


ORIGINAL ARTICLE

Short-term intraperitoneal catheters: An ambulatory care intervention for refractory ascites secondary to cirrhosis during COVID-19

Natalie LY Ngu,^{*,†}  Patricia Anderson,^{*,†} Jo Hunter,^{*,‡} Anita Figredo,[§] Timothy Papaluca,^{*} Stephen Pianko,^{*,†} Anouk Dev,^{*,†} Sally Bell^{*,†} and Suong Le^{*,†}

^{*}Department of Gastroenterology and Hepatology, [‡]Pharmacy Department, [§]Hospital in the Home, Monash Health and [†]Faculty of Medicine, Nursing and Health Sciences, Monash University, Melbourne, Victoria, Australia

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Correspondence

A/Prof Suong Le, Department of Gastroenterology and Hepatology, Level 3, Monash Medical Centre, 246 Clayton Rd, Clayton, Victoria 3168, Australia. Email: suong.le@monashhealth.org.au

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Abstract

Background and Aim: Patients with refractory ascites have frequent hospital admissions, which pose exposure risks in the context of the COVID-19 pandemic. The aim of this study was to investigate the safety and efficacy of a novel 12-week, multi-disciplinary ambulatory care program allowing frequent low-volume ascitic drainage through a tunneled, intraperitoneal catheter (IPC).

Methods: Adult patients with cirrhosis complicated by refractory ascites were recruited through a liver clinic in a tertiary health service in Melbourne, Australia from April to December 2020. All patients were enrolled in a 12-week multidisciplinary program including medical, nursing, dietetics, and pharmacy support. A Rocket Medical IPC was inserted on day 1 with 1–2 L of ascitic fluid drained over 1–3 sessions per week either at the patients' homes or at the hospital day ward. Patients' demographics, death, complications, and self-reported outcomes were recorded.

Results: Twelve patients were enrolled with a median of 65-day (interquartile range [IQR]: 16.5–93) IPC duration between April and December 2020 across two periods of COVID-related lockdown in Melbourne, Australia. There were no IPC-related deaths. Early removal was necessitated in three patients due to leakage, nonadherence, and bacteremia. On day 30, the median self-reported health score increased from 50 (IQR: 50–70) to 78 (IQR: 50–85), attributable to a reduction in symptom burden.

Conclusion: A multidisciplinary IPC program including the use of short-term IPC was safe and associated with a self-reported improvement in perceptions of health. In the context of the COVID-19 pandemic, the program aimed to reduce patient and clinician exposure, which is maintaining engagement and management of decompensated cirrhosis.

Introduction

The COVID-19 pandemic has created challenges in how healthcare systems provide care for patients with cirrhosis complicated by refractory ascites. The consequences of refractory ascites can include spontaneous bacterial peritonitis,¹ high healthcare resource utilization, and reduced health-related quality of life.² As the most common complication of decompensated cirrhosis,^{3,4} ascites necessitates frequent face-to-face interactions with the healthcare system through elective large-volume paracentesis (LVP), emergency department presentations, and acute hospitalization. The development of ascites is a predictor of mortality, both as a component of the Child–Pugh score and as an independent variable.⁵

The clinical utility of long-term intraperitoneal catheters (IPCs) as an adjunct therapy to LVP and standard medical therapy (SMT) for patients with cirrhosis and portal hypertension

remains poorly defined in the literature. However, IPCs have been shown to be safe and cost-effective in management in palliative patients with malignant ascites.⁶

We investigated the safety and efficacy of a novel ambulatory care program developed with hospital in the home (HITH) to allow frequent low-volume ascitic drainage through a long-term tunneled, IPC (Rocket Medical IPC) in patients with advanced cirrhosis.

Methods

We conducted a prospective feasibility study at Monash Health, the second largest healthcare service in Australia, from April to December 2020. Adult patients with cirrhosis and refractory ascites were recruited through an existing liver outpatient clinic service for decompensated cirrhosis. Ascites was deemed refractory if requiring LVP at least twice in the previous 8 weeks despite

fluid and dietary sodium restriction and on maximal tolerated doses of diuretics. The patients must have had a diagnosis of cirrhosis of any etiology based on clinical, laboratory, imaging, and endoscopic findings and be an adult patient with the capacity to give informed consent. In addition, the patients had to meet the criteria for admission in the local HITH program, including residing in the catchment area and absence of previously documented safety concerns for staff. We excluded patients immediately eligible for liver transplantation, those with prior spontaneous bacterial peritonitis, active infection, loculated ascites, or hepatic hydrothorax.

Ethics approval was granted through the Monash Health Human Research Ethics Committee. Patients provided written informed consent for both the study and the IPC insertion procedure. The authors designed, implemented the study, and collected and analyzed the data. Rocket Medical provided training on the use of the IPC but did not provide in-kind nor financial support and was not involved in the design, conduct, analysis, or reporting of the study.

Intervention. We developed a novel model of care for community-based management of refractory ascites secondary to cirrhosis during COVID-19 to reduce presentations to the hospital. The intervention involved the insertion of a tunneled IPC and enrolment into a multi-faceted HITH program, which included scheduled ascitic fluid drainage, multidisciplinary team care, and intensive nutritional support. Following admission to HITH, the patients received home visits by nurses for ascitic drainage and fortnightly liver clinic reviews on-site at the hospital. The drainage schedule was individualized, with 1–2 L drained by HITH nurses over 1–3 sessions per week, without human albumin infusions. Patients were provided with discount vouchers for taxi transport to appointments. Any medical or other concerns identified by the patient or visiting nurses were escalated to the treating HITH doctor who would perform a telehealth consultation or escalate to the liver clinic doctor who would organize a face-to-face consultation. Any emergency concerns were directed to the nearest emergency department by ambulance.

All patients received oral antibiotic prophylaxis (norfloxacin 400 mg daily or trimethoprim/sulfamethoxazole 160 mg/800 mg daily). An ascitic fluid sample was taken for cell count, microscopy, and culture at every drainage in a bland specimen jar and in an anticoagulated blood collection tube. A diagnosis of peritonitis was made if the ascitic fluid polymorphonuclear (PMN) cell count was greater than 250/mm³ with concomitant features of infection such as abdominal pain, fever, elevated serum white cell count, or elevated C-reactive protein or if an organism was cultured on Gram stain of ascitic fluid.

This program ran for a 12-week period, at which point the IPC was removed or replaced. Indications for earlier removal included complications such as polymicrobial peritonitis, sepsis, IPC obstruction, leakage, or resolution of ascites. Patients continued to receive SMT including dietary sodium minimization, 1.5 L fluid restriction, and the use of diuretics at the maximum tolerated doses. The diuretics were one or both of spironolactone, a mineralocorticoid receptor antagonist, and frusemide, a loop diuretic. Doses were prescribed and changed by the liver clinic clinicians according to weight, peripheral edema, or development of hyperkalemia, hyponatremia, and renal impairment.

Procedure. The Rocket IPC (Rocket Medical Pty Ltd) was chosen due to local clinician experience (interventional radiologists and community nursing teams) and prior approval by the Therapeutic Goods Administration.⁷ Compared with the market alternative PleurX (UK Medical Ltd., Basingstoke, UK), the Rocket IPC is easier to insert and has lower lifetime costs.⁸

The IPC insertion was performed by an experienced interventional radiologist with ultrasound guidance using an aseptic technique. Patients received appropriate blood products if the International Normalized Ratio was more than 1.7 and/or if the platelet count was less than 50 × 10⁹/L.

Outcomes. The primary composite endpoint was safety, which included death related to IPC (death that would not have been expected in the absence of IPC insertion), rates of bleeding at the insertion site, bacterial peritonitis (ascitic fluid PMN cell count ≥250 cells/mm³ and presence of clinical features of infection, for example, fever, abdominal pain), and cellulitis (acute erythema, warmth, and tenderness at the insertion site). Secondary endpoints were IPC attrition rates and longitudinal change in the quality of life (EuroQol 5 Dimensions [EQ-5D] and Chronic Liver Disease Questionnaire [CLDQ]). The EQ-5D consists of two separate components, a visual analog scale that assesses overall health state (0 being worst imaginable to 100 being best imaginable health state) and a descriptive assessment of five dimensions (mobility, personal care, usual activities, pain, and anxiety/depression) at three levels (no problems, some problems or extreme problems). Total scores ranged from 5 to 15, with better quality of life indicated by lower scores.⁹ The CLDQ consists of 29 items in the domains of fatigue, activity, emotional function, abdominal symptoms, systemic symptoms, and worry and has been found to show a gradient between those (i) with and without cirrhosis and (ii) Child–Pugh A compared with Child–Pugh B or C class cirrhosis.¹⁰

Statistical analysis. The Stata/IC 16.1 (StataCorp LLC, College Station, TX, USA) was used for the analysis. Descriptive statistics were used for quantitative outcome measures to include all primary and secondary outcomes. Comparisons between groups were performed using the Students' *t* test for parametric continuous data, Wilcoxon rank sum test for nonparametric continuous data, or χ^2 test for categorical variables, as required. Statistical significance was established at *P* < 0.05. Medians and interquartile ranges were determined for nonparametric outcomes.

Results

Twelve patients were referred and accepted for the IPC program, of which eight patients met inclusion criteria. The additional four patients were also accepted for palliative management of refractory ascites due to Child–Pugh C class cirrhosis (*n* = 3) and metastatic ovarian cancer in a patient with concomitant cirrhosis (*n* = 1). Baseline characteristics are shown in Tables 1 and 2. All patients were ineligible for liver transplantation due to active alcohol use (*n* = 6), frailty/functional status (*n* = 3), active intravenous drug use (*n* = 1), or non-hepatocellular carcinoma malignancy (*n* = 2). The median total ascitic fluid volume drained in the 3 months prior to IPC insertion was 30.3 L (IQR: 27.5–33.6 L).

Table 1 Baseline characteristics

Characteristic	
Total patients, <i>n</i>	12
Male sex, <i>n</i> (%)	8 (67%)
Age, years, median (IQR)	59 (47–74)
Etiology of liver disease	
Alcohol	8 (67%)
Hepatitis C	1 (8%)
Non-alcoholic fatty liver disease	1 (8%)
Alcohol and hepatitis C	1 (8%)
Hepatitis B/D	1 (8%)
Comorbidities	
Renal disease	5 (42%)
Cardiovascular disease [†]	3 (25%)
Diabetes mellitus	3 (25%)
Hyponatremia (<135 mmol/L)	7 (58%)
SAAG > 11	11 (92%)
Non-HCC malignancy	2 (17%)

[†]Cardiovascular disease was determined to be present if the patient had a history of coronary artery disease, ischemic cardiomyopathy, cerebrovascular disease or peripheral artery disease.

HCC, hepatocellular carcinoma; IQR, interquartile range; MELD, Model for End-Stage Liver Disease Score; SAAG, serum albumin to ascites gradient.

Primary endpoint: Safety. With a median duration of 77 days (IQR 15–96), the primary endpoint was reached in three patients requiring early removal of the IPC; however, there were no deaths related to the IPC and no bleeding events (Table 2). Peritonitis with methicillin-susceptible *Staphylococcus aureus* bacteremia and cellulitis necessitating IPC removal occurred in one patient (11%), and cellulitis alone occurred in one patient (11%). The IPC was not removed in this patient during treatment for cellulitis at week 9 but subsequently removed at week 11 due to nonadherence. Persistent insertion site leakage occurred in one participant, requiring IPC removal. Two patients died with an IPC in situ in whom the device was inserted for end-of-life ascites management in the context of liver failure, with one case complicated by metastatic hepatocellular carcinoma. Over a 6-month follow up period, three patients died at 214, 64, and 122 days from IPC removal due to liver failure (*n* = 2) and metastatic ovarian cancer (*n* = 1), respectively.

Secondary endpoints. IPC attrition was 100%, with all IPCs removed at the completion of the program and one patient completing two full-length programs (87 and 83 days). The decision to replace the IPC in this patient was made by the multidisciplinary team due to persistent drainage of the maximal volume of ascitic fluid (2 L three times per week) as well as patient self-reported improvement in quality of life and tolerance of the IPC.

At 30 days following IPC insertion, the median self-reported health score on a vertical visual analog scale increased from a median of 50 (IQR: 30–70) to 78 (IQR: 50–85) (*P* = 0.39), attributable to a reduction in symptom burden (Table 3, Fig. 1).

Liver disease severity. Liver disease severity was stable measured by Child–Pugh class or median Model for End-Stage Liver Disease (MELD) score at 30 and 90 days from baseline (Table 3). There was no significant change in oral diuretic dosage from a baseline median spironolactone dose of 100 mg (IQR: 25–225 mg) and frusemide 40 mg (IQR: 0–60 mg), at 30 or 90 days from insertion. Three patients with persistent ascites received transjugular intrahepatic portosystemic shunt (TIPS) insertion following IPC if there was no documented history of hepatic encephalopathy or other relative/absolute contraindication (Table 2).

Discussion

In this novel pilot study of short-term IPC use for the management of refractory ascites during the COVID-19 pandemic, we have demonstrated safety and improvement in patient perceptions of health. This novel intervention aims to reduce the frequency of emergency hospital presentations and admissions, and elective LVP, in this immunosuppressed population with historically high healthcare resource utilization. These findings suggest that the use of the IPC within a multidisciplinary, liver-specific program can be safe and effective for patients immediately ineligible for liver transplantation due to low MELD scores, insufficient period of abstinence from alcohol, or those likely to clinically improve with intensive optimization of their malnutrition and or sarcopenia. We will continue to exclude patients with Child–Pugh C class cirrhosis due to the high infection and morbidity risks, including local incidence of bacteremia and bacterial peritonitis, which will narrow the eligible cohort to Child–Pugh B class patients.

Although used extensively in malignant ascites cohorts,⁶ there is limited uptake in patients with end-stage liver disease due to the complexity of psychosocial factors and episodic decompensation. These contribute to inconsistent engagement with healthcare services and potentially preventable hospital admissions.¹¹ This program addresses these issues by providing a patient-centered model of care with increased intensity of clinician support between conventional outpatient appointments from an MDT team. The 12-week duration was chosen due to the risk of IPC-related infection¹² but also to provide time to build patient engagement, medication adherence, and assess nutritional improvement. We have observed 100% attrition rates, suggesting the improvements may be sustainable in this population, who are often difficult to engage in ambulatory care.

While the improvement in QoL measures did not reach statistical significance due to the small sample size, qualitative feedback through patient interviews, and direct feedback suggests high levels of patient acceptability of the IPC, particularly when compared with the alternative of frequent LVP. Patients with decompensated liver disease experience a high symptom burden comparable to that of other end-stage chronic disease and worse than that experienced by those with compensated liver disease.¹³ Distressing symptoms drive poor HRQoL, which is associated with increased mortality and hospitalization.² Improvements in HRQoL are likely multifactorial and remain a major clinical objective for this cohort who otherwise have limited treatment options. Benefits that have not been captured through standardized tools include attempts at reducing the financial burden that

Table 2 Descriptive patient characteristics

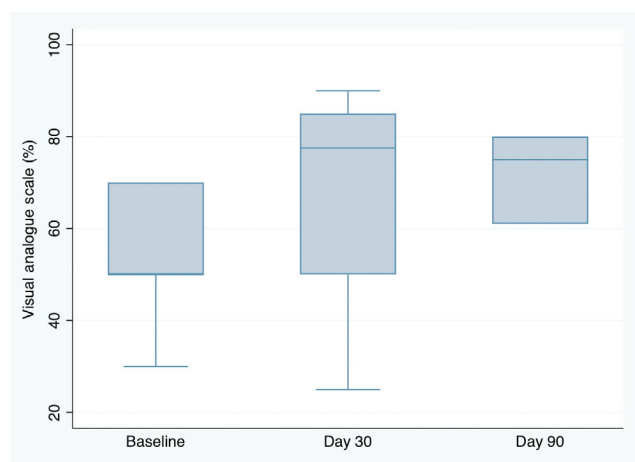
	Age (years)	Sex	Liver disease etiology	Baseline MELD	Child-Pugh	Ascitic fluid drained in 3 months prior	Duration, days	Reason for removal	Complication	Cause of death	Time to death, days	TIPS after IPC
1	39	Male	Alcohol	8	B8	11.7	77	Routine				
2	60	Male	Alcohol	9	B9	27.4	90	Nonadherence	IPC site cellulitis	Liver failure	214	x
3	25	Female	Alcohol	14	C14	0	40	Resolution of ascites				
4	60	Female	Alcohol	22	C11	51.65	5	Death		Liver failure	5	
5	56	Female	NAFLD	17	B7	27.86	18	Complication	IPC site leakage	Metastatic ovarian cancer	122	x
6	74	Female	Alcohol	13	A5	NA	138	Routine				
7	77	Male	Alcohol	11	B8	10.17	87	Routine				
8	53	Male	Hepatitis C	17	B7	30.35	119	Routine				
9	74	Male	Hepatitis Delta	33	C11	34.3	7	Complication	Cellulitis, bacterial peritonitis, and bacteremia	Liver failure	64	
10	59	Male	Hepatitis C and Alcohol	24	B7	30.25	15	Death		HCC	15	
11	41	Male	Alcohol	17	B8	52.42	96	Routine				
12	76	Male	Alcohol	21	B8	31.5	52	Nonadherence				x

HCC, hepatocellular carcinoma; IPC, intraperitoneal catheter; MELD, Model for End-Stage Liver Disease; NA, not available; NAFLD, non-alcoholic fatty liver disease; TIPS, transjugular intrahepatic portosystemic shunt.

Table 3 Liver disease severity, visual analog scale (VAS), and diuretic dosing at baseline, 30 days, and 90 days

Characteristic, median (IQR)	Baseline	30 days	<i>P</i> value	90 days	<i>P</i> value
MELD-Na score	17 (12–22)	18 (9–21)	0.21	17 (10–21)	0.34
Child–Pugh Score	8 (7–10)	7 (7–8)	0.55	7 (7–8)	0.46
VAS Score	50 (50–70)	78 (50–85)	0.39	75 (60–80)	NA
Spironolactone oral dose (mg)	100 (25–225)	75 (0–200)	0.79	100 (50–100)	0.11
Furosemide oral dose (mg)	40 (0–60)	40 (40–60)	0.68	40 (40–60)	0.65

IQR, interquartile range, mg milligrams; MELD, Model for End-Stage Liver Disease; NA, not available.

**Figure 1** Visual analog scale (EQ-5D).

frequent healthcare interactions have on this population through provision of discounted taxi vouchers. HRQoL measures will continue to be analyzed as part of a larger cost-effectiveness analysis, which is currently underway.

Distinct from current published data, the program we describe is truly multidisciplinary. Components included home-based drainage, specialized clinician review when required, dietitian management, and provision of appropriate nutritional supplements; and pharmacist consultation to assist with titration of diuretics, auditing vaccination administration, and clarifying differences in prescribed *versus* actual medication use. With overall coordination by a specialist nurse, the program increased healthcare interactions and promoted engagement with healthcare services, therefore improving the direct benefits to patients beyond the IPC management alone. The main disadvantage is increased ambulatory care costs; however, a 12-week feasibility nonblinded randomized control trial comparing LVP to long-term IPC in a similar cohort demonstrates preliminary evidence of safety and cost-effectiveness.¹⁴

Although excluded from this study, patients eligible for liver transplantation may also benefit from the holistic approach provided by this program. Common co-existing issues of malnutrition, substance use, and mental health can be intensively addressed through close, multidisciplinary support. The IPC program could therefore be utilized as a bridge to TIPS insertion or to liver transplantation in the absence of non-modifiable barriers to hepatic recompensation. Due to the risk of precipitating hepatic encephalopathy with TIPS, particularly those with

previous episodes, the IPC may also be a useful alternative strategy for refractory ascites in those ineligible for liver transplantation.

A major concern with the use of IPC is the risk of infection in this population, thus all patients in our cohort received daily prophylactic antibiotics. Cohort studies of IPC use in cirrhosis.¹²

References 12, 15, 16 have demonstrated variable rates and definitions of bacterial peritonitis, as elevations in ascitic fluid PMN cell count can be attributed to dysfunction of peritoneal macrophages in some cases, reflecting dysregulated immunity associated with a chronic liver disease rather than acute infection.¹⁷ A cohort study of 33 patients demonstrated microorganism growth from ascitic fluid in 38% over a median 117.5 days (95% confidence interval 48–182 days)¹²; however, this was not correlated with clinical features of sepsis or peritonitis. A case series of eight patients demonstrated IPC site cellulitis in two patients, with the IPC removed in one patient at day 219.¹⁵ The widely accepted definition of spontaneous bacterial peritonitis by the International Ascites Club consists of an ascitic fluid PMN cell count greater than or equal to 250 cells/mm³ as a threshold to commence empirical antibiotic therapy, although specificity is increased at 500 cells/mm³.¹⁸ We employed a modified definition to include clinical features of infection at the time of a PMN count of at least 250 cells/mm³, to ensure intravenous antibiotic administration is not delayed but avoids unnecessary IPC removal. PMN count fluctuated over the course of the program in all patients. The patient with *S. aureus* infection had a peak PMN count of 2589 cells/mm³, which correlated with abdominal pain, skin warmth, and erythema at the IPC site, and elevated serum inflammatory markers. Other patients in the cohort also demonstrated elevated PMN counts; however, in the absence of clinical infective features, no changes to treatment were made.

In our cohort, IPC removal due to peritonitis/bacteremia and leakage refractory to sutures, both occurred in patients with Child–Pugh C cirrhosis. The Child–Pugh classification system is commonly used to describe the severity and approximate 1-year survival rates.¹⁹ Although a multivariate analysis performed in the cohort study mentioned previously¹² demonstrated no association between Child–Pugh class and peritonitis due to typical enteric microorganisms, this cannot be extrapolated to our patient, in whom methicillin-susceptible *S. aureus* was demonstrated in both ascitic fluid and blood cultures who met criteria for Child–Pugh C classification. Due to safety concerns in this vulnerable group, we will exclude those with Child–Pugh C cirrhosis in a future randomized controlled study. We acknowledge

limitations including the small sample size and that no patients had a histological diagnosis of cirrhosis. Patients not meeting inclusion criteria ($n = 4$) were included to further evaluate this novel intervention and will be excluded in the follow-on evaluation of IPC use in this cohort.

In conclusion, short-term tunneled IPC for the management of refractory ascites in patients with cirrhosis was overall safe and associated with improved patient perceptions of health; however, the risk of serious infection, particularly in those with Child–Pugh C cirrhosis, remains. In the context of the COVID-19 pandemic, the program aimed to reduce face-to-face interactions, limit nosocomial infection to this vulnerable population while improving overall healthcare engagement. The study will continue to explore the safety and cost-effectiveness of this novel intervention during and after the COVID-19 pandemic.

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