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## Treatment of refractory ascites with an automated low flow ascites pump in patients awaiting liver transplantation

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## ABSTRACT

**Background:** For patients with liver cirrhosis awaiting liver transplantation who suffer from refractory ascites (RA), standard treatment consists of repeated large volume paracentesis. The automated low-flow ascites-pump (alfapump) offers an innovative treatment alternative for patients with RA, if TIPSS is contraindicated or ineffective. This study addresses the feasibility of alfapump treatment in patients awaiting liver transplantation.

**Methods:** Between 2012 and 2018, patients listed for liver transplantation who were treated with an alfapump were included in this retrospective single centre study.

**Results:** Of 22 patients listed for liver transplantation and treated with an alfapump, 14 were finally transplanted. Alcohol-related liver disease was the most common aetiology for liver cirrhosis ( $n = 11$ ), followed by hepatitis C, hepatitis B and NASH. Mean age at listing was 56.3 years and 68.2% of patients were male. The average daily ascites volume pumped by the device was 1076 ml. During transplant surgery, no alfapump-related complications occurred. The alfapump was removed at the end of the transplant procedure in eight patients and left in place in three patients for up to 104 days, whereas three patients had the pump removed prior to the transplantation. Overall survival was significantly better in patients that were finally transplanted (log-rank  $p < 0.0001$ ). Five patients (22.7%) required at least one alfapump-related re-intervention.

**Conclusion:** Treatment with an alfapump in patients on the liver transplant waiting list with refractory ascites is feasible. The alfapump did not affect the transplant procedure and was explanted in most patients at the end of the transplant surgery.

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## Abbreviations

FFP	Fresh frozen plasma
LVP	Large volume paracentesis
LT	Liver transplantation
MOF	Multi-organ failure
PLT	Platelet concentrates
PRBC	Packed red blood cells
RA	Refractory ascites
TIPSS	Transjugular intrahepatic portosystemic shunt

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E-mail address: [federico.storni@insel.ch](mailto:federico.storni@insel.ch) (F. Storni).<sup>1</sup> equal contribution as last authors.<https://doi.org/10.1016/j.liver.2021.100037>2666-9676/© 2021 The Authors. Published by Elsevier Masson SAS. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

## Introduction

Patients with liver cirrhosis and portal hypertension frequently develop ascites during the evolution of the disease as a consequence of systemic inflammation, splanchnic vasodilation, low systemic vascular resistance and reduced effective arterial blood volume leading to an increased reabsorption of sodium and water [1,2]. In the initial phase, ascites is controlled with optimized fluid and salt management and diuretic treatment with an aldosterone antagonist in combination with a loop diuretic [3,4]. Refractory ascites (RA) is defined as ascites that cannot be mobilised by medical therapy or that recurs early after large volume paracentesis (LVP). Survival in patients with RA is as low as 50% at one year [5,6].

Standard treatment of RA consists of repeated large-volume paracentesis in combination with albumin substitution [6,7]. However, LVP offers only temporary relief of ascites-associated symptoms.

Furthermore, LVPs require frequent hospital visits that are associated with a decreased quality of life and considerable costs [8,9]. Alternatively, RA can be treated with a transjugular intrahepatic portosystemic shunt (TIPSS) that reduces portal pressure and therefore the main driver for the development of ascites [7,10]. Several studies and meta-analyses have shown that TIPSS is effective in reducing the need for paracentesis and improves survival compared to LVP and albumin replacement therapy [11–13]. However, TIPSS has a number of relative contraindications that are associated with an unfavourable outcome including pre-existing hepatic encephalopathy, or reduced cardiac function [14–16].

In patients with a contraindication for TIPSS, the alfapump offers an alternative treatment option for RA. Efficacy regarding removal of ascites and a decrease in paracentesis frequency have been demonstrated in the Pioneer study [17] in 2013. In 2017, standard of care treatment (LVP) was compared with alfapump therapy in a randomized controlled trial. This trial confirmed the efficacy of treatment with the alfapump compared to standard of care treatment at a comparable risk [18]. These results have been recently confirmed in a meta-analysis summarizing the available evidence to date [19]. Furthermore, treatment with the alfapump was associated with an improved nutritional status [18] and quality of life [8] compared to standard of care with LVP.

Liver transplantation is the only curative treatment option in most patients with liver cirrhosis and RA. Depending on the availability of donor organs, waiting time on the list may exceed one year. Therefore, finding the ideal bridging treatment for patients with RA on a liver transplant waiting list is of great importance.

The aim of this study was to evaluate safety and feasibility of treatment with the alfapump and to describe first experiences regarding the intra- and perioperative aspects of liver transplantation in patients with this device in situ.

## Material and methods

This study is a retrospective analysis of data collected from patients listed for liver transplantation in a tertiary care university transplant centre who were treated with an alfapump for RA between 2012 and 2018. Within this timeframe, all patients treated with an alfapump while being on the waiting list for liver transplantation were included, whereas patients with an alfapump that were not on the waiting list for liver transplantation were excluded. Follow-up visits took place as standard of care for patients with the alfapump and/or patients listed for liver transplantation every one to three months according to the clinical need. For this analysis, patients were followed up until the last visit prior to July 2020 or death. The decision regarding the insertion of a TIPSS or an alfapump was taken by an interdisciplinary team consisting of hepatologists and transplant surgeons.

Primary outcome of this analysis was feasibility of liver transplantation in patients with an alfapump in situ. Secondary endpoints were survival of patients with an alfapump listed for liver transplantation, efficacy of alfapump measured as total und daily volume pumped, cause of death in patients with and without LT, evolution of liver-disease prior to transplantation based on Child-Pugh stage, MELD and MELD-Na score and technical complications.

The study has been approved by the Ethics Committee of the Canton Bern, Switzerland (KEK 073–2012).

## Statistics

Continuous data are reported as mean and standard deviation (SD) and median and range in case of normal distribution or otherwise as median and range and compared by unpaired *t*-test and Wilcoxon-Mann-Whitney test. Categorical data are presented as percentages. Kaplan Meier Survival curves and Log-rank test were

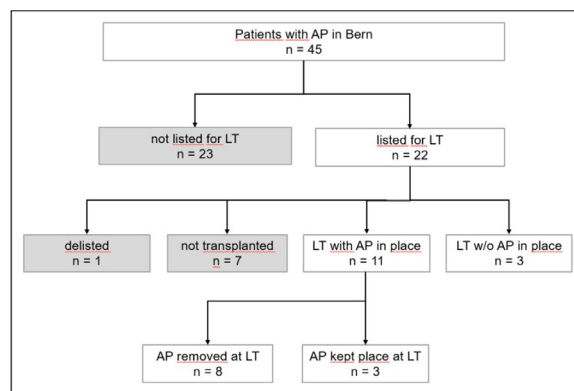


Fig. 1. Overview of patient selection.

used to display and compare survival of patients with and without liver transplantation.

Statistical analyses were performed using IBM SPSS Version 25.0 (Chicago, Illinois, USA) and GraphPad Prism version 8 for Windows, GraphPad Software, La Jolla, California, USA.

## Results

From 12/2012 to 07/2018, 45 patients in total have been treated with an alfapump in our centre. Of these, 22 have been listed for liver transplantation (LT) before or while being treated with the alfapump and consequently included in this analysis (Fig. 1). The decision to implant an alfapump was taken jointly by the hepatologist and the transplant surgeon.

### Disposition at listing for LT

At listing for LT, mean patient age was  $56.3 \pm 8.8$  years and 68.2% of patients were male. Transplanted patients were younger ( $53.6 \pm 8.7$  years) at listing than those that deceased prior to LT ( $61.0 \pm 7.2$  years). Alcoholic liver disease was the most frequent aetiology of liver cirrhosis (11/22; 50%), followed by hepatitis C (4/22; 18.2%) and hepatitis B (3/22; 13.6%) (Table 1). Four patients suffered from a HCC within Milan criteria. Of these, three patients had an underlying alcohol-related cirrhosis and one a hepatitis C-related cirrhosis. Scores and laboratory parameters at listing for LT and at alfapump implantation are specified in Table 1 and Table 2, respectively.

### Disposition at LT

Of the initially 22 patients listed for LT and concomitantly treated with an alfapump, 14 were finally transplanted (50% female), whereas eight male patients died prior to LT, seven while being on the transplant list and one after having been delisted seven weeks prior to death due to progressive liver disease. The average duration on the waiting list for transplanted patients was  $289 \pm 152$  days and for those that were not transplanted  $191 \pm 192$  days. Mean age at LT was  $54.3 \pm 8.4$  years. At transplantation, 11 patients had the alfapump still in situ, whereas three patients had the pump explanted prior to LT.

The amount of ascites pumped in patients that were finally transplanted was  $214.5 \pm 217.9$  L on average, resulting in a mean daily volume of  $1121 \pm 421$  ml. Transplanted patients had the alfapump for a mean duration of  $177 \pm 131$  days. Scores and laboratory parameters at LT are specified in Table 2.

**Table 1**  
Baseline study population.

	w/o LT n = 8	with LT n = 14	all patients n = 22
Male/female n (%)	8/0 (100/0)	7/7 (50/50)	15/7 (68.2/31.8)
Age at listing for LT (years)			
mean/SD	61.0 ± 7.2	53.6 ± 8.7	56.3 ± 8.8
median (range)	61.0 (52–72)	55.0 (39–70)	56.5 (39–72)
Age at alfapump implantation (years)			
mean/SD	61.1 ± 7.5	53.9 ± 8.5	56.5 ± 8.7
median (range)	61.0 (53–73)	55.5 (40–71)	56.5 (40–73)
Underlying chronic liver disease			
- Alcohol	6 (2 HCC)	5 (1 HCC)	11 (3 HCC)
- Hepatitis B		3	3
- Hepatitis C	1**	3 (1 HCC)	4 (1 HCC)
- NASH	1	1	2
- Wilson's disease		1	1
- Turner-associated cholestasis		1	1
Child-Pughscore* mean, SD	9.4 ± 1.4	8.9 ± 0.9	9.0 ± 1.1
median, range	9.0 (8–12)	9.0 (8–11)	9.0 (8–12)
stage A (n)	0	0	0
B (n)	6	12	18
C (n)	2	2	4
MELD score* mean, SD	15.8 ± 3.6	14.7 ± 6.5	15.1 ± 5.5
median, range	15.5 (11–23)	12.5 (7–29)	14.5 (7–29)
MELD-Na score* mean, SD	19.9 ± 5.3	18.5 ± 5.7	19.0 ± 5.4
median, range	21 (13–26)	17 (11–29)	18.5 (11–29)
Albumin (g/L)* mean, SD	30.3 ± 9.0	26.9 ± 6.7	28.1 ± 7.6
median, range	28 (15–45)	26.5 (18–41)	27 (15–45)
Bilirubin (μmol/L)* mean, SD	46.4 ± 20.5	43.1 ± 32.3	44.3 ± 28.1
median, range	40.5 (15–76)	34 (11–110)	39 (11–110)
Creatinine (μmol/L)* mean, SD	195.6 ± 210.6	129.2 ± 72.1	153.4 ± 138.1
median, range	109.5 (67–695)	113.5 (58–331)	109.5 (58–695)
INR* mean, SD	1.41 ± 0.24	1.28 ± 0.20	1.33 ± 0.22
median, range	1.38 (1.1–1.8)	1.26 (1.0–1.6)	1.26 (1.0–1.8)

\* at listing for LT.

\*\* cured hepatitis C an autoinflammatory syndrome.

### Surgery (LT)

Mean LT duration was 251 ± 49 min. Intra-operative requirement for packed red blood cells, fresh frozen plasma and thrombocyte units was 9.5 ± 6, 16 ± 9 and 4 ± 2.7, respectively. The alfapump was removed in eight patients at the end of the LT, and kept in place in three patients for another 15, 93 and 104 days post LT. One patient experienced postoperative bleeding not related to the alfapump. Two patients required temporary postoperative renal replacement therapy.

### Survival

Mortality after LT was 28.6% (n = 4) during the observation period, whereas the 90 day mortality after alfapump implantation was 7.1%. Reasons for death were primary non-function of the graft (2 days post LT), intracerebral bleeding (3 days post LT, the donor liver was re-transplanted in another recipient), pulmonary metastases of a HCC (one year post LT) and septic shock (3 years post LT, after re-transplantation) (Table 3). In all four patients, mortality was not related to the alfapump. As expected, survival in transplanted patients was significantly better than in patients not transplanted (Fig. 2). In patients not transplanted, mortality was 100% with a 90 day mortality after implantation of the alfapump of 25%. Death occurred mostly in the context of infection and/or progressive liver disease (Table 3). Overall 90 day mortality after alfapump implantation was 13.6% in this series.

### Complications before LT

Of the patients who were finally transplanted, the alfapump had to be removed in three patients prior to LT. One patient had an intra-abdominal and one a systemic infection, the latter in combination

with a pump dysfunction. In a third patient with advanced malnutrition, a pump pocket skin lesion in combination with a dysfunctional peritoneal catheter led to the explantation of the pump (Table 4).

Of the 8 patients who died while on the waiting-list, one patient had a pump pocket empyema that was clearly linked to the alfapump system, whereas three patients suffered from an abdominal infection with an uncertain link to the pump system. Three patients died from progressive liver disease, one of them with an infection of unclear focus, and one patient presented with a small bowel perforation not directly related to the pump catheter system.

### Laboratory follow-up

Of the patients going on to transplantation, 11 were Child-Pugh stage B and three stage C at the time of alfapump implantation (Table 2), whereas 10 were Child-Pugh stage B and four stage C at LT. Mean MELD was 15.1 ± 2.8 and 18.4 ± 7.4, respectively. While having the alfapump in situ, creatinine increased from 113.6 ± 35.7 to 157.7 ± 91.4 μmol/L, bilirubin from 40.7 ± 30.3 to 63.9 ± 82.9 μmol/L and the INR from 1.31 ± 0.25 to 1.42 ± 0.41 in patients that were finally transplanted. Albumin levels remained in the same range (27.7 ± 2.7 vs. 28.5 ± 5.8 g/L) within the same period of time, although albumin was not administered in the context of continuous ascites drainage by the alfapump. Zinc levels were considerably low at alfapump implantation (7.1 ± 1.8 nmol/L, normal level >12 nmol/L).

### Discussion

For patients with refractory or difficult to treat ascites, therapeutic options are limited. Large volume paracentesis is a well established procedure and associated with a low risk for complications [20,21]. However, the repetitive accumulation of significant amounts of

**Table 2**  
Summary at alfapump implantation and LT.

	at AP impl. all patients n = 22	at AP impl. w/o LT n = 8	at AP impl. with LT n = 14	p°	at LT n = 14	p'
Male/female n (%)	15/7 (68.2/31.8)	8/0 (100/0)	7/7 (50/50)		7/7 (50/50)	
Age (years)						
- mean, SD	56.5 ± 8.7	61.0 ± 7.5	53.9 ± 8.3	0.060	54.3 ± 8.4	
- median (range)	56.5 (40–73)	61.0 (53–73)	55.5 (40–71)		56.0 (41–71)	
Child-Pugh Score						
- mean, SD	9.1 ± 0.4	8.9 ± 0.4	9.2 ± 0.4	0.071	9.4 ± 0.6	0.435
- median (range)	9.0 (8–10)	9.0 (8–9)	9.0 (9–10)		9.0 (9–11)	
Stage A	0	0	0		0	
Stage B	19	8	11		10	
Stage C	3	0	3		4	
MELD score						
- mean, SD	16.0 ± 5.3	16.4 ± 6.4	15.1 ± 2.8	0.515	18.4 ± 7.4	0.297
- median (range)	15.0 (8–25)	15.0 (12–21)	16.0 (8–25)		18.0 (10–32)	
MELD-Na score						
- mean, SD	17.3 ± 4.5	17.0 ± 3.6	17.5 ± 5.0	0.808	22.3 ± 6.7	0.026*
- median (range)	17.5 (11–25)	17.0 (12–22)	18.0 (11–25)		22.0 (13–35)	
Albumin (g/L)						
- mean, SD	27.1 ± 3.7	26.1 ± 5.1	27.7 ± 2.7	0.433	28.5 ± 5.8	0.626
- median (range)	27.0 (20–33)	26.5 (20–33)	27.5 (23–33)		30.0 (16–37)	
Bilirubin (μmol/L)						
- mean, SD	36.8 ± 26.4	29.9 ± 17.5	40.7 ± 30.3	0.367	63.9 ± 82.9	0.268
- median (range)	24.0 (10–115)	23.5 (11–66)	31.5 (10–115)		26.0 (8–286)	
Creatinine (μmol/L)						
- mean, SD	119.6 ± 38.8	130.1 ± 44.3	113.6 ± 35.7	0.349	157.7 ± 91.4	0.097
- median (range)	116.0 (41–195)	123.0 (74–195)	115 (41–182)		123.5 (89–421)	
INR						
- mean, SD	1.30 ± 0.21	1.28 ± 0.14	1.31 ± 0.25	0.758	1.42 ± 0.41	0.297
- median (range)	1.30 (1.00–1.80)	1.33 (1.11–1.44)	1.27 (1.00–1.80)		1.35 (1.09–2.66)	
Zinc (nmol/L)						
- mean, SD	6.9 ± 1.9	6.5 ± 2.3	7.1 ± 1.8	0.547	n.d.	
- median (range)	6.6 (4.7–11.3)	5.9 (4.7–11.3)	6.8 (5.0–10.2)			
Selenium (nmol/L)						
- mean, SD	0.71 ± 0.17	0.71 ± 0.21	0.70 ± 0.15	0.876	n.d.	
- median (range)	0.7 (0.4–1.0)	0.7 (0.5–1.0)	0.7 (0.4–0.9)			
Vitamin D (25OH) (nmol/L)						
- mean, SD	31.9 ± 18.4	33.6 ± 26.2	30.8 ± 11.9	0.771	n.d.	
- median (range)	27 (12–86)	29 (12–86)	26 (17–50)			
BMI* (kg/m <sup>2</sup> )						
- mean, SD	24.5 ± 5.4	25.9 ± 6.0	23.7 ± 5.1	0.384	23.0 ± 3.5	0.389
- median (range)	23.9 (16.9–36.0)	25.3 (16.9–35.0)	22.5 (17.1–36.0)		23.3 (17.8–31.6)	
Hand grip (kg)						
- mean, SD	23.1 ± 7.8	27.1 ± 6.8	20.3 ± 7.5	0.074	n.d.	
- median (range)	24.9 (10.3–34.1)	27.9 (13.8–34.1)	17.7 (10.3–31.7)			

\*Dry body weight.

\* Significant increase at LT.

p° comparison of patients with and without LT at baseline.

p' comparison of patients with LT at implant alfapump and at LT.

ascites has a negative effect on patient mobilization, nutritional uptake and quality of life in general [8,22–25].

Alternatively, patients can be treated with a TIPSS, what is associated with a significant reduction of ascites and an improved survival [10–12]. However, reduction of ascites usually takes weeks to several months and shunting of the liver via the TIPSS is associated with a relevant risk for hepatic encephalopathy (HE) [14].

The alfapump represents an alternative treatment in patients with RA in whom TIPSS is contraindicated or not feasible. With an alfapump in place, full control of ascites is possible right after the implantation of the pump, what is an advantage if ascites control is required for months rather than for years. However, in case of a very short waiting time (less than three months), paracentesis might be the best option with regard to invasiveness and costs.

After implantation of an alfapump, no regular albumin substitution is recommended in contrast to the recommendations in the context of large volume paracentesis. In this study, albumin was administered only in the context of recommended indications such as hepatorenal syndrome - acute kidney injury (HRS-AKI) and spontaneous bacterial peritonitis (SBP). In this series, albumin levels remained at the same level after AP implantation until

transplantation without regular substitution of albumin and despite continuous ascites drainage leading to a considerable loss of albumin and proteins.

From alfapump implantation to LT an increase in mean MELD, MELD-Na, bilirubin and creatinine was observed. This is compatible with a progression of the underlying liver disease while being on the waiting list for LT. In patients with a three months post transplant follow-up, mean creatinine was only slightly lower compared to LT ( $152.1 \pm 55.6 \mu\text{mol/L}$  vs,  $168.5 \pm 101.1$ ).

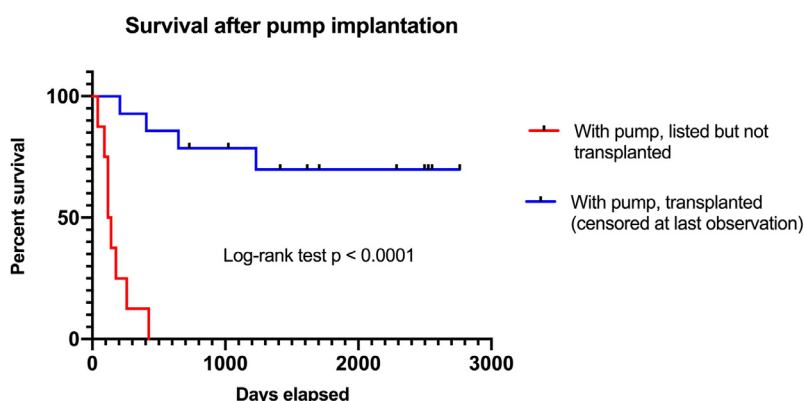
#### Pump outcome in patients with LT

In this series, 14 patients were finally transplanted. In 3 patients alfapump was removed before LT; one patient suffered from a skin ulceration of the pump pocket in combination with a pump dysfunction, one patient had a systemic infection of unclear origin in combination with a pump dysfunction and a third patient suffered from a bacterial peritonitis with *Klebsiella pneumoniae*.

The alfapump was removed in 8 patients at the end of LT and left in place in 3 patients. Reasons for leaving the alfapump in place after LT were severe coagulopathy or hemodynamic instability at the end

**Table 3**  
Cause of death pre- and post-transplant.

	Pre-LT	Post-LT
Deceased n (%)	8 (100)	4 (28.6)
Male n (%)	8 (100)	3 (75)
Reason of death		
- Progressive liver disease	2	
- Progressive liver disease and infection of unclear focus	1	
- Progressive liver disease and peritonitis ( <i>Enterococcus faecium</i> and <i>candida</i> )	1	
- Abdominal wall phlegmon with communication into abdominal cavity, death due to multi-organ failure, pump not explanted	1	
- Septic shock with probable abdominal focus and explantation of the alfapump; patients died 2 days later due to multi-organ failure	1	
- Pump pocket empyema and bacterial peritonitis with consecutive explantation of the alfapump; patient died three weeks later due to multi-organ failure	1	
- Small bowel perforation with peritonitis, pump removed during bowel surgery, exitus 4 days later	1	
- Primary graft non-function, exitus letalis on day of transplantation		1
- Intracerebral bleeding 3 days after transplantation		1
- Metastatic hepatocellular carcinoma in the lung one year after transplantation		1
- Sepsis with MOF after re-transplantation, 3 years after initial LT with explantation of the alfapump		1



**Fig. 2.** Survival in patients treated with alfapump. Patients with an implanted AP ( $n = 22$ ) listed for LT (intention to treat). The LogRank test compares survival of patients finally transplanted with patients that were not transplanted.

of the transplant procedure. In one patient the alfapump was reactivated post LT to drain ascites.

*Liver transplantation*

Based on the patients we analysed in this series, there is no evidence that therapy with the alfapump is an obstacle to liver transplantation. As described in Table 3, 8 patients with alfapump out of 22 died on the waiting list for liver transplantation. This high mortality was mostly the consequence of the polymorbidity and fragility of these patients and not primarily related to the alfapump. The position of the alfapump, in the wall of the right upper abdominal quadrant, did not interfere with the surgical transplant procedure.

*Mortality before and after LT*

Within the observation period of this study, seven patients died while being on the waiting list and one after being delisted due to progressive liver disease. In two of these patients, death was attributed to progressive liver disease, whereas in another two patients progressive liver disease in combination with an infection of unknown origin and a peritonitis (*Enterococcus faecium* and *candida*) were the most likely cause of death. Three patients died following abdominal wall phlegmon, pump pocket empyema and septic shock with probable intraabdominal focus, respectively, and one patient following small bowel perforation unrelated to the alfapump system with consecutive complications of peritonitis (Table 3). Whereas in the patient with the pump pocket empyema a link between the infection and the alfapump was clearly given, a causative involvement of

the alfapump could neither be confirmed nor excluded in the other patients with septic complications, since infections and especially bacterial peritonitis are frequently observed complications in patients with advance decompensated liver cirrhosis. The alfapump was not a reason for an a priori exclusion from LT in any of the patients of this series. However, in case of serious infection, sepsis or multi-organ failure with or without relation to the alfapump, patients might have been temporarily or permanently precluded from LT.

Of 14 patients who received a liver transplant, one died due to primary graft non-function after intraoperative hyperkalemia, cardiac instability and cardiopulmonary resuscitation, and one due to an intracerebral bleed on postoperative day 3 after an initially good evolution post-transplant with extubation on postoperative day 2. Neither of these two patients had signs for an infection or sepsis with or without relation to the alfapump. One patient died after re-transplantation as a consequence of sepsis with multi-organ failure three years after the initial LT and alfapump explantation, and one because of a HCC-related metastatic lung disease one year after LT and pump removal. Reason for death was unrelated to the alfapump in all four patients.

*Technical adverse events*

Most frequently observed technical adverse event leading to revisional surgery in this as well as in other series was blocking of the peritoneal catheter [26]. This finally led to a change in the catheter used in subsequent studies and non-study implantations. Pump exchange due to technical device problems was required in two patients in this series Table 4.

**Table 4**  
Technical alfapump data.

Pump performance Patient group	w/o LT	with LT	all
Patients per group	8	14	22
Ascites pumped by alfapump until LT or end of observation, total amount (L)			
- mean, SD	169.0 ± 147.8	214.5 ± 217.9	198.0 ± 192.8
- median (range)	144.3 (36.7–496.0)	125.6 (11.3–653.2)	144.3 (11.3–653.2)
Ascites pumped by alfapump until LT or end of observation, per day (ml)			
- mean, SD	996 ± 253	1121 ± 421	1076 ± 367
- median (range)	931 (703–1357)	990 (452–2093)	961 (452–2093)
Pump in situ, days			
- mean, SD	160 ± 114	177 ± 131	171 ± 122
- median (range)	117 (40–389)	141 (24–476)	128 (24–476)
<b>Technical adverse events</b>			
Peritoneal catheter revision*	0	4	4
Bladder catheter revision	1	0	1
Pump exchange	1	1	2
Smart charger exchange	0	1	1

\* 4 events in 2 patients.

Limitations of this observational study include the lack of a control group with repeated large volume paracentesis as standard of care treatment and the retrospective analysis of the data. Furthermore, patients with alcoholic liver cirrhosis are overrepresented in this series.

## Conclusions

The alfapump expands the therapeutic options for RA in patients waiting for LT. However, TIPSS should be considered in all patients with RA as treatment option prior to the implantation of an alfapump since TIPSS is associated with an improved survival and the alfapump is approved for patients with exclusion criteria for TIPSS only. Careful patient selection is mandatory, taking into account the expected time on the liver transplant waiting list. On average, the alfapump was in situ for 6 months and the mean volume of ascites transported was approximately one litre per day. Pump-related re-interventions were most frequently required due to peritoneal catheter problems. The alfapump did not interfere with the transplant procedure and no surgical complications related to the alfapump could be identified in this series. The alfapump was removed at the end of the liver transplantation in most patients but kept in place in a few patients for a limited period of time. Pre-transplant mortality was associated with progressive liver disease, while post-transplant mortality was independent of the alfapump. The work presented here shows that ascites management with an alfapump in patients on the waiting list for LT is a feasible treatment option in carefully selected candidates. Furthermore, LT was not negatively affected by the alfapump in situ in this series. Surgical revisions were mainly related to catheter-associated technical problems. Technical improvements and optimization of management will further reduce the need for revisions in future patients.

## Author contributions

F.S., J.S., V.B., A.D.G. and G.S. collected and interpreted data and wrote the manuscript.

## Financial disclosure

F.S., A.D.G. and G.S. received speaker fees from Sequana Medical.

## Conflicts of interest

All authors declare no conflict of interests.

## Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.liver.2021.100037.

## References

- [1] Sola E, Gines P. Renal and circulatory dysfunction in cirrhosis: current management and future perspectives. *J Hepatol* 2010;53(6):1135–45.
- [2] Bernardi M, Moreau R, Angeli P, Schnabl B, Arroyo V. Mechanisms of decompensation and organ failure in cirrhosis: from peripheral arterial vasodilation to systemic inflammation hypothesis. *J Hepatol* 2015;63(5):1272–84.
- [3] Gines P, Cardenas A, Arroyo V, Rodes J. Management of cirrhosis and ascites. *N Engl J Med* 2004;350(16):1646–54.
- [4] Hernandez-Gea V, Aracil C, Colomo A, et al. Development of ascites in compensated cirrhosis with severe portal hypertension treated with beta-blockers. *Am J Gastroenterol* 2012;107(3):418–27.
- [5] Moore KP, Wong F, Gines P, et al. The management of ascites in cirrhosis: report on the consensus conference of the International Ascites Club. *Hepatology* 2003;38(1):258–66.
- [6] EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. *J Hepatol* 2018;69(2):406–60.
- [7] Tsochatzis EA, Bosch J, Burroughs AK. Liver cirrhosis. *Lancet* 2014;383(9930):1749–61.
- [8] Stepanova M, Nader F, Bureau C, et al. Patients with refractory ascites treated with alfapump(R) system have better health-related quality of life as compared to those treated with large volume paracentesis: the results of a multicenter randomized controlled study. *Qual life Res: Int J Qual Life Aspect Treatment Care Rehabil* 2018;27(6):1513–20.
- [9] Kwan SW, Allison SK, Gold LS, Shin DS. Cost-effectiveness of transjugular intrahepatic portosystemic shunt versus large-volume paracentesis in refractory ascites: results of a markov model incorporating individual patient-level meta-analysis and nationally representative cost data. *J Vascul. Int Radiol: JVIR* 2018;29(12):1705–12.
- [10] Rossle M, Ochs A, Gulberg V, et al. A comparison of paracentesis and transjugular intrahepatic portosystemic shunting in patients with ascites. *N Engl J Med* 2000;342(23):1701–7.
- [11] Bureau C, Thabut D, Oberti F, et al. Transjugular intrahepatic portosystemic shunts with covered stents increase transplant-free survival of patients with cirrhosis and recurrent ascites. *Gastroenterology* 2017;152(1):157–63.
- [12] Salerno F, Camma C, Enea M, Rossle M, Wong F. Transjugular intrahepatic portosystemic shunt for refractory ascites: a meta-analysis of individual patient data. *Gastroenterology* 2007;133(3):825–34.
- [13] Bai M, Qi XS, Yang ZP, Yang M, Fan DM, Han GH. TIPS improves liver transplantation-free survival in cirrhotic patients with refractory ascites: an updated meta-analysis. *World J Gastroenterol* 2014;20(10):2704–14.
- [14] Bureau C, Metivier S, D'Amico M, et al. Serum bilirubin and platelet count: a simple predictive model for survival in patients with refractory ascites treated by TIPS. *J Hepatol* 2011;54(5):901–7.
- [15] Copelan A, Kapoor B, Sands M. Transjugular intrahepatic portosystemic shunt: indications, contraindications, and patient work-up. *Semin Intervent Radiol* 2014;31(3):235–42.
- [16] Piecha F, Radunski UK, Ozga AK, et al. Ascites control by TIPS is more successful in patients with a lower paracentesis frequency and is associated with improved survival. *JHEP Rep: Innovat. Hepatol* 2019;1(2):90–8.
- [17] Bellot P, Welker MW, Soriano G, et al. Automated low flow pump system for the treatment of refractory ascites: a multi-center safety and efficacy study. *J Hepatol* 2013;58(5):922–7.

- [18] Bureau C, Adebayo D, Chalret de Rieu M, et al. Alfapump(R) system vs. large volume paracentesis for refractory ascites: a multicenter randomized controlled study. *J Hepatol* 2017;67(5):940–9.
- [19] Lepida A, Marot A, Trepo E, Degre D, Moreno C, Deltenre P. Systematic review with meta-analysis: automated low-flow ascites pump therapy for refractory ascites. *Aliment Pharmacol Ther* 2019;50(9):978–87.
- [20] De Gottardi A, Thevenot T, Spahr L, et al. Risk of complications after abdominal paracentesis in cirrhotic patients: a prospective study. *Clin Gastroenterol Hepatol* 2009;7(8):906–9.
- [21] Pache I, Bilodeau M. Severe haemorrhage following abdominal paracentesis for ascites in patients with liver disease. *Aliment Pharmacol Ther* 2005;21(5):525–9.
- [22] Orr JG, Homer T, Ternent L, et al. Health related quality of life in people with advanced chronic liver disease. *J Hepatol* 2014;61(5):1158–65.
- [23] Bhanji RA, Carey EJ, Watt KD. Review article: maximising quality of life while aspiring for quantity of life in end-stage liver disease. *Aliment Pharmacol Ther* 2017;46(1):16–25.
- [24] Jara M, Bednarsch J, Malinowski M, et al. Predictors of quality of life in patients evaluated for liver transplantation. *Clin Transp* 2014;28(12):1331–8.
- [25] Kim HY, Jang JW. Sarcopenia in the prognosis of cirrhosis: going beyond the MELD score. *World J Gastroenterol* 2015;21(25):7637–47.
- [26] Stirnimann G, Berg T, Spahr L, et al. Treatment of refractory ascites with an automated low-flow ascites pump in patients with cirrhosis. *Aliment Pharmacol Ther* 2017;46(10):981–91.