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REVIEW

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Advancements in ascites management: a comprehensive narrative review of the Alfa Pump system

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Abstract

Ascites remains a significant challenge in patients with cirrhosis, posing difficulties in management and affecting prognosis. This review examines the current understanding of ascites, including its underlying mechanisms, symptoms, and treatment options, with a specific focus on the innovative Alfa Pump device. The review begins by discussing traditional approaches to managing ascites while also addressing their limitations and potential complications. It then explores the emergence of the Alfa Pump system, a novel implantable device designed to tackle refractory ascites by continuously draining fluid from the abdomen while minimizing circulatory issues. Through a synthesis of current literature and clinical evidence, this narrative review underscores the importance of a multidisciplinary approach in the management of ascites, with a particular emphasis on the evolving role of the Alfa Pump in improving outcomes and quality of life for patients with refractory ascites.

Keywords Ascites, Alfa Pump, Diuretics, TIPs

Introduction

Ascites, derived from the Greek word "askos" meaning a bag or sac, is the pathological accumulation of fluid in the peritoneal cavity of the abdomen [1, 2]. Generally, a fluid buildup of 25 mL (about 0.85 oz) is considered ascites [3]. Severe cases can lead to painful breathing and restricted movement [4]. Ascites is a common complication of cirrhosis, occurring in about 50% of patients with cirrhosis, and has a mortality rate of around 50% over 3 years [2, 5, 6]. The prognosis is particularly poor for refractory ascites, with a survival rate of 20% within 1 year [7]. Typically, males have minimal intraperitoneal fluid, while females have around 20 mL, influenced by their menstrual cycle [2].

Ascites can result from portal hypertension (SAAG ratio ≥ 1.1) or non-portal hypertension causes (SAAG ratio < 1.1). Portal hypertension is associated with chronic liver disease (cirrhosis), hepatic congestion, fulminant hepatic failure, Budd-Chiari syndrome, and massive hepatic metastases. Other causes include non-hepatic pathologies such as congestive heart failure, constrictive pericarditis, and tricuspid insufficiency. Non-portal hypertension causes involve hypoalbuminemia (nephrotic syndrome, protein-losing enteropathy, severe malnutrition with anasarca), infections (bacterial,

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tuberculous, fungal peritonitis, HIV-associated peritonitis), and malignancies (peritoneal carcinomatosis, primary mesothelioma, pseudomyxoma peritonei, hepatocellular carcinoma). Other contributing factors include chylous ascites, pancreatic ascites, nephrogenic ascites, urine ascites, ovarian diseases, familial Mediterranean fever, vasculitis, granulomatous peritonitis, and eosinophilic peritonitis. Lifestyle factors include viral hepatitis, alcohol use disorder, intravenous drug use, type 2 diabetes mellitus, and hypercholesterolemia [1, 3, 8].

Ascites pathophysiology involves several theories [9]. The underfilling theory suggests portal hypertension increases fluid filtration from abdominal vessels, reducing blood volume and activating renin and aldosterone, resulting in sodium and water retention. The overflow theory attributes sodium retention to impaired excretion or liver dysfunction, causing fluid buildup [9, 10]. The arterial vasodilation theory (Fig. 1) combines these mechanisms, linking vasodilation with blood volume reduction and sodium retention. The forward theory (Fig. 2) further incorporates increased splanchnic pressure and lymph production [9, 11]. Overproduction of vasodilators like prostaglandin E, prostacyclin, and nitric oxide causes a hyperdynamic state, lowering vascular resistance and raising venous flow, exacerbating ascites [12]. Reduced atrial natriuretic peptide response and increased shear stress elevate sodium retention, leading to complications like hepatorenal syndrome, and hyponatremia in refractory ascites [12–16].

Signs and symptoms of ascites vary based on the etiology. Generally, patients present with abdominal distension, discomfort, weight gain, early satiety, dyspnea, and shortness of breath [2]. Bacterial infections may cause fever, abdominal tenderness, and confusion. Malignant ascites may present with generalized abdominal pain, weight loss, shifting dullness, and a tender abdomen. Peritoneal carcinoma can lead to a palpable Sister Mary Joseph nodule, and upper abdominal malignancy may present with a Virchow node [1, 17]. Heart failure-related ascites presents with dyspnea, orthopnea, peripheral edema, jugular venous congestion, and chest crepitations. Chylous ascites causes diarrhea, steatorrhea, night

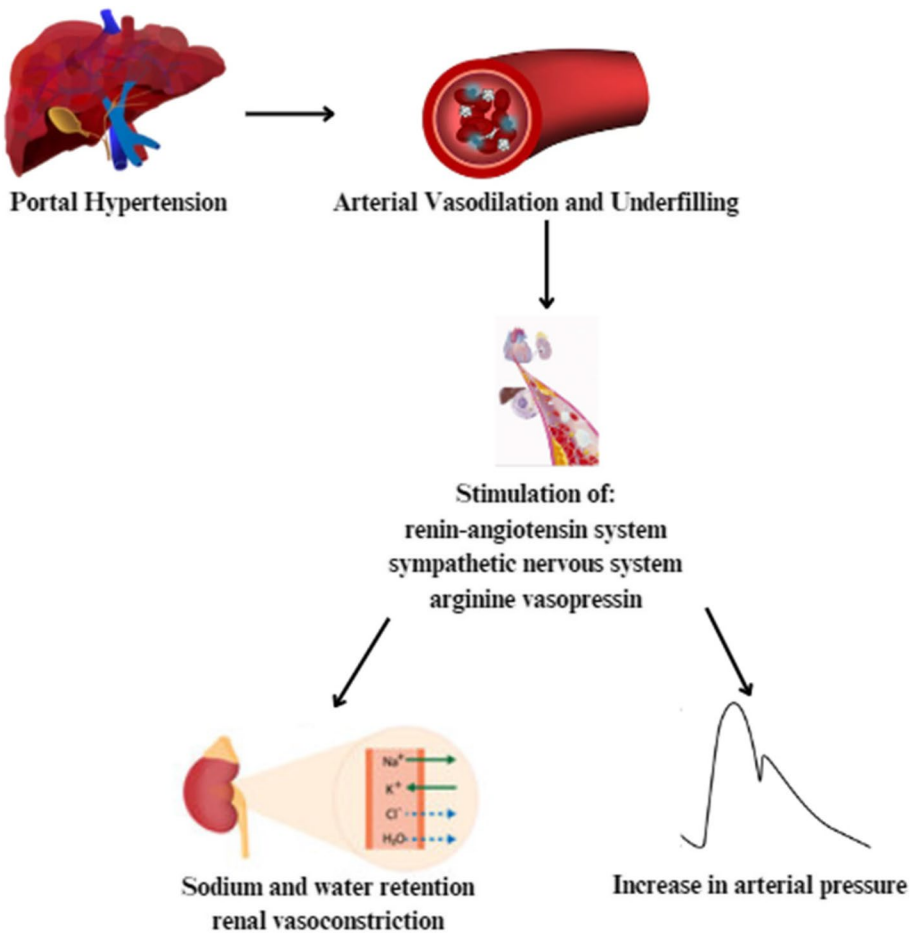

Fig. 1 Theory of arterial vasodilation

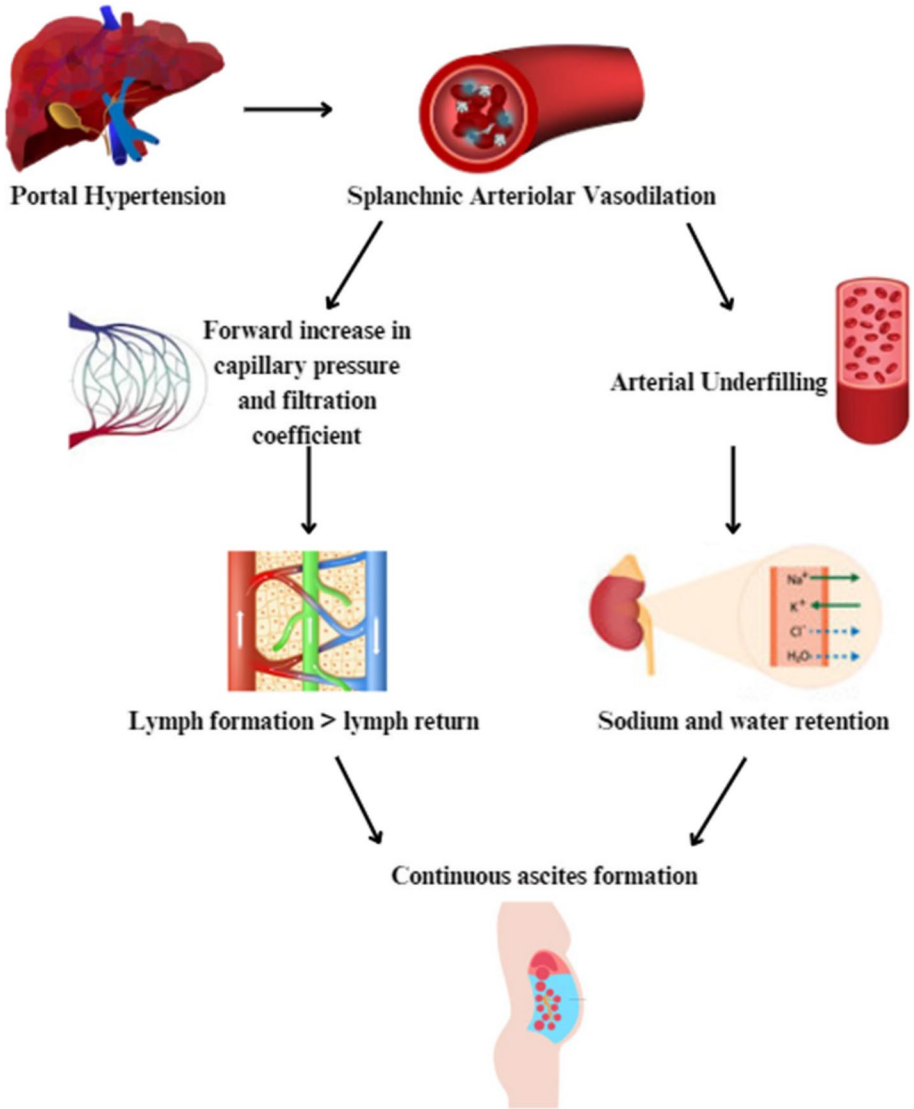

Fig. 2 Forward theory of ascites formation

sweats, fever, nausea, early satiety, malnourished appearance, edema, and enlarged lymph nodes [18]. Hepatic diseases, especially cirrhosis, often present with jaundice, spider angiomata, palmar erythema, muscle wasting, visible abdominal collaterals, and gynecomastia.

Refractory ascites

According to the International Ascites Club, refractory ascites is defined as ascites that cannot be mobilized or recurs early despite medical therapy [21, 22]. Approximately, 10% of ascites patients per year develop refractory ascites due to insufficient natriuretic response to diuretics or diuretic-related side effects [23, 24]. Beyond the typical complications associated with ascites, such as spontaneous bacterial peritonitis, electrolyte abnormalities, and renal dysfunction, refractory ascites introduces additional issues like a constant sense of fullness, decreased appetite, various hernias, nutritional deficiencies, and sarcopenia [24]. Recurrent ascites, defined as ascites recurring at least three times a year despite sodium restriction and diuretic therapy, can be a precursor to refractory ascites [23].

Refractory ascites is diagnosed when ascites cannot be mobilized, recurs within 4 weeks of abdominal paracentesis, and shows a lack of response to maximal doses of diuretics for at least 1 week. Other diagnostic criteria include persistent ascites despite sodium restriction,

mean weight loss of less than 0.8 kg over 4 days, and urinary sodium excretion less than sodium intake [12].

The prognosis for refractory ascites is poor, with complications including dilutional hyponatremia, hepatorenal syndrome, spontaneous bacterial empyema, hepatic hydrothorax, spontaneous bacterial peritonitis, and umbilical hernia. Additionally, patients with comorbidities such as diabetes, age over 60, and hepatocellular carcinoma have reduced survival rates similar to those with general ascites [12].

Current treatments

The treatment and management of ascites depend on its type, severity, and degree of liver failure [19, 20]. Uncomplicated ascites is managed with salt restriction, diuretic therapy, and therapeutic paracentesis. Patients may also be referred for liver transplantation if they have liver cirrhosis. Complicated ascites, which includes conditions like spontaneous bacterial peritonitis, hepatorenal syndrome, or hyponatremia, requires treating these conditions in addition to reducing ascites [25].

There is a spectrum of treatment options for refractory ascites. These include well-established approaches such as large volume paracentesis, transjugular intrahepatic portosystemic shunt (TIPS), peritoneovenous shunt, and the use of vasopressin receptor antagonists (vaptans) [25, 26]. Large-volume paracentesis (LVP) is the first-line treatment of refractory ascites. Plasma volume expansion is needed to prevent post-paracentesis dysfunction [27]. LVP provides only transient alleviation of symptoms associated with ascites. It can also lead to circulatory dysfunction after paracentesis requiring albumin infusions. Moreover, the need for frequent hospital visits associated with LVP results in a diminished quality of life and substantial costs. It had been shown that compared to large volume paracentesis, TIPS resulted in a greater reduction in the ascites volume and the need for repeated paracentesis. TIPS placement induces decompression of the portal circulation by shunting an intrahepatic portal branch into a hepatic vein [22]. This causes a decrease in portal pressure which [28, 29] leads to improvement in systemic hemodynamics and increased effective blood volume, thereby improving renal perfusion and favoring salt and water excretion as early as 4 weeks after TIPS insertion [28]. However, it was associated with hepatic encephalopathy and cardiac decompensation [46]. Tolvaptan, a vaptan, is a V2- receptor blocker that reduces the expression of aquaporin-2 and inhibits water reabsorption in the collecting ducts [31]. Recent studies and meta-analysis show that tolvaptan is effective in the treating refractory cirrhosis particularly in those with underlying liver cirrhosis and hepatitis C. However, further studies need to be carried out to establish greater efficacy of tolvaptan [31, 32].

Even with these treatment options, liver transplantation remains the only curative treatment [12]. Following LT, clinical ascites can be present for 3 to 4 months. It is therefore crucial that patients continue to adhere to their low-sodium diet post-transplantation until ascites is eliminated [30].

Given the grim situation of treatments for refractory ascites, it is essential to explore and invest in modern solutions.

Automated low-flow ascites pump (Alfa Pump)

A promising and beneficial novel treatment option has emerged in the form of the automated low-flow ascites (ALFA) pump, offering a new dimension in managing refractory ascites. The Alfa Pump is frequently regarded as an effective treatment option for refractory ascites in patients who are not suitable candidates for TIPS and LVP, particularly those awaiting liver transplant. Currently, the Alfa Pump is approved for use in refractory liver ascites and malignant ascites. The United States Food and Drug Administration has also granted the Alfa Pump for treatment of recurrent ascites [35]. Alfa Pump is a class III medical device that is implanted and designed to facilitate the automated movement of ascitic fluid from the peritoneal space to the urinary bladder, where it is subsequently expelled. The device can be implanted within 1 h under general or local anesthesia, and once implanted, it can be charged wirelessly through a handheld charger that also allows for the personalized programming and monitoring of the device. The charger is placed positioned over the pump area twice daily for a maximum duration of 20 min each time [33–37].

In 1998, Rozenblit and coauthors introduced the initial mechanical device aimed at actively transferring ascites from the peritoneal cavity to the urinary bladder. Despite this, none of these systems has achieved widespread clinical applicability primarily due to technical challenges [37, 38]. The inaugural prototypes were developed in 2005, and the founders illustrated the technical viability of the method.

The Alfa Pump made its debut in 2011 [39]. A pivotal clinical trial for market introduction is currently in progress in the USA and Canada (POSEIDON; NCT03973866), with an expected completion date in 2024. The device enjoys full reimbursement in Switzerland and holds innovative treatment status (NUB status 1) under specific conditions in Germany. In Israel, reimbursement is available under certain circumstances. In the UK, usage is recommended with special considerations for clinical governance, consent, audit, or research [41, 42].

Mechanism

The Alfa Pump is an implantable pump system that is designed to move ascitic fluid from the abdominal cavity to the urinary bladder through catheters specially routed into the peritoneal and bladder. Alfa Pump removes 500 mL to 2.5 L per day. Four pressure sensors within the Alfa Pump monitor abdominal and bladder pressure, offering insights into flow rate and system dynamics. The pump initiates a pumping cycle only when the bladder pressure falls below a specific threshold. Simultaneously, pumping ceases promptly if the peritoneal cavity pressure experiences a significant drop, indicating insufficient accessible fluid for the Alfa Pump [40] (Fig. 3).

The Alfa Pump employs a gear pump, where fluid is propelled forward between rotating gears to achieve the desired volume. This requires a specific number of motor turns, coupled with motor speed, determining the Alfa Pump's flow rate. As ascites is transported, it passes through multiple pressure sensors, with changes in their values confirming the active movement of fluid.

The overseeing physician for a patient with an implanted Alfa Pump utilizes the Alfa Pump programmer—a computer equipped with flow control software. Flow control allows for the programming of the target daily volume, pumping schedule, frequency, and the ability to toggle the Alfa Pump on and off [43].

It is important to provide pre- and postimplantation care to the patients. Mostly, the patient undergoes hospitalization 24–48 h before the implantation procedure. Paracentesis is carried out to confirm the absence of ongoing spontaneous bacterial peritonitis and to drain the abdomen. It is essential to retain 1–2 L of ascites before implantation to verify the proper functioning of the pump before surgical closure and to reduce the risk of ascitic fluid leakage. Intravenous antibiotic prophylaxis is initiated on the day of implantation and continued for 48 to 72 h. The consideration of nonselective beta-blockers should also be reassessed in each patient who is preselected for Alfa Pump implantation in accordance with existing guidelines [44, 45].

Effectiveness

Among patients who had underwent Alfa Pump implantation, 62% no longer required large volume paracentesis, showcasing a noteworthy decrease in the need for this procedure over time (average follow-up time ranging from 6 to 24 months) [47]. The study cited acute kidney injury (AKI) and poor circulatory tolerance after pump insertion as safety issues hindering the pump's efforts in controlling ascites. Notably, the reduced reliance on paracentesis correlated with an early and sustained enhancement in nutritional status. In the study conducted by Bureau et al., a significant improvement in brachial circumference, tricipital skinfold thickness, and hand grip strength was observed during the initial 3 months following Alfa Pump placement when compared to the control group [48–50].

Survival outcomes with the Alfa Pump system have not been explicitly evaluated in the existing published studies. However, a recent meta-analysis indicates that

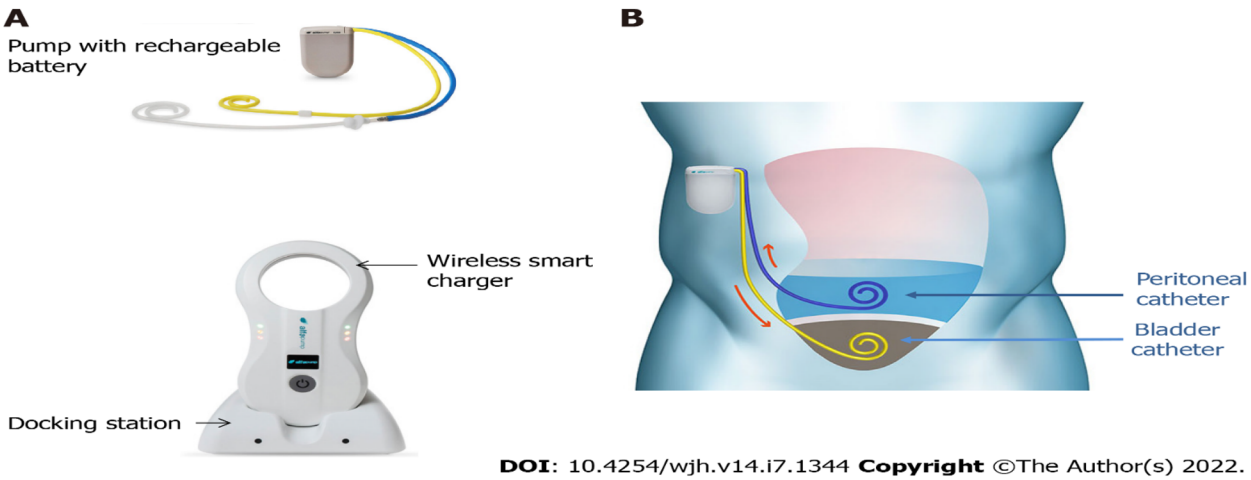

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Fig. 3 Alfa Pump® device and principles of its implantation. **A** The system consists of the following: (1) A pump, which contains a rechargeable battery and is connected to a peritoneal catheter and a bladder catheter, and (2) charging accessories. The charger collects information and charges the pump through transduction; the docking station must be connected to the electrical network. **B** The pump is positioned subcutaneously, under the costal margin (preferably on the right side), so that the patient is not hindered when sitting. The bladder must be full at the time of insertion of the bladder catheter; conversely, only a small amount of ascites is left in place for insertion of the peritoneal catheter, so that the pump can be tested before parietal closure. Images courtesy of Sequana Medical

survival is at least comparable to that of patients undergoing large-volume paracentesis (LVP) [51, 52]. In a prospective study documenting the real-world, long-term (24-month) use of the Alfa Pump in 106 patients ineligible for TIPS insertion, the median survival was reported as 10.1 months [53].

Alfa Pump insertion is generally safe and successful, thereby improving nutrition and quality of life of patients [50, 54]. A total of 20–30% of the patients may develop AKI, spontaneous bacterial peritonitis (SBP), and/or urinary tract infection (UTI) [33, 41, 47, 55]. There is also an elevated risk of developing electrolyte abnormalities and postoperative bleeding. Additionally, patients may encounter issues related to device malfunction including catheter and pump dysfunction, potentially necessitating re-intervention [33, 47, 49, 56].

Other uses

A study performed in 2018 highlighted the use of Alfa Pump in those with malignant ascites. Since most patients with malignant ascites have a preserved liver function, the Alfa Pump can be used in such patients who also have a life expectancy greater than 6 months. Unlike in cirrhosis patients, these patients have a decreased risk of typical cirrhosis-associated complications like spontaneous bacterial peritonitis, esophageal variceal bleeding, or a decreased synthetic liver function [57].

Contraindications

The implantation of the Alfa Pump device is absolutely contraindicated in cases of loculated ascites, untreatable obstructive uropathy, the presence of an active bacterial infection during implantation (especially spontaneous bacterial peritonitis, urinary infection, or abdominal skin infection), and an expected survival of less than 3 months. It is crucial to exercise special caution with frail patients, and their nutritional status should be thoroughly evaluated and optimized before considering implantation [58].

Cost

The expenses associated with the Alfa Pump encompass the device's current cost (EUR22,500), operating room fees, and the costs related to a brief hospital stay [37] Given the promising results of the Alfa Pump, further investment and consideration in this direction can revolutionize the landscape of ascites treatment and management.

Conclusion

Ascites can present with a wide array of symptoms, from simple to complex cases, thereby offering a spectrum of available treatment options. The newly implemented Alfa Pump has since shown promise for the treatment of refractory ascites. Its ability to improve fluid management may result in a tailored-treatment approach by resulting in fewer hospital stays and a higher quality of life, all while supporting optimal nutritional status. Additionally, the device's prospective cost savings, even after initial implementation, further boost its appeal as an encompassing ascites management solution. However, it is important to note that despite its emerging success, additional research is needed to effectively evaluate its long-term efficacy and safety in various diverse patient populations. Furthermore, factors including affordability and accessibility might have an impact on how widely the Alfa Pump may be used in existing healthcare environments. As we conclude, the beneficial aspects highlighted by current findings should be balanced with a commitment to addressing these limitations to allow a thorough and well-informed integration of the Alfa Pump in clinical practice.

Disclaimer

The authors declare that this work is original and backed by scientific research and facts.

Authors' contributions

All authors contributed to and reviewed the publication, critically revised the manuscript, approved the final version to be published, and agreed to be accountable for all aspects of the work.

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Availability of data and materials

All data analyzed during this study are included in the published article.

Declarations

Competing interests

The authors declare that they have no competing interests.

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