesso técnico é 100% e enquanto os drenos abdominais de longa duração permanecem in situ não existe necessidade de paracenteses de grande volume adicionais, sendo que os cateteres permaneceram in situ por uma duração entre 3 e 436 dias. No que toca à segurança, a lesão renal ocorreu em 17 a 50% dos doentes, mas apenas se drenados >1,5 litros/dia; a infeção inclui a celulite e a peritonite que ocorreu em 7 a 58% dos doentes, geralmente resolúveis com a antibioterapia e/ou a remoção do dispositivo. Os drenos abdominais de longa duração não parecem ter um impacto negativo na mortalidade. Relativamente à qualidade de vida, os dados entre os estudos parecem contraditórios, sendo que a maioria reporta um efeito global neutro. ***Conclusão:*** Os drenos abdominais de longa duração devem ser considerados no futuro como uma opção na ascite refratária associada à doença hepática terminal, no entanto, estudos de maior qualidade são necessários para confirmar a sua segurança e benefícios no controlo de sintomas. Esta opção poderá ser importante na melhoria das necessidades paliativas desta população.

Introduction

Ascites is the most common complication of advanced chronic liver disease, with an incidence of 5–10% of patients annually in the compensated stage [1]. The main pathophysiological mechanism involved appears to be sodium retention due to overactivation of the renin-angiotensin-aldosterone system and sympathetic nervous system, which culminates in an accumulation of fluid in the extracellular space [1]. The emergence of ascites has a significant impact on quality of life (QoL), and is associated with complications such as bacterial peritonitis (BP), ventilatory dysfunction, abdominal hernias, worsening of renal function, and can result in hospitalization [1, 2]. Initial therapy includes loop diuretics and aldosterone antagonists [1]. However, as liver disease progresses to end-stage liver disease (ESLD), patients may develop refractory ascites (RAs), as this approach becomes ineffective and is hindered by complications.

At ESLD, survival ranges from 6 months to 1 year, with few validated therapies available [1]. Liver transplantation, the most effective treatment, is not feasible for the majority of patients, and many are also unsuitable candidates for transjugular intrahepatic portosystemic shunt. Furthermore, other palliative interventions, such as surgical peritoneovenous shunts, are used sparingly due to the high rate of associated complications [2, 3], while the Alfapump® system is available only in select centers and has a significant complication rate of 85% [1–3]. Consequently, most patients resort to large-volume paracentesis (LVP) as their only option, requiring regular hospital visits lasting several hours, potentially leading to complications (10–15%) such as post-paracentesis circulatory dysfunction and worsening

kidney function, often necessitating albumin replacement [1, 2].

A topic in hepatology that has recently gained prominence is the necessity for palliative care for this population. Similar to other conditions, these patients experience reduced survival rates and a significant symptomatic burden, which greatly impacts their QoL [1, 2, 4]. Given these challenges, the utilization of long-term abdominal drains (LTAD) has emerged as a novel therapeutic opportunity increasingly used in RA associated with ESLD. The use of this approach in the ESLD population is associated with several concerns including the risk of infectious and worsening renal function [2–4].

Objectives

This review aims to describe the safety, effectiveness, and impact on the QoL of LTAD in ESLD-related ascites.

Methods

A systematic review of research articles on the utilization of LTADs for advanced chronic liver disease, published from 1 January 2001 to 1 June 2024, was conducted. The literature search and the verification of inclusion and exclusion criteria were performed by two independent reviewers (D.S., A.G.). An initial search was conducted using PubMed-MEDLINE, Embase, and Google Scholar. Medical subject headings (MeSH) applied were the following: (cirrhosis OR chronic liver disease) AND refractory ascites AND (permanent-tunneled peritoneal catheter OR tunneled catheter OR indwelling catheter OR long-term abdominal drains). The methodology followed Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) recommendations (see online supplementary material at https://doi.org/10.1159/000543713). Screening and testing for eligibility were performed based on English-written abstracts. A grid was constructed to assess articles for eligibility and select them for inclusion, according to specific inclusion and exclusion criteria.

Inclusion Criteria

- English full-text articles from peer-reviewed journals, including online publications ahead of print, within the specified time frame.
- Retrospective and prospective studies, including cohort, case series, case-control, randomized controlled trials and case reports.
- Studies involving adults.
- Studies on the safety, effectiveness, and benefits of LTADs in chronic liver disease-associated RAs.

Exclusion Criteria

- Review articles (systematic and non-systematic), comments, letters, and book chapters.
- Conference abstracts, oral communications, and posters.
- Papers focused on children or adolescents or authored by pediatric institutions.
- Studies on LTADs used only for ascites unrelated to chronic liver disease or those that did not separately report data for chronic liver disease-related ascites.

The full text of selected relevant studies was then evaluated by two researchers (D.S. and A.G.) independently, according to the inclusion criteria described above. Other authors (P.G. and I.C.) intervened in case of disagreement. The quality of the studies was assessed using the Newcastle-Ottawa Scale (NOS), which awarded stars based on factors such as participant selection, comparability of study groups, and outcome measurement.

In this systematic review, the outcomes used to evaluate LTAD were categorized into three domains: effectiveness, safety, and QoL. Effectiveness was assessed by measuring technical success in LTAD implantation and the need for additional LVP while the device remained in situ. Safety outcomes focused on both infectious and noninfectious complications and mortality rates. Finally, QoL was assessed using both subjective and objective methods.

Results

One hundred thirty-nine references were initially identified in PubMed-MEDLINE, Embase, and Google Scholar. After the irrelevant titles were removed, 49 records underwent screening, resulting in 16 eligible articles and 33 exclusions. The study selection process is shown in Figure 1.

NOS quality assessment and limitations for all the 16 articles selected for review are summarized in Table 1. The main characteristics of the articles selected for review are summarized in Table 2.

The included studies presented heterogeneity in design, reported on different types of LTAD, and were generally of low quality, with many having limited statistical power due to small sample sizes. Infection and kidney injury were defined more heterogeneously across the studies. To clarify these definitions, we have summarized them in Table 3.

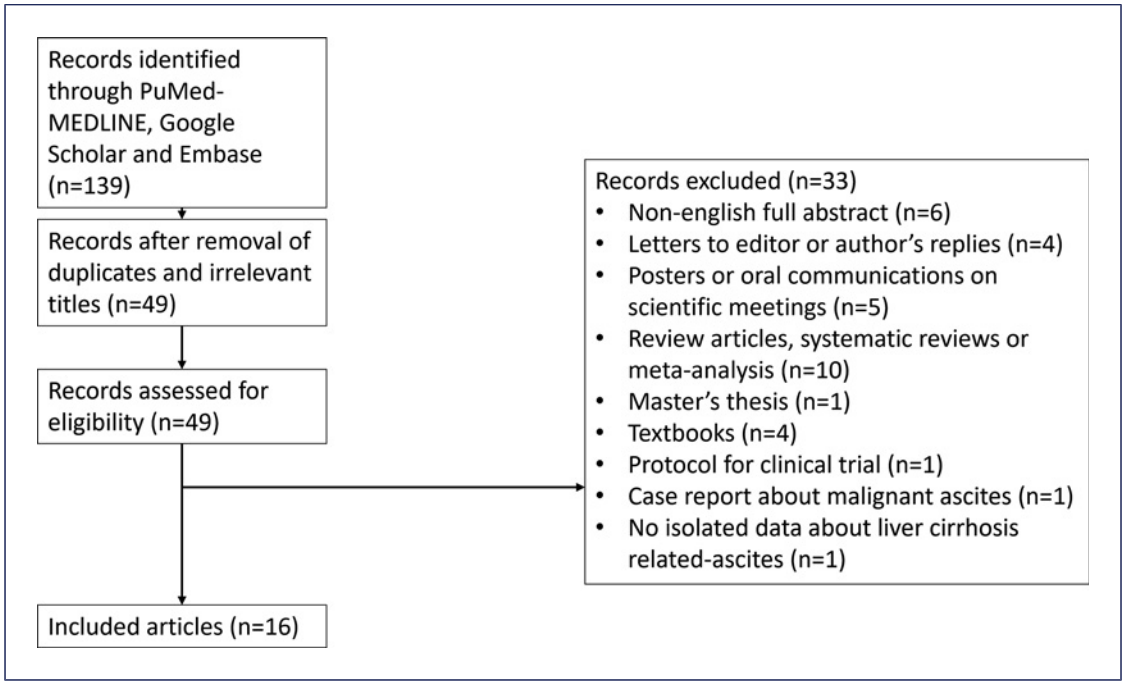

Fig. 1. Flowchart of the search process.

A total of 1,056 patients with ESLD were analyzed, 647 of whom received LTAD. The reported age range across studies spanned from 44 to 83 years. Male patients comprised between 43% and 79% of the sample, while females ranged from 21% to 57%. The underlying etiologies also varied widely. Alcohol-related causes were the most frequent, representing 29–81% of cases. Other common causes included metabolic-associated steatotic liver disease, affecting 16%–41% of patients, and viral hepatitis, which accounted for up to 39% in certain studies. Less common etiologies included cryptogenic causes, autoimmune liver diseases, and other metabolic or cardiac conditions.

Liver disease severity was assessed using the Model for End-Stage Liver Disease (MELD) score in 13 of the 16 studies, with scores ranging from 5 to 31. The Child-Pugh score was employed in 9 studies; among these, 4 reported scores ranging from 5 to 11, while the remaining 4 studies categorized patients by stage, resulting in 61 patients classified as Child-Pugh B and 48 as Child-Pugh C.

Patients were managed in various settings, including at home (n = 440) and in hospitals (n = 185), with some studies not specifying the primary drainage location. Ascites drainage was performed by patients, caregivers, or nurses, though most studies did not specify who conducted the procedure.

Effectiveness

Both non-tunneled and tunneled catheters, with either one or two cuffs, were utilized. LTAD implantation was typically performed by interventional radiologists or hepatologists under ultrasound guidance and occasionally supplemented by fluoroscopy.

Technical success in LTAD implantation was 100% in all analyzed studies, regardless of the catheter type, with PleurX® and Rocket® being the most commonly reported. Although not all studies evaluated effectiveness – defined as the absence of the need for additional drainage via LVP while the LTAD remained in situ – those that did, reported that additional drainage was rarely necessary. When additional drainage was required, it was typically due to transient catheter blockage or dislodgment. In the cohort of 647 patients with LTAD, catheter placement durations ranged from 1 to 436 days.

Safety

Safety was assessed based on complications associated with the device, which can be either infectious or noninfectious, as well as mortality following drain implantation. Infectious complications include primary BP, cellulitis, and secondary BP, while noninfectious complications encompass renal injury, hyponatremia, leakage, blockage, displacement, and hemorrhage.

Table 1. Study design, sample size, and quality of the included studies

Authors, country, and year of publication	Study design	Sample size	Limitations	Newcastle-Ottawa Score
Hingwala et al. [5] Canada 2017	Retrospective cohort	13 patients, 13 with LTAD	Retrospective study; lack of controls; small sample	Poor Quality
Tergast et al. [6] Germany 2023	Retrospective cohort	250 patients, 152 with LTAD	Retrospective study; not differentiate the data between patients with Alfapump® and LTAD	Good quality
Cooper et al. [7] United Kingdom 2020	Randomized controlled trial	14 patients, 6 with LTAD	Small sample	Good quality
Kimer et al. [8] Denmark 2020	Randomized controlled trial	13 patients, 6 with LTAD	Small sample	Good quality
Macken et al. [9] United Kingdom 2017	Retrospective cohort	7 patients, 7 with LTAD	Small sample; retrospective study; lack of controls	Poor quality
Kathpalia et al. [10] United States of America 2015	Retrospective cohort	149 patients, 149 with LTAD	Retrospective study; lack of controls; small sample	Poor quality
Macken et al. [11] United Kingdom 2020	Randomized controlled trial	36 patients, 17 with LTAD	Small sample	Good quality
Ngu et al. [12] Australia 2021	Prospective cohort	12 patients, 12 with LTAD	Small sample; included some patients with ESLD and malignancy	Poor quality
Martin et al. [13] United States of America 2016	Retrospective cohort	36 patients, 36 with LTAD	Small sample; retrospective study; lack of controls; short period of study	Poor quality
Lungren et al. [14] United States of America 2013	Retrospective cohort	188 patients (but only 7 with ESLD), 7 of the ones with ESLD with LTAD	Retrospective study; small sample	Poor quality
Tergast et al. [15] Germany 2022	Retrospective cohort	223 patients, 152 with LTAD	Retrospective study	Good quality
Corrigan et al. [16] United Kingdom 2020	Retrospective cohort	25 patients, 25 with LTAD	Retrospective study; lack of controls; small sample	Poor quality
Riedel et al. [17] Denmark 2018	Prospective cohort	25 patients, 7 with LTAD	Small sample; included some patients without ESLD	Good quality
Reinglas et al. [18] Canada 2016	Retrospective cohort	33 patients, 33 with LTAD	Lack of controls; retrospective study; small sample	Poor quality
Solbach et al. [19] Germany 2016	Prospective cohort	24 patients, 24 with LTAD	Lack of controls; small sample	Poor quality

Table 1 (continued)

Authors, country, and year of publication	Study design	Sample size	Limitations	Newcastle-Ottawa Score
Paparoupa et al. [20] Germany 2020	Case report	1 patient with LTAD	Lack of controls; small sample	Poor quality
647 patients with LTAD, from a total of 1,056 patients with ESLD				

LTAD, long-term abdominal drains; ESLD, end-stage liver disease.

Infectious complications were reported with an incidence ranging from 7 to 58%, with the primary complications being BP and cellulitis at the insertion site. Notably, some authors reported similar rates in control groups [11, 15, 17]. There is no consensus regarding the use of prophylactic antibiotics during LTAD implantation or on the optimal duration of therapy (periprocedural versus throughout the duration of catheter placement). The antibiotics used across studies included quinolones, co-trimoxazole, and cephalosporins. Reinglas et al. [18] reported a higher risk of infection in an uncontrolled study where catheters remained in place for more than 3 months. However, none of the studies were controlled or had follow-up periods longer than 3 months, making it difficult to compare this increased risk to standard care practices. The infection rates varied based on antibiotic use: from 0 to 48% without prophylaxis, 0–58% with periprocedural antibiotics, and 6–33% with maintenance antibiotic therapy. Most infections were managed conservatively with antibiotics, and in some cases, catheter removal was necessary. Secondary BP was also identified as a potential risk by Paparoupa et al. [20].

Concerning noninfectious complications, kidney injury incidence ranged from 17% to 50%. This wide range may be due to the large discrepancy in the volume of fluid drained between studies and the use (or absence) of albumin replacement. Albumin administration was inconsistently reported, and in most studies, it was not routinely used. Only two studies, Kathpalia et al. [10] and Martin et al. [13], routinely administered albumin, with dosages of 8 g and 12 g per liter removed, respectively. Controlled studies also demonstrated a relatively high incidence of kidney injury in control groups. Tergaist et al. [6] highlighted the relationship between fluid drainage volume and kidney injury, estimating a threshold of 1.5 L/day above which the risk of complication significantly increases. Below this threshold, even without albumin replacement, the risk of kidney injury appears to be similar to standard of care, where albumin is routinely administered. Hyponatremia was another noted risk, which, according to Tergaist et al. [6], only becomes apparent after exceeding the 1.5 L/day drainage threshold.

Most studies also reported minor complications such as leakage, blockage, and displacement, which were generally self-limited or resolved conservatively. For instance, was typically resolved with an additional suture at the catheter insertion site, while blockage or displacement was addressed through catheter replacement. The incidence of leakage, obstruction, and displacement ranged from 12 to 29%, 4–17, 6%, and 6–10%, respectively, across the studies. No bleeding complications were reported.

Some authors [15, 19] have noted successful LTAD placement in patients who later underwent liver transplantation, even in cases involving infections related to the device, without significant complications. This suggests that LTAD could potentially be used as a bridge to transplantation in the future, supported by reports involving a total of 10 patients.

Few studies assessed the impact of LTAD on mortality. Riedel et al. [17] reported no impact on mortality. Kathpalia et al. [10] reported a higher mortality rate in patients with BP associated with LTAD. However, it is important to note that no antibiotic prophylaxis was administered during the procedure and that the type of catheter utilized was unspecified. Conversely, Tergast et al. [15] reported a lower mortality (hazard ratio of 0.57 on 90-day mortality) in their cohort of patients with LTAD.

Quality of Life

Few studies assessed QoL using self-reported questionnaires and interviews, with inconsistent results across studies. QoL was measured using scales such as the EuroQol 5-dimensions (EQ-5D), Chronic Liver Disease Questionnaire (CLDQ), Integrated Palliative Care

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Table 2. The main characteristics of the included studies

Authors, country, and year of publication	Catheter used	Albumin use and dosage	Antibiotic prophylaxis	Number of days LTAD remained in situ	Amount of fluid drained	Necessity of additional LVP	Rate of infection	Rate of renal dysfunction	QoL	Other complications or benefits
Hingwala et al. [5] Canada 2017	Argyle™ Peritoneal Dialysis Catheters	Only if drainage of >5 L/day at 6 g of albumin 25% for each liter drained	Yes, but only before LTAD implantation	146	Not reported	Not reported	7% (probably not related to LTAD)	Not reported	Not reported	Not reported
Tergast et al. [6] Germany 2023	Not reported	Not used routinely	Not reported	Not reported	~1.64 L/day	Not reported	Not reported	Increased but only if drained >1.5 L/day	Not reported	Hyponatremia risk increased if drained >1.5 L/day
Cooper et al. [7] United Kingdom 2020	Rocket® LTAD	Not reported	Not reported	Not reported	1-2 L/day on 2–3 times per week	Not reported	Not reported	Not reported	Mixed results on symptom control, evaluated by several questionnaires (IPOS, SFLDQoL, EQ-5D-5L, ZBI-12)	Not reported
Kimer et al. [8] Denmark 2020	PleurX® LTAD	Not used routinely; 83% of patients received for other indications	Yes, daily	127	Up to 2 L/day on up to 3–4 times per week	Yes, in only 1 patient due to clotting of the catheter	33% rate of peritonitis. Responded well to antibiotics. No need to remove the device	0%	There was no difference between the groups in QoL, as measured by the Cirrhosis-Associated Ascites Symptom Score	Hyponatremia, and hepatic encephalopathy, possibly not correlated with the device
Macken et al. [9] United Kingdom 2017	Rocket® LTAD	Not reported	Yes, daily	8–436	Not reported	None	28% rate of cellulitis, one case needing removal of the device	Not reported	Not reported	A case of encephalopathy from unknown origin
Kathpalia et al. [10] United States of America 2015	Not reported	Used routinely with a dosage of 8 g/L removed	Not used routinely	3–5	Up to 3 L drained every 8 h	Not reported	10% rate of peritonitis	Not reported	Not reported	Increased mortality in patients with peritonitis
Macken et al. [11] United Kingdom 2020	Rocket® LTAD	None	Yes, daily	52–90	1-2 L/day on 2–3 times per week	Only 1 patient	6% rate of peritonitis and 23% rate of cellulitis, both rates comparable to LVP	35% of patients had worsening renal function, but similar to controls	Most QoL domains declined in the LTAD cohort, even though interviews suggested that participants found LTAD acceptable and experienced better symptom management	Lower costs in LTAD group

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Table 2 (continued)

Authors, country, and year of publication	Catheter used	Albumin use and dosage	Antibiotic prophylaxis	Number of days LTAD remained in situ	Amount of fluid drained	Necessity of additional LVP	Rate of infection	Rate of renal dysfunction	QoL	Other complications or benefits
Ngu et al. [12] Australia 2021	Rocket® LTAD	None	Yes, daily	77	Up to 2 L 3 times a week	Not reported	11% rate of peritonitis and 11% rate of cellulitis	Not reported	QoL, as measured by self-reported health scores on a visual analog scale, showed improvement, although it was not statistically significant	Not reported
Martin et al. [13] United States of America 2016	Not reported	Used routinely with a dosage of 12 g/L removed	Not used	3	Up to 3 L drained every 8 h for 72 h	None	0%	0%	Not reported	Minor complications only
Lungren et al. [14] United States of America 2013	PleurX® LTAD	Not reported	Yes, but only before the procedure	Not reported	Not reported	Not reported	0%	Not reported	Not reported	Not reported
Tergast et al. [15] Germany 2022	PleurX® LTAD	Not used routinely	Only before LTAD implantation but high incidence of prior SBP precluding daily prophylaxis	Not reported	0.5–2.5 L/day	Not reported	58%, but similar to controls after propensity score matching	21%, but similar to controls	Not reported	No complications in patients with LTAD undergoing liver transplant. Lower mortality in patients with LTAD
Corrigan et al. [16] United Kingdom 2020	PleurX® LTAD	Not used routinely. Periprocedural if >5 L drained at 6–10 g/L drained	Not used routinely	50% patients had LTAD in situ for >200 days	Not reported	Not reported	8% rate of peritonitis and 12% of cellulitis	Not reported	Not reported	No major complications
Riedel et al. [17] Denmark 2018	PleurX® LTAD	Not reported	Yes, routinely only before LTAD implantation but high rate of prophylactic antibiotics for other reasons	2–336	Not reported	Not reported	Approximately 26% rate of peritonitis, similar to controls	0%	No differences in rates of hospital admissions or days hospitalized per month between groups	No differences in mortality. Lower electrolyte disturbances In LTAD patients

Table 2 (continued)

Authors, country, and year of publication	Catheter used	Albumin use and dosage	Antibiotic prophylaxis	Number of days LTAD remained in situ	Amount of fluid drained	Necessity of additional LVP	Rate of infection	Rate of renal dysfunction	QoL	Other complications or benefits
Reinglas et al. [18] Canada 2016	PleurX® LTAD	Not reported	Not used routinely	48–182	2-7 L/week	Not reported	48% rate of peritonitis, including spontaneous and catheter-related peritonitis. Catheter-related peritonitis happened usually 3 months after implantation. 9% rate of cellulitis	17%	Not reported	Minor complications only
Solbach et al. [19] Germany 2016	PleurX® LTAD	Not used	Only before LTAD implantation but high incidence of prior SBP precluding daily prophylaxis	2–222	1.909 L/day	None	8.3% rate of peritonitis and cellulitis	50% had a transient and mild increase in creatinine on week 12	Not reported	5 patients were transplanted after LTAD implantation and none had complications on the follow-up period. Minor and transient risk of hyponatremia at week 4. Increase in appetite
Paparoupa et al. [20] Germany 2020	ASEPT® Peritoneal drainage system	Not reported	Probably already on antibiotics for a pneumonia	1	Not reported	Removed early because of complications	Secondary peritonitis because of a perforation of ascending colon	Not reported	Not reported	Not reported

LTAD, long-term abdominal drains; ESLD, end-stage liver disease; IPOS, Integrated Palliative Care Outcome Scale; SFLDQoL, Sheffield Profile for Liver Disease Quality of Life; EQ-5D-5L, 5-level-5-dimensions-euroqol; ZBI-12, Zarit Burden Interview-12.

Outcome Scale (IPOS), Sheffield Profile for Liver Disease Quality of Life (SFLDQoL), EuroQol-5-level-5-dimensions (EQ-5D-5L), Cirrhosis-Associated ascites Symptom (CAS) score, and Zarit Burden Interview-12 (ZBI-12). Macken et al. [11] and Cooper et al. [7] also conducted interviews with patients and nurses for qualitative data. Riedel et al. [17] extrapolated QoL from monthly hospital admissions and days hospitalized.

Kimer et al. [8] reported that the median CAS score indicated relatively poor health-related QoL at baseline. There was no significant difference between groups throughout the trial.

Riedel et al. [17] reported that for patients with ESLD, the median number of admissions was similar between the LTAD and control groups (0.6 vs. 0.8; $p = 0.40$). The median length of hospitalization was 5.2 days, with no significant difference between LTAD (3.1 days) and LVP (6.6 days; $p = 0.14$).

In Cooper et al. [7], the LTAD group showed mixed outcomes. Physical symptom scores ranged from 1 to 18, with most patients showing stabilization or slight improvement by the final visit. Emotional symptoms scored between 0 and 11, following a similar trend. Communication and practical issues scores started between 0 and 7, with slight improvements or stable results over time. ZBI-12 scores indicated reduced caregiver burden, dropping from 39 to 30. EQ-5D-5L scores varied, with some patients improving (e.g., 0.31–0.34), while others declined (e.g., 0.92 to 0.68). VAS scores also showed variability, with some improving significantly (e.g., 40–90) and others declining (e.g., 70 to 50). SFLDQoL scores showed fluctuation in symptoms, effect, and memory domains, with improvements (e.g., symptoms 63–87) and declines (e.g., effect 63 to 33). Distress and loneliness scores generally stabilized or improved, while sleep, hopelessness, and stigma scores showed varied trends. Ngu et al. [12] reported a rise in the median self-reported health score on a visual analog scale, from 50 (IQR: 30–70) to 78 (IQR: 50–85), though the change was not statistically significant ($p = 0.39$).

In contrast, Macken et al. [11] documented a decrease in QoL in the LTAD group compared to improvements in the LVP group. By week 12, the EQ-5D-5L score in the LTAD group slightly declined to 0.59, while the LVP group increased to 0.57, with a mean difference of 0.02. ZBI-12 scores showed a minor rise in caregiver burden for the LTAD group (17.9–18.0), while the LVP group saw a more substantial increase (14.6–20.0). IPOS-physical scores increased in the LTAD group (10.6–14.0), while decreasing in the LVP group (15.6–12.2). The LTAD group showed a slight decrease in IPOS-emotional scores (6.5), compared to a larger reduction in the LVP group (4.5). Both groups started with a mean IPOS-communication score of 2.4, but by week 12, the LTAD group remained at 2.4, while the LVP group improved to 1.8.

Discussion

LTADs have the potential to transform patient care by enabling home-based ascites drainage. Despite their extensive use in malignancy ascites with significant benefits in symptom burden and QoL, LTADs are not formally recommended for use in ESLD by most hepatology guidelines. However, some centers have begun implementing LTAD for this purpose. In 2022, a consensus document on LTAD insertion, supported by British Association for the Study of the Liver and the British Society of Gastroenterology, was published [4]. Concerns about infectious and non-infectious complications remain the primary barriers to wider LTAD use in ESLD.

Technical success rate appears to be very high across all the studies [5–20], with more recent research reporting that catheters can remain in situ for over a year [9]. Although most of the studies reported shorter catheter duration, it is essential to consider that these patients predictably have a life expectancy of only 6 months following a diagnosis of RA. This approach is generally offered to patients who are not candidates for more effective approaches like liver transplant or transjugular intrahepatic portosystemic shunt. Notably, both Tergaist et al. [15] and Solbach et al. [19] reported no complications in liver transplant patients with LTAD, suggesting its potential as a bridge to transplantation.

Drainage success with LTAD appears promising, as it can reduce diuretic dosage, with additional LVP rarely required. This probably stems from the fact that complications such as blockage or displacement, which could impede drainage, are easily resolved. Thus, LTAD demonstrate effectiveness in facilitating ascites drainage.

The variety of LTAD types, differing implantation protocols and inconsistent use of prophylactic antibiotics contribute to significant variability in outcomes. Furthermore, the amount and frequency of liquid drainage can differ widely and protocols for albumin replacement remain a topic of debate. These factors explain the wide range of complications, including kidney injury and infection rates across studies.

Significant improvements have been made in LTAD devices and their management. Initially, non-tunneled abdominal drains were used, posing a significantly higher

Table 3. Definitions of peritonitis and kidney injury in the included studies

Authors, country, and year of publication	Peritonitis definition	Kidney injury definition
Hingwala et al. [5] Canada 2017	"Peritonitis was defined as having a white cell count of >100 cells/μL with >50% polymorphonuclear leukocytes or a positive ascites culture, cloudy effluent, or abdominal pain"	Not reported
Tergast et al. [6] Germany 2023	Not reported	"Definition of acute kidney injury: increase in sCr ≥0.3 mg/dL (≥26.5 mmol/L) within 48 h; or a percentage increase sCr ≥50% from baseline which is known, or presumed, to have occurred within the prior 7 days"; "Definition of severe acute kidney injury: increase of sCr >threefold from baseline or sCr ≥4.0 mg/dL (353.6 mmol/L) with an acute increase ≥0.3 mg/dL (26.5 mmol/L) or initiation of renal replacement therapy"
Cooper et al. [7] United Kingdom 2020	Not reported	Not reported
Kimer et al. [8] Denmark 2020	Not reported	Not reported
Macken et al. [9] United Kingdom 2017	Not reported	Not reported
Kathpalia et al. [10] United States of America 2015	"Neutrophil count >250/mm^3 irrespective of culture results"	Not reported
Macken et al. [11] United Kingdom 2020	"Increased inflammatory markers, >250/mm^3 polymorphonuclear cells in the ascitic tap and or a positive ascitic fluid culture"	Not reported
Ngu et al. [12] Australia 2021	"Bacterial peritonitis (ascitic fluid polymorphonuclear cell count ≥250 cells/mm^3 and presence of clinical features of infection, for example, fever, abdominal pain), and cellulitis (acute erythema, warmth, and tenderness at the insertion site)"	Not reported
Martin et al. [13] United States of America 2016	Not reported	Not reported
Lungren et al. [14] United States of America 2013	Not reported	Not reported
Tergast et al. [15] Germany 2022	"The diagnosis of spontaneous bacterial peritonitis is based on neutrophil count in ascitic fluid of >250/mm^3"	"Increase in sCr ≥0.3 mg/dL (≥26.5 lmol/L) within 48 h or a percentage increase sCr ≥50% which is known, or presumed, to have occurred within the prior 7 days"

Table 3 (continued)

Authors, country, and year of publication	Peritonitis definition	Kidney injury definition
Corrigan et al. [16] United Kingdom 2020	Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 2017, Peritoneal infection – "A disorder characterized by an infectious process involving the peritoneum."	Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 2017 – Acute Kidney Injury – "A disorder characterized by the acute loss of renal function (within 2 weeks) and is traditionally classified as pre-renal (low blood flow into kidney), renal (kidney damage) and post-renal causes (ureteral or bladder outflow obstruction)"
Riedel et al. [17] Denmark 2018	Not reported	Not reported
Reinglas et al. [18] Canada 2016	"An adverse event was defined as any complication occurring to the patient which could be related to the catheter"	Not reported
Solbach et al. [19] Germany 2016	"The diagnosis of bacterial peritonitis was made on the basis of clinical presentation and ascites cell count (total cell count >500/μL or neutrophil-segmented granulocytes >250/μL)."	Not reported
Paparoupa et al. [20] Germany 2020	Not reported	Not reported

sCr, serum creatinine.

risk of infection [2]. The tunnel creates a wider path between the peritoneal cavity and the skin, within the subcutaneous tissue. Subsequent innovations included the incorporation of cuffs providing additional protection against infection, by promoting granulation tissue growth outside the cuff sealing the tract. Unlike peritoneal dialysis, catheters which have one cuff just outside the peritoneal cavity and the other in the subcutaneous tissue, LTAD usually have only one cuff in the subcutaneous tissue. They also incorporate safety valves to prevent air and fluid from entering and to minimize fluid leakage. These mechanisms prevent infection by hampering the translocation of bacteria from the skin to the peritoneum. Antibiotic prophylaxis was not routinely administered across studies and there is ongoing debate regarding whether it should be solely periprocedurally or continued for maintenance. Standardizing clinical practice, particularly regarding the use of antibiotics, is essential for improving patient outcomes. Infection risk is a major concern in this population due to their known dysfunctions in the neutrophilic and reticuloendothelial systems, as well as low levels of immunoglobulins in ascitic fluid [18]. The primary infections of concern are cellulitis and BP. One study [15] reported a 58% rate of spontaneous BP in patients submitted only to LVP, a procedure typically not associated with such risk. Therefore, caution is warranted when interpreting results from non-controlled studies in LTAD patients, as these may be more attributable to the underlying disease than to device-related factors. So, as rightly mentioned by Macken et al. [4], it is important to exclude spontaneous BP or bacterascites before implanting an LTAD. There is no consensus on the timing for safe implantation after these conditions have been resolved. Additionally, for patients receiving comfort care, prioritizing symptomatic control may be more important.

Another important consideration is that LTAD often induce a local inflammatory response, leading to elevated neutrophil counts in ascitic fluid. This increase may not always indicate infection [8], posing a question that future studies should address. Additionally, the isolation of microorganisms from ascitic fluid drained through LTAD may reflect device colonization rather than contamination from the ascitic liquid itself, a phenomenon that is more likely to occur when devices are in situ for extended periods [8]. Alternatively, a different type of bacterascites

may occur, where the microorganisms originate from the skin rather than the enteric microbiome.

Therefore, to accurately diagnose BP in LTAD patients, it is advisable to perform a diagnostic tap for cell count and culture from both peritoneum and the LTAD, as recommended in the consensus document published [4]. Once BP is diagnosed, it is essential to differentiate between LTAD-associated BP and spontaneous BP. This distinction is crucial, as device explantation and targeted antibiotic therapy against gram-positive microorganisms may be beneficial for the former group. However, most of the analyzed studies do not differentiate between these two subtypes, hampering strong conclusions about the risk of device-related BP in patients with LTAD.

Since granulation tissue growth around the cuffs takes time to develop, the tract is not sealed at the time of the implantation. Therefore, periprocedural antibiotic prophylaxis seems rational despite one study that did not employ it reported acceptable infection rates [16]. Furthermore, as LTAD can potentially lead to BP it is advisable to exclude BP before implantation [4].

It is important to note that most reported infections are easily resolved with antibiotics or through device explantation. Once the infection is addressed, the device can often be safely reimplanted [9].

Kidney injury is a major concern for ESLD patients due to their constant state of relative hypovolemia [1], making them more susceptible to worsening kidney function in the presence of precipitating factors. Additionally, kidney injury worsens the prognosis [1] of these patients, highlighting the importance of preserving kidney function. It is hypothesized that grade III ascites can reduce renal venous flow due to increased intra-abdominal pressure. Furthermore, LVP performed without albumin replacement is associated with deteriorating kidney function, likely due to the rapid drainage of large volumes of fluid over a short period – sometimes exceeding 10 L within a few hours – aggravating the relative hypovolemia state. Therefore, it stands to reason that draining smaller amounts of fluid more frequently may be a safer approach.

Although few of the analyzed studies focused on this subject, LTAD appear to be safe when smaller volumes – particularly <1.5 L/day – are drained 2–3 times a week, even without albumin replacement [6]. In controlled studies [11, 15], kidney injury incidence seems comparable between patients submitted to LVP and LTAD, despite only the LVP group receiving routine albumin replacement. No study has conclusively reported an increased risk of hyponatremia, hepatic encephalopathy, or kidney injury when adhering to these limits and no post-paracentesis circulatory dysfunction have been observed within this range. However, caution is warranted in interpreting these findings, as some LTAD patients have reduced their diuretic dosage while using the devices, whereas some LVP patients have not, which could bias interpretation [19]. Nonetheless, the fact that LTAD patients could reduce their diuretic dosage and did not require additional LVP seems to confer additional protection against kidney injury, given the association between diuretic use and kidney complications. Other complications include leakage (usually self-limiting but can be addressed with an extra suture if it persists), LTAD blockage, or displacement which may necessitate replacement.

Bleeding is another potential complication associated with LTAD, particularly concerning in the ESLD population due to compromised hemostasis [1, 4]. It often originates from the abdominal wall vessels, such as the superior and inferior epigastric arteries, as well as portosystemic collateral vessels. To mitigate this risk, the peritoneal wall is usually accessed, away from the epigastric arteries, which are generally located 4 cm lateral to the umbilical scar. Ultrasound guidance, particularly Doppler, is utilized to ensure avoid vessels in the chosen tract. It is also advisable to check platelet count and coagulation parameters and to discontinue anticoagulants and antiplatelet medications prior LTAD implantation [4]. Despite being a high-risk procedure in a vulnerable population, bleeding rates reported with LTAD implantation are typically low and often self-limiting [4], as our analysis showed.

Rare but severe complications include bowel perforation and death; however, the latter may be attributed to other causes in this specific case [20]. The most recent evidence suggests that LTAD do not negatively affect mortality, likely due to improved periprocedural management [15, 17]. Additionally, several cases documented LTAD use for extended periods [9] supporting the notion of its safety, especially when considering the limited life expectancy of this population.

Paradoxically, it has been reported that Child-Pugh classification and MELD scores, do not correlate with the rate of infection. Thus, LTAD appear to be safe even in patients with advanced disease [18].

Unfortunately, limited studies have focused on assessing the QoL in this population, despite this being a primary objective for the use of these devices. While conducting valid studies in palliative care is challenging, it is essential to implement randomized controlled trials using appropriate scales to assess symptom control in both patients and their families. Only the CAS score is

specifically designed to assess the impact of ascites on QoL, but none of the self-reported questionnaires have been validated in this setting.

Data from analyzed studies are contradictory, with most reporting an overall neutral effect [8, 12, 17] or mixed results on QoL [7]. Additionally, Macken et al. [11] found that most QoL domains declined in the LTAD cohort, despite interviews indicating that participants found LTAD acceptable and experienced improved symptom management. As noted by Macken et al. [11], LTAD studies on malignant ascites similarly show inconsistent QoL improvements in questionnaire-based assessments, despite supportive evidence from qualitative data. These inconsistent results may be attributed to the lack of a validated QoL questionnaire specific to ascites and the chronic, incurable nature of RAs. With proper instruction from healthcare professionals, patients can effectively manage LTAD independently or with the assistance of a caregiver, facilitating more convenient and autonomous ascites drainage. As highlighted Macken et al. [4], the presence of caregivers and supportive social conditions are fundamental to successful device management. Moreover, LTAD may alleviate symptoms by preventing the development of tense ascites, as observed in the LVP approach.

Conclusion

LTAD are an alternative for palliative care in ESLD. Further research is needed to clarify their role as a bridge to transplantation. Caution is advised, as many supporting studies have small sample sizes and are of poor quality, leaving key questions unanswered. Nonetheless, technical advances in catheter design and procedural management have been significant. The ongoing REDUCe2 trial in the United Kingdom is expected to provide important insights into LTAD safety and effectiveness. More research is required, particularly on the impact of LTAD on QoL in ESLD patients, an area that remains underexplored. This review underscores the importance of palliative care in ESLD, highlighting LTAD as a potentially valuable option for RA and urging hepatologists to consider them in palliative strategies.

Statement of Ethics

As this study was a systematic review ethics approval was not required.

Conflict of Interest Statement

The authors declare no conflicts of interest.

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Author Contributions

Diogo Simas and André Gonçalves contributed equally to the conception and design of the study. Both authors independently conducted bibliographic research, screened the articles, and drafted the manuscript. Plácido Gomes, Isabel Caetano, Pedro Russo, and Catarina Martins critically reviewed the manuscript. All the authors approved the final manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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