Improvement in Quality of Life and Decrease in Large-Volume Paracentesis Requirements With the Automated Low-Flow Ascites Pump

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The automated low-flow ascites pump (alfapump) is an implantable device that drains ascites directly into the urinary bladder. We studied its safety (absence of serious complications) and efficacy (decreased large-volume paracentesis [LVP] requirement and improved quality of life [QoL]) in the management of ascites in a cohort of North American patients with cirrhosis and recurrent ascites ineligible for transjugular intrahepatic portosystemic shunt (TIPS). QoL was measured by the Chronic Liver Disease Questionnaire (CLDQ) and Ascites Questionnaire (Ascites Q). Following alfapump implantation, patients were monitored for ascites control, laboratory abnormalities, QoL, adverse events, and survival at 12 months. A total of 30 patients (60.0 ± 9.9 years; 57% male; Model for End-Stage Liver Disease score, 11.4 ± 2.7) received an alfapump, mostly by an interventional radiology approach (97%), followed by longterm prophylactic antibiotics. The alfapump removed a mean ascites volume of 230.6 ± 148.9 L/patient at 12 months, dramatically reducing the mean LVP frequency from 2.4 ± 1.4/patient/month before pump implantation to 0.2 ± 0.4/patient/month after pump implantation. All surviving patients had improved QoL (baseline versus 3 months; CLDQ, 3.9 ± 1.21 versus 5.0 ± 1.0; Ascites Q, 51.7 ± 21.9 versus 26.7 ± 18.6; $P < 0.001$ for both) and a better biochemical index of nutritional status (prealbumin 87.8 ± 37.5 versus 102.9 ± 45.3 mg/L at 3 months; $P = 0.04$). Bacterial infections (15 events in 13 patients), electrolyte abnormalities (11 events in 6 patients), and renal complications (11 events in 9 patients) were the most common severe adverse events. By 12 months, 4 patients died from complications of cirrhosis. Alfapump insertion may be a definitive treatment for refractory ascites in cirrhosis, especially in patients who are not TIPS candidates.

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The appearance of ascites in cirrhosis heralds the onset of decompensation[1]; predisposes the patient to the development of bacterial peritonitis, hyponatremia, and acute kidney injury (AKI)[2]; and reduces survival.[3] Abdominal fullness leads to early satiety, reduced caloric intake, and eventual malnutrition, whereas tense ascites predisposes the patient to the development of hernias with their specific complications. Patients with ascites therefore have a poor quality of life (QoL).[4]

The treatment of ascites refractory to diuretic therapy[5] is either repeated large-volume paracentesis (LVP) with albumin infusions,[6] or the insertion of a transjugular intrahepatic portosystemic shunt (TIPS) in the appropriate patient.[7] The definitive treatment for difficult-to-control ascites with liver dysfunction is liver transplantation. However, patients with ascites

Abbreviations: AE, adverse event; AKI, acute kidney injury; alfapump, automated low-flow ascites pump; ALP, alkaline phosphatase; ALT, alanine aminotransferase; Ascites Q, Ascites Questionnaire; AST, aspartate aminotransferase; CLDQ, Chronic Liver Disease Questionnaire; GI, gastrointestinal; HE, hepatic encephalopathy; INR, international normalized ratio; LVP, large-volume paracentesis; MELD, Model for End-Stage Liver Disease; MOSAIC, Multicenter, Open-Label Study of the Alfapump System in Cirrhosis With Recurrent Ascites; NASH, nonalcoholic steatohepatitis; PI, principal investigator; QoL, quality of life; SAE, serious adverse event; SBP, spontaneous bacterial peritonitis; SD,

standard deviation; TIPS, transjugular intrahepatic portosystemic shunt; UTI, urinary tract infection; WBC, white blood cells.

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and a low Model for End-Stage Liver Disease (MELD) score have a low priority for liver transplantation.[8] Thus, many patients are dependent on LVP as the only means of managing their ascites, which imposes a significant health care burden without improving their longterm QoL.

The automated low-flow ascites pump (alfapump; Sequana Medical NV, Ghent, Belgium) is a subcutaneous, implantable, and rechargeable device that automatically transfers ascitic fluid into the urinary bladder, which is then discharged as urine. The device effectively carries out a continuous low-rate paracentesis for approximately 16 hours per day.[9] With an expected battery life of 3 years or more, the alfapump can potentially keep patients relatively ascites free, but there are concerns of increased infection risks.[10] Therefore, the aims of this first feasibility study in North America in patients with recurrent ascites were to determine the safety of the alfapump system as measured by the absence of serious complications related to the device and to evaluate the efficacy of the pump as measured by reduction in the requirement for LVP and improvement in QoL using Chronic Liver Disease Questionnaire (CLDQ)[11] and Ascites Questionnaire (Ascites Q).[12]

Patients and Methods

The Multicenter, Open-Label Study of the Alfapump System in Cirrhosis With Recurrent Ascites (MOSAIC) study was a prospective, open-label, feasibility study, approved by the Food and Drug Administration in the United States and by the Medical Devices Bureau of Health Canada, conducted in these countries to determine whether it was feasible to implant this device and use it as a tool to control ascites in patients with cirrhosis. Therefore, no control group was included in the design of the study. The ethics committees of all participating centers approved the study (www.clinicaltrials.gov, number NCT02400164). All authors had access to the study data and approved the final manuscript.

Adult patients with cirrhosis aged above 21 years requiring ≥1 LVP per month for a minimum of 2 of the prior 3 months despite diuretics were assessed for the study. Other inclusion criteria were ineligibility for or refusal of TIPS insertion, expected survival of >3 months, and MELD score ≤21. Ineligibility for TIPS insertion was left to the discretion of the principal investigator (PI) at each site and could include

a past history of spontaneous encephalopathy, age above 70 years, cardiac failure, pulmonary hypertension, or technical issues, such as total occlusion of portal vein or polycystic liver disease. Exclusion criteria were loculated ascites, >2 systemic or local abdominal infections in the previous 6 months, recent intra-abdominal surgery, history of bladder cancer, ischemic or inflammatory bowel disease, urinary bladder outlet obstruction, functioning TIPS or surgical portosystemic shunt, previous solid organ transplant, serum bilirubin of >85 μmol/L (5 mg/dL), serum creatinine >132 μmol/L (1.5 mg/dL), estimated glomerular filtration rate <30 mL/minute/1.73 m^2; hepatic encephalopathy (HE) greater than stage 2 in the prior 2 weeks, spontaneous bacterial peritonitis (SBP), or urinary tract infection (UTI) within 24 hours of alfapump insertion. All patients signed informed consent.

ALFAPUMP INSERTION

Of the 30 enrolled patients, 29 (97%) received their alfapump via an interventional radiological approach under either intravenous sedation or general anesthesia (1 patient had surgical implantation). This interventional radiology approach was different from the insertion technique used in all European countries when the alfapump was inserted via a surgical approach. Under ultrasound guidance, the peritoneal catheter was inserted into the right lower quadrant, followed by insertion of the bladder catheter immediately superior to the pubic symphysis. A pocket was then created in the upper quadrant of the abdomen between the skin and muscle layers to house the alfapump. Both the peritoneal and bladder catheters were then tunneled, connected to the pump, and fixed in place with sutures, followed by closure of the alfapump pocket. All patients received intravenous antibiotics prior to alfapump insertion, followed by daily oral antibiotic. The patients in the United States received 750 mg of ciprofloxacin daily as prophylaxis, whereas the patients in Canada received norfloxacin 400 mg daily. Oral antibiotic use was continued as long as the pump was in situ. Patients were instructed to charge the pump daily. The pump was programmed to run for approximately 16 hours per day during hours that they were awake. The initial daily pump volume was calculated from the historical paracentesis volume. The daily pump volume, timing, and duration of pump activity were adjusted as necessary at subsequent visits.

Ascites volume transported by the alfapump was monitored remotely using a sensor in the pump and was reported initially daily for 1 week and weekly thereafter. Patients were reviewed following hospital discharge initially weekly for 1 month and monthly till the study endpoint at 3 months. Extended follow-up occurred at 6, 9, and 12 months. The study extended to 2 years in the United States only. The protocol did not mandate the use of albumin, and therefore, PIs were not required to systematically record the amount of albumin given. However, albumin infusion was provided at implantation. Further albumin infusions were allowed and administrated at the discretion of the investigator for LVP, SBP, AKI, or hyponatremia.

ENDPOINTS

The primary endpoint was safety, reported as the incidence and severity of serious adverse events (SAEs) related to the device and/or the catheters, the implantation procedure, and/or the alfapump therapy. Secondary endpoints included the efficacy of the alfapump system as assessed by the reduction in percutaneous paracentesis frequency, including percutaneous paracenteses of all volumes and the reduction in the cumulative volume of ascites removed through all such paracentesis events; patient QoL using the CLDQ[11] and the ascites-specific Ascites Q[12]; and survival. A higher CLDQ score means a better QoL, and a higher Ascites Q score denotes more symptoms from abdominal distension.

STATISTICAL ANALYSIS AND SAMPLE SIZE

Statistical analysis was performed using SPSS Statistics, version 23 (IBM, Armonk, NY). A descriptive analysis was performed for all primary and secondary variables. Continuous variables were described using means, medians, standard deviations (SDs), 95% confidence intervals, and minimum and maximum values of each distribution. Categorical variables were described using frequencies and percentages of each category.

Changes from the baseline of the primary and secondary endpoint variables used the Student *t* test for paired data. The Wilcoxon signed-rank test was used to analyze all nonparametric data.

The safety of the alfapump system was evaluated by SAEs occurring during the study.

No formal sample size calculation was done for this feasibility study. A sample size of 30 patients was selected, assuming an underlying event rate of 5% for

these SAEs, in order to provide nearly an 80% chance of identifying such an event.

Results

Between April 2015 and January 2017, 36 patients were screened, and 30 were enrolled, 15 of whom had diuretic-resistant ascites and the remaining 15 of whom had diuretic-intolerant ascites. The results provide statistical analyses for the first 12-month period after alfapump implantation and only provide a description for events that occurred for the period of 12-24 months. Figure 1 shows patient disposition, while Table 1 shows patient demographics and baseline laboratory data. Patients were mostly middle-aged men, with a median paracentesis history of 11.9 months (range, 2.5-104.9 months). Baseline Child-Pugh score was 7.9 ± 0.9, and MELD score was 11.4 ± 2.7.

The median observation time for all patients was 360.5 days (interquartile range, 152.0-380.0 days). Of the 18 patients who were withdrawn over the 24-month period, 10 were due to SAEs; 3 underwent liver transplantation; 1 had resolution of ascites following eradication of hepatitis C virus infection; and 4 died unrelated to the pump (Fig. 1). Of the patients withdrawn for SAE, 1 in 10 subsequently died, resulting in a total of 5 deaths.

The 14 nonfatal withdrawals resulted in pump explants: 3 at liver transplantation; 1 because of ascites resolution; and 10 due to SAEs of pump failure or catheter-related complications (n = 3), infections (n = 4), or skin erosion at the pump pocket site (n = 3). All patients who had the pump explanted preferred that the pump remain in place.

SAFETY

There were 37 SAEs in 19 (63.3%) patients within the first 3 months. Of these, 12 events (32.4% of all SAEs) occurring in 10 (33.3%) patients were possibly related to the device, implantation procedure, or the alfapump therapy, while 25 unrelated (67.6%) events occurred

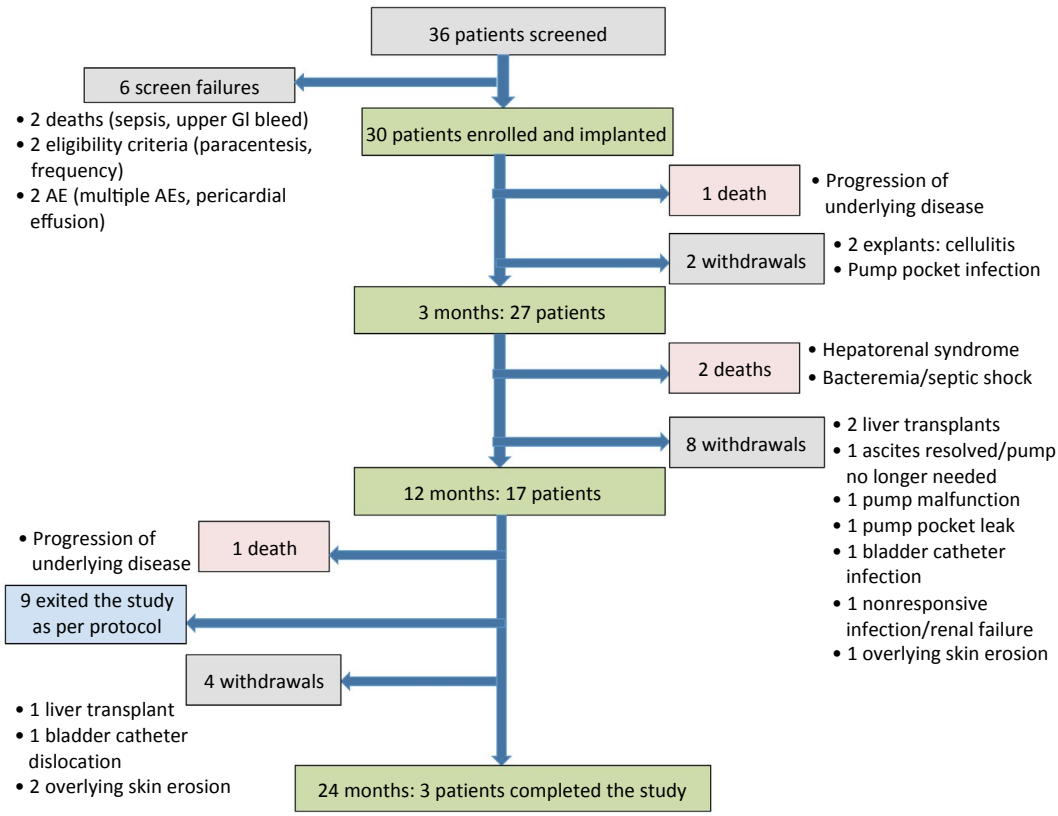

FIG. 1. Patient disposition.

TABLE 1. Patient Demographics and Baseline Laboratory Data

Category	Value (n = 30)
Age, years	60.0 ± 9.9 (32-72)
Sex	
Male	17 (56.7)
Female	13 (43.3)
Type of refractory ascites	
Diuretic-resistant	15 (50)
Diuretic-intolerant	15 (50)
Etiology of liver cirrhosis	
Alcohol	9 (30)
NASH	9 (30)
Hepatitis C	3 (10)
Hepatitis C and alcohol	3 (10)
Alcohol and NASH	2 (6.7)
Primary biliary cirrhosis	2 (6.7)
Other	2 (6.7)
Hematology	
Hemoglobin, g/L	108.8 ± 13.9 (79-139)
WBC, $\times 10^9$/L	5.6 ± 2.4 (2.1-11.0)
Platelet count, $\times 10^9$/L	140 ± 78 (44-364)
INR	1.3 ± 0.2 (1.0-1.6)
Biochemistry	
Serum Na^+, mmol/L	134 ± 5 (119-141)
Serum K^+, mmol/L	4.4 ± 0.7 (3.4-6.8)
Serum creatinine, μmol/L	93 ± 23 (44-124)
Liver panel	
AST, IU/L	42 ± 19 (22-99)
ALT, IU/L	26 ± 14 (7-69)
ALP, IU/L	150 ± 79 (50-344)
Total bilirubin, μmol/L	24 ± 16 (7-75)
Serum albumin, g/L	34 ± 6 (20-46)
Child-Pugh score	7.9 ± 0.9 (7-11)
MELD score	11.4 ± 2.7 (7-16)
Number of paracentesis of any volume, per month*	3.18 ± 1.83
Number of paracentesis of ≥5 L, per month*	2.33 ± 1.39

NOTE: Data are given as mean ± SD (range) or n (%).
*In the 3 months prior to alfapump implantation.

in 9 (30.0%) patients. The corresponding number of events for the 12-month follow-up period was 79 SAEs: 27 related (34.2%) in 13 (43.3%) patients, and 52 unrelated (65.8%) in 17 (56.7%) patients (Table 2).

Bacterial infections (15 events in 13 [43.3%] patients), electrolyte abnormalities (11 events in 6 [20.0%] patients), and renal complications (11 events in 9 [30.0%] patients) were the most common SAEs in the first 12 months, followed by abdominal complaints in patients with preexisting umbilical or inguinal hernias, felt to be related to intermittent incarceration of hernia contents (9 events in 9 [30.0%] patients; Table 2).

Cellulitis over either the pump pocket or the catheter sites were the most common infections within the first 12 months. These were felt to be related to pressure on the skin over the pump from clothing and, therefore, could not be prevented by the prophylactic antibiotic. Unrelated infections were UTI (n = 3) without concomitant ascites infection, SBP (n = 1), spontaneous bacteremia (n = 1), bacterial endocarditis (n = 1), and septic shock (n = 1). The last 3 events occurred in the same patient in that particular sequence without any evidence of pump pocket infection. She subsequently died. Two episodes each of UTI and SBP occurred 12 months after pump implantation. There was no correlation between the infection rate and the implant sequence, nor was there an obvious correlation between the infection rate and the time since implant.

The most common electrolyte abnormality (10 of 11 events) was hyponatremia (serum sodium of <130 mmol/L). Two episodes of hyponatremia were related to pump rates being set too high and recovered after reducing the pump rates. The remaining 8 episodes of hyponatremia were chronologically related to concomitant diuretic use, which was not prohibited during the study. These settled after discontinuing diuretics. Renal function for the entire cohort remained relatively stable despite not mandating albumin infusions (serum creatinine at baseline: 93 ± 23 versus 107 ± 34 μmol/L at 12 months). A total of 11 reports of AKI in 9 patients occurred beyond 7 days after implantation: 2 related episodes were possibly due to high pump rates, and 9 unrelated episodes were due to concurrent diuretic use or infection. AKI episodes increased the mean baseline serum creatinine for these episodes from 105 ± 28 μmol/L to a mean peak value of 209 ± 56 μmol/L. There were 5 of these episodes that completely resolved; 3 partially improved; and 3 did not improve and resulted in death. Because albumin infusion was not mandated by the protocol, there was no requirement to record the amount of albumin used in these patients and for what indication. However, for the busiest site that enrolled 11 patients, the median amount of albumin given for all indications over the 12-month study period was 525 g (range, 25-4925 g; median

TABLE 2. SAEs in the Study Patients

	3-Month Follow-up		12-Month Follow-up	
	Number of Events	Number of Patients (n = 30)	Number of Events	Number of Patients (n = 30)
Related to the alfapump				
Total	12	10 (33.3)	27	13 (43.3)
Postoperative bleeding	1	1 (3.3)	1	1 (3.3)
Leakage of ascites into pump pocket	2	2 (6.7)	2	2 (6.7)
Wound dehiscence	1	1 (3.3)	1	1 (3.3)
Pump malfunction	2	2 (6.7)	4	3 (10)
Bladder catheter malfunction	1	1 (3.3)	3	3 (10)
Peritoneal catheter malfunction	0	0 (0.0)	1	1 (3.3)
Hematuria	1	1 (3.3)	1	1 (3.3)
Bacterial infection	3	3 (10)	9	8 (26.7)
Hyponatremia	1	1 (3.3)	2	1 (3.3)
AKI	0	0 (0.0)	2	2 (6.7)
Skin erosion over pump	0	0 (0.0)	1	1 (6.7)
Unrelated to the alfapump				
Total	25	9 (30)	52	17 (56.7)
Deep vein thrombosis of the arm	0	0 (0.0)	1	1 (3.3)
AKI	5	3 (10)	9	7 (23.3)
Anemia	2	2 (6.7)	2	2 (6.7)
Anasarca	0	0 (0.0)	1	1 (3.3)
Bacterial infections	0	0 (0.0)	3	2 (6.7)
Dehydration	1	1 (3.3)	1	1 (3.3)
Diabetic complications	2	2 (6.7)	3	2 (6.7)
Exacerbation of chronic abdominal pain	1	1 (3.3)	1	1 (3.3)
Gastroenteritis	1	1 (3.3)	1	1 (3.3)
GI bleed	0	0 (0.0)	2	2 (6.7)
HE	0	0 (0.0)	2	2 (6.7)
Hyperkalemia	1	1 (3.3)	1	1 (3.3)
Hyponatremia	7	4 (13.3)	8	4 (13.3)
Hypotension	0	0 (0.0)	1	1 (3.3)
Hypovolemia shock	0	0 (0.0)	1	1 (3.3)
Incarcerated umbilical hernias	0	0 (0.0)	2	2 (6.7)
Incomplete bowel obstruction	0	0 (0.0)	1	1 (3.3)
Pulmonary hypertension	0	0 (0.0)	1	1 (3.3)
Ruptured umbilical hernias	0	0 (0.0)	2	2 (6.7)
Septic shock	0	0 (0.0)	1	1 (3.3)
UTI	2	2 (6.7)	3	2 (6.7)
Urinary retention	2	1 (3.3)	2	1 (3.3)
Worsening of ascites	1	1 (3.3)	3	1 (3.3)

NOTE: Data are given as n (%). Each patient may have had more than 1 SAE.

study period, 12 months; range 3-12 months). Supporting Table 1 shows the changes in serum albumin over the 12-month period. Essentially, the serum albumin oscillated around the baseline value of 34.4 ± 6.4 g/L.

REINTERVENTIONS

All reinterventions were performed by the same radiologist who did the pump insertion, with the exception of 1 site, which only included 1 patient, where the

same surgeon inserted the pump and explanted it at a later date. At the 2 sites with the highest enrollment, which included 21 patients combined, nearly 80% of the reinterventions occurred in the first 5 patients, suggesting a learning curve effect.

Excluding pump explants, there were 18 reinterventions in 14 patients with some patients requiring multiple procedures simultaneously. The most common reason for intervention was related to the peritoneal catheter (7 dislocations, 1 kinked catheter, and 1 malfunction). A total of 3 bladder catheters were replaced, whereas 1 was repositioned.

A total of 9 pumps were replaced: 7 were related to primary pump issues (3 blocked pump gears, 3 insufficient communication/charging/end of pump life, and 1 malfunction at the initial implant); 1 blocked pump was replaced in conjunction with a peritoneal catheter replacement; and 1 pump nearing its expected end of life was replaced at the time of bladder catheter replacement. Pump failure was thought to be due to humidity-related pump circuitry failure.

EFFICACY

After alfapump implantation, 13 patients required no further percutaneous paracentesis. Supporting Table 2 shows that for those patients who required no further paracentesis after pump implant had significantly fewer paracentesis procedures per month in the preceding 3 months (2.7 ± 1.1 versus 3.5 ± 2.2; $P = 0.04$). For the entire cohort, the mean time to the first paracentesis (n = 17) of any volume was 103.0 ± 95.4 days, while the time to the first LVP (>5 L; n = 12) was 108.6 ± 99.6 days. A reduction of paracentesis requirement for the entire cohort was maintained at 3 and 12 months after pump implantation (Fig. 2A). The mean total ascites volume removed by the alfapump was 79.1 ± 33.7 L/patient at 3 months and 230.6 ± 148.9 L/patient at 12 months (Fig. 2B). In contrast, the mean total ascites volume removed by percutaneous paracentesis was 6.6 ± 10.3 L/patient at 3 months and 19.1 ± 29.8 L/patient at 12 months. The reasons for LVPs at 3 months and 12 months are detailed in Table 3.

QUALITY OF LIFE

QoL was impaired at baseline with the mean baseline CLDQ value at 3.9 ± 1.2 and the mean baseline Ascites Q value at 51.7 ± 21.9. Significant improvement in QoL was observed as early as 1 month after alfapump implantation, and it was maintained at 3 months with both instruments and at 12 months with Ascites Q questionnaire (Fig. 3).

SURVIVAL AND PATIENT OUTCOMES

There were 4 deaths (13.3%) during the study, with 1 further death occurring 192 days after withdrawal from the study. The causes of all deaths were related to the underlying liver disease or complications related to cirrhosis, and none were attributed to pump implantation or pump therapy. Three patients underwent liver transplant at days 104, 133, and 413 after pump insertion. Of all contactable patients

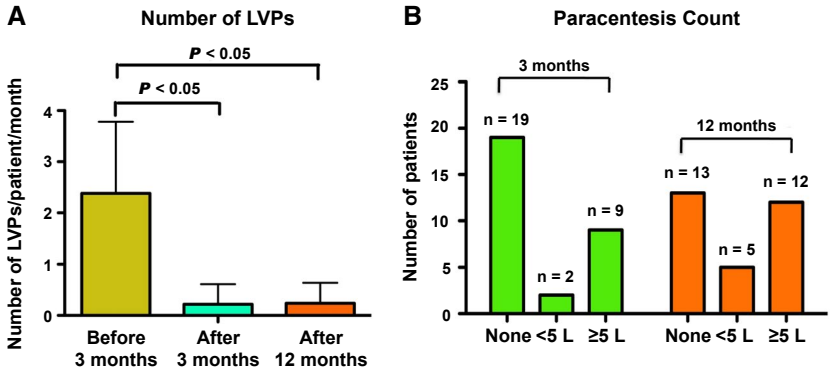

FIG. 2. (A) The number of LVPs/patient/month comparing the period in the 3 months prior to alfapump insertion versus the postinsertion period. Data are shown as mean ± SD. (B) The number of patients who needed various volumes of paracentesis by 3 and 12 months. Please note that patients who died and patients who had early explants due to SAEs were not counted as responders.

TABLE 3. Reasons for LVP at 3- and 12-Month Follow-up

	3-Month Follow-up		12-Month Follow-up	
Reason for LVP	Number of Patients*	Number of LVPs	Number of Patients*	Number of LVPs
Total	9	20	12	59
Pump malfunction	1	1	2	3
Pump pocket fluid collection	0	0	1	2
Peritoneal catheter blocked	2	6	2	12
Bladder catheter dislocation	1	1	2	6
Bladder catheter occlusion	0	0	1	8
PI decision	1	2	3	4
Patient preference/request	1	1	1	1
Renal dysfunction	3	8	4	19
Urinary retention	1	1	1	2
Unknown	0	0	1	2

*Some patients may have more than 1 reason for LVP.

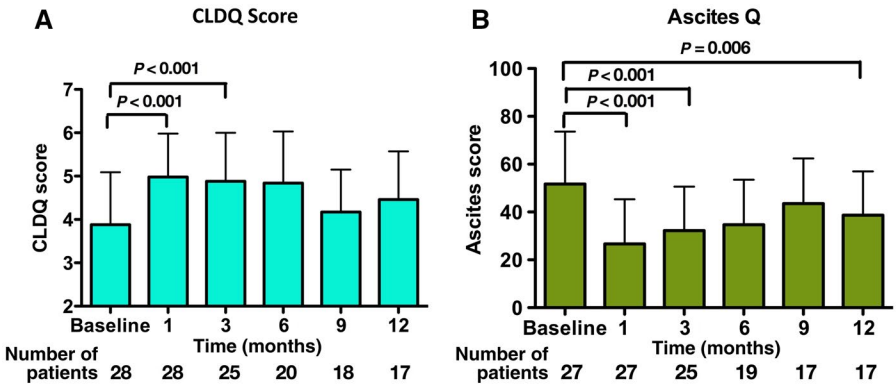

FIG. 3. Change in QoL as measured by (A) CLDQ score and (B) Ascites Q score in the study patients. Data are shown as mean ± SD. For Ascites Q, a lower score means improvement; for CLDQ, a higher score means improvement.

after study completion, there were 17 (56.7%) patients alive at the end of the 12-month period with a pump in situ but without a liver transplant (Fig. 4). A total of 3 patients in the United States and 7 patients in Canada were still alive with a functioning pump at more than 24 months. Patients experienced improved nutritional states as documented by an improved prealbumin level at 3 months and maintained at 12 months (Fig. 5). No other measurement of nutritional improvement, such as increase in psoas muscle thickness, was available because no serial computed tomography scans were planned for this study. Of all of the patients who were alive at the end of the study period, 4 patients had undergone hernia repairs, while 2 were waiting for their operation. Those patients who underwent hernia repairs reported further improvement in their QoL.

Discussion

This MOSAIC study demonstrates the utility, safety, and efficacy of the alfapump system in the management of patients with recurrent ascites. This is the first North American study using the alfapump as a management tool for recurrent ascites. Like the previous European studies,[9,10,13-16] we encountered a significant number of technical issues, and bacterial infections occurred in at least 40% of the study patients. Despite this, we demonstrated that the insertion of the alfapump system was effective in reducing the requirement for LVP. Furthermore, the control of ascites was associated with a significant improvement in QoL, better biochemical index of nutritional status, and improved medium-term survival.

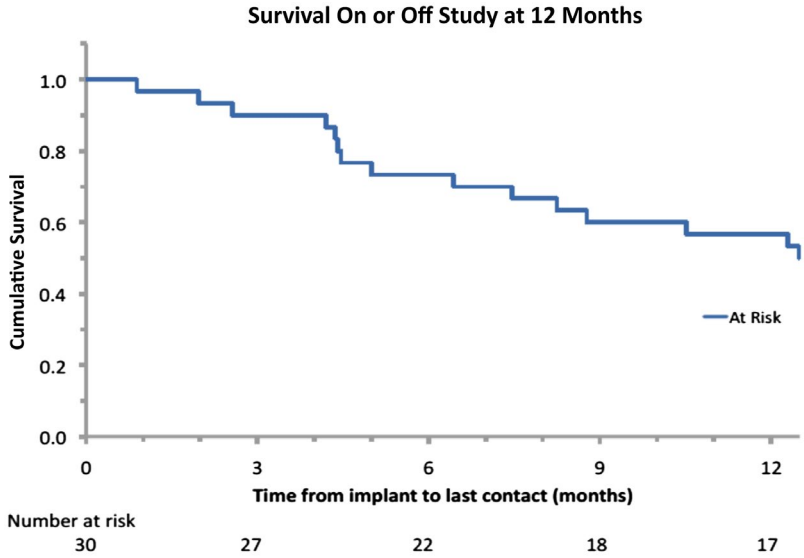

FIG. 4. The overall survival for up to 12 months after enrollment in the study. Last contact is indicated by study withdrawal, death, or the end of the study.

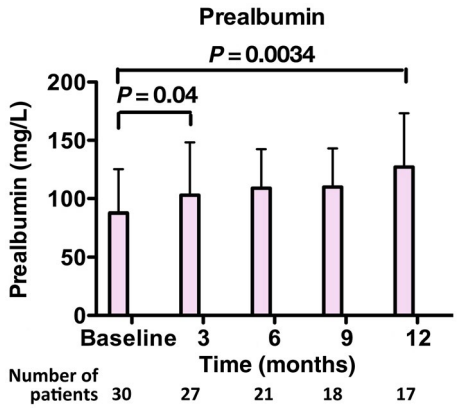

FIG. 5. Prealbumin levels in the study patients. Data are shown as mean ± SD.

This study differs from all of the previous European studies in that patients had the alfapump implanted almost exclusively as an interventional radiological procedure, which was a first for all radiologists involved. Such an approach has been reported in the literature[17] and, in skilled hands, is a minimally invasive procedure with equal success. The follow-up period of >12 months for at least half of the patients (17/30) also allows for the assessment for longer-term issues.

The major technical issues were related to pump malfunction, dislodgement or blockage of catheters, and skin erosions over the pump. Because the majority of the pumps were implanted at 2 sites, the minimal experience attained by the remaining sites made the procedure technically challenging. The introduction partway through the study of a peritoneal dialysis catheter with all of the drainage openings in the pigtail end of the catheter reduced the likelihood of the peritoneal catheter openings being clogged by omentum or tissue debris.[15] Using a purse string suture to anchor the catheters and turning on the pump immediately after implantation were the other 2 changes made during the study period, which may have decreased the catheter dislodgement issues. Drainage of ascites prior to pump implantation and leaving sutures in situ for 3 weeks may reduce the likelihood of wound dehiscence.[9] It is anticipated that with increasing experience, coupled with improved design of the catheters, reinterventions would be required less often for future studies.

Bacterial infections are a common occurrence in patients with cirrhosis and ascites.[18] Therefore, bacterial infections remain a concern in patients who received the alfapump, which is a foreign body.[10] Routine prophylactic antibiotic use has reduced the number of bacterial infections,[10] and therefore, despite the presence of the alfapump, the incidence of SBP and, hence, UTI was infrequent. However,

cellulitis over the pump pocket and over the catheter sites remains a major issue. The skin is constantly subjected to pressure from clothing on one side and the pump on the other. The absence of subcutaneous fat over these sites and the presence of diabetes in some patients may have contributed to the development of cellulitis. Better patient selection and frequent inspection of wound sites may reduce the incidence of abdominal wall erosion. Instructing patients to wear protective padding over the alfapump may reduce the friction between the skin over the pump and the overlying clothing. Prompt treatment of cellulitis with antibiotics may also decrease its extent and duration.

For the 17 patients who required an LVP during the study, the time to the first LVP after alfapump implantation was delayed to more than 3 months, consistent with other reports of alfapump use in the literature.[10,13-15] The majority of the postimplantation LVPs were related to pump or catheter malfunction, which is higher than in published studies.[10,14] However, planned future improvements in pump and catheter design should reduce this complication, with a corresponding reduced requirement for percutaneous paracentesis, thereby significantly reducing overall costs. Albumin infusions were generally given with LVPs but were not mandated at any other times. Therefore, there was no formal accounting of albumin use during the study. However, anecdotally, 33% of all study patients from 1 site had significantly reduced albumin requirements without compromising their prognoses, potentially allowing for a further reduction in health care costs.

Several patients in the study were still receiving diuretics, which may have precipitated hyponatremia because many of these episodes were chronologically related to the use of diuretics. Future studies should focus on fine-tuning the alfapump drainage rate to match the patient's rate of ascites accumulation, thereby avoiding concomitant diuretic use and potentially reducing electrolyte abnormalities and AKI. In contrast to the published randomized controlled trial[14] or the postmarketing observation study,[13] there were no AKI episodes within the first 7 days following implantation in this study. This difference in AKI occurrence cannot be readily explained on the basis of the severity of liver disease or renal dysfunction because all 3 studies enrolled patients with similar Child-Pugh and MELD scores. Other parameters that are not readily comparable include the frequency of diuretic use and doses and the alfapump rates and albumin use not associated with LVPs. All of these could affect the volume status of these patients and, hence, the risk for AKI development. The fact that 2 cases of AKI associated with the alfapump therapy resolved with a reduction of the drainage rate suggests that excessively high drainage rates should be avoided, especially in patients with borderline baseline renal dysfunction.

Once ascites was under control, there was a significant improvement in QoL, which was obvious as early as 1 month and well maintained into 3 months, and the improvement was attributed to a reduction in abdominal symptoms and an increase in activity score. The total CLDQ score of the current cohort at baseline was similar to another cohort of patients with refractory ascites treated with the alfapump system[19] with similar improvements reported at 1 and 3 months. Elimination of ascites also allowed surgical correction of umbilical and inguinal hernias, enhancing body image and further improving QoL.

Nutritional status as measured by prealbumin improved with alfapump therapy as early as 3 months after pump implantation, similar to what was observed in studies following alfapump insertion[14] or TIPS.[20-22] Anecdotally, patients put on more fat and muscle weight. This may be partly related to an increased caloric intake following elimination of ascites. Attenuation of the increased resting energy expenditure associated with ascites[23] and improved absorption of nutrients[24] have also been proposed as possible mechanisms. Because this study was not designed to primarily assess the effects of the alfapump treatment on the patients' nutritional status, no other formal assessment of nutritional status was conducted. It would be appropriate in future studies to include formal assessment of changes in nutritional status, such as serial psoas muscle measurements with the alfapump therapy.

The overall good survival of these patients within the study, with 17 (57%) of the enrolled 30 patients being alive without a liver transplant at 12 months, may be attributed to careful patient selection or to their relatively low baseline MELD score. In a real-life experience of European patients with higher baseline MELD scores who received an alfapump, only 3 of 21 patients remained in that study at a median of 153 days.[13] This observation suggests that patients with MELD scores >21 may not be appropriate candidates for alfapump as a definitive treatment for ascites. Rather, these patients could receive an alfapump as a means of improving their QoL while waiting for a liver transplant.

In conclusion, the alfapump system, implanted as an interventional radiological procedure, is a feasible treatment for recurrent ascites in patients with cirrhosis who are not suitable for TIPS insertion, especially in those with relatively preserved liver function. Prophylactic antibiotics seem to reduce the incidence of bacterial infections, which appear to be no higher than expected in this population despite the presence of a foreign body. Appropriate ascites drainage rates and diuretic withdrawal may decrease the risks for electrolyte and renal abnormalities. These patients can improve their nutritional state and enjoy a better QoL with reasonable medium-term survival without liver transplantation.

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