

Systematic Review

Preventive and Treatment Interventions for Abdominal Ascites of Patients with Liver Cirrhosis: A Systematic Review of Randomized Controlled Trials

Ferya Çelik¹, Hicran Bektaş²

Department of Internal Medicine Nursing, Akdeniz University Faculty of Nursing, Antalya, Turkey

ORCID iDs of the authors: F.Ç. 0000-0002-2473-192X; H.B. 0000-0002-3356-3120

Cite this article as: Çelik, F., & Bektaş, H. (2021). Preventive and treatment interventions for abdominal ascites of patients with liver cirrhosis: A systematic review of randomized controlled trials. *Florence Nightingale J Nurs*, 29(2), 250-262.

Abstract

AIM: This systematic review aimed to evaluate the efficacy of preventive and therapeutic approaches used in the management of ascites in liver cirrhosis.

METHOD: Literature review was done in "Scopus, Web of Science, CINAHL, ScienceDirect, PubMed MEDLINE, Ulakbim National Database, and Cochrane Library" databases using the keywords, "ascites, refractory ascites, liver cirrhosis, intervention, prophylaxis, treatment, nursing management, prevention, ascites management, randomized controlled trials," and 2,447 articles were obtained. The studies with low bias risk were included. This systematic review was planned by following the recommendations of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement.

RESULTS: A total of 11 randomized controlled trials were included. When the included studies were examined, ascites treatment approaches were evaluated in all of the studies; however, preventive approaches were not evaluated. It was found that mannitol, a diuretic drug, helps ascites management by contributing to weight loss, decrease in abdominal circumference, and urinary sodium excretion. The automatic low-flow ascites pump also reduced the need for large-volume paracentesis. There was a decrease in weight and abdominal circumference measurements when band compression was applied to the umbilicus.

CONCLUSION: Therapeutic approaches were found to be effective. It was thought that the lack of nursing practices and the prevention of ascites formation in the abdomen was an important deficiency. Randomized controlled trials were recommended for the prevention of abdominal ascites formation and the side effects of treatment on the patient.

Keywords: Ascites, ascites management, liver cirrhosis, nursing management.

Introduction

Abdominal ascites is defined as the accumulation of excess fluid in the abdominal cavity. It can occur owing to liver diseases, malignancy, or heart failure and has been discussed in the perspective of liver cirrhosis in this systematic review. More than 50% of patients with liver cirrhosis develop ascites within 10 years (Biecker, 2011). Ascites development negatively affects the working and social life of the patient; escalates hospital admissions and chronic treatment costs; and causes problems such as spontaneous bacterial peritonitis, respiratory dysfunction, and umbilical hernia. Liver transplantation is recommended as the final treatment of ascites (European Association for the Study of the Liver, 2018). However, it cannot be performed in every patient with ascites because of the cost of the procedure,

the low number of donors, and contraindications for liver transplantation in some patients (Zhao et al., 2018). There is no specific treatment for liver cirrhosis. Therefore, the aim of treatment is to minimize the progression of the disease and prevent complications. In this context, nurses play an important role as they provide comprehensive and continuous patient care as a member of the multidisciplinary team (Gimenes et al., 2017). Nurses need to access and evaluate evidence-based research results so that they can safely meet the comprehensive and complex needs of patients with liver cirrhosis, prevent complications, maintain their care, use critical thinking skills in improving patient outcomes and complication management, and reduce complication-related hospital admissions and hospitalizations. Formation of ascites in the abdomen can also lead to secondary symptoms, such as excess fluid volume,

fluid-electrolyte imbalance, activity intolerance, anorexia, inadequate nutrition, dyspnea, the deterioration of skin integrity, risk of injury, chronic pain, or infection (Bulechek et al., 2017; Carpenito-Moyet, 2005; Gimenes et al., 2017). Therefore, preventive and therapeutic approaches to the development of ascites gain importance.

Sodium restriction and diuretic administration have an important place among the preventive approaches. In patients with ascites, a sodium-restricted diet of 4.6–6.9 g/day is recommended. It is stated that ascites can develop in patients at least 3 times in 12 months despite a sodium-restricted diet and diuretic treatment (European Association for the Study of the Liver, 2018). The development of ascites despite preventive measures brings therapeutic approaches to the fore. The methods used in the treatment of ascites are drug therapies, interventional methods, and liver transplantation. In addition to these, there are new treatment methods such as automated low-flow ascites pump (Arroyo, 2013; Stirnimann et al., 2017) and complementary approaches such as umbilical tape application (Xing et al., 2012).

It is recommended that the use of diuretics, which is among the drug treatment methods, should be planned in a way that the daily weight loss will not be more than 0.5 kg in patients without peripheral edema and 1 kg in patients with edema (European Association for the Study of the Liver, 2018). Midodrine and sotalolol are other treatment options used in ascites management (Biecker, 2011; European Association for the Study of the Liver, 2018). Large-volume paracentesis application, which is one of the interventional methods, is recommended as the first treatment option in the management of excessive ascites. The use of diuretics or large-volume paracentesis application provides a symptomatic improvement in ascites management instead of an ultimate treatment (European Association for the Study of the Liver, 2018). Transjugular intrahepatic portosystemic shunt (TIPS) is recommended for ascites management if paracentesis is not tolerated after 4 or more applications, patients do not improve, or there is a contraindication (Moore et al., 2003; Zhao et al., 2018). Transjugular intrahepatic portosystemic shunt helps refractory ascites recovery by reducing portal venous pressure (Rössle & Gerbes, 2010). With the automated low-flow ascites pump, one of the new treatment methods, the ascites fluid in the abdominal cavity is discharged through the bladder. It is stated that in

patients with decompensated cirrhosis or refractory ascites, the automated low-flow ascites pump reduces the ascites fluid and the need for paracentesis (European Association for the Study of the Liver, 2018).

Nurses caring for patients with liver cirrhosis have responsibilities in the prevention and treatment of ascites. Prevention interventions include training on nutrition, abstinence from alcohol, and monitoring the side effects of diuretic medications, kidney function, and hepatic encephalopathy symptoms, weight, abdominal circumference, and the amount of fluid intake and excretion. It has been stated that nurses should follow patients closely at home in the treatment of ascites. They are recommended to evaluate electrolyte values and renal functions after paracentesis and to question for abdominal discomfort or bleeding (Fullwood & Purushothaman, 2014). This systematic review aimed to evaluate the effectiveness of preventive and therapeutic approaches used in the management of abdominal ascites in patients with liver cirrhosis.

Method

Study Design

The study was designed as a systematic review.

Search Process and Study Selection

This systematic review was planned by following the recommendations of the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement (Moher et al., 2015).

Studies included in this systematic review were selected according to the PICOS Model proposed by the Joanna Briggs Institute (P: Population (the type of participants), characteristics of the participants; I: Intervention (the type of interventions), characteristics of the intervention; C: Comparison (the type of comparisons), characteristics of comparison groups; O: Outcome (the type of outcomes), outcomes; S: Study designs (the type of studies), study design) (The Joanna Briggs Institute, 2014).

P: Regardless of sex, race, socio-economic class, and etiology, patients aged more than 18 years with liver cirrhosis associated with ascites development constituted the target group of this systematic review.

I: The use of preventive and therapeutic interventions in patients with cirrhosis constituted the intervention groups of this systematic review.

C: The studies included in the systematic review were compared in terms of evaluating the effectiveness of preventive and therapeutic interventions in patients with cirrhosis.

O: The effects of interventions implemented to prevent and treat ascites development in patients with cirrhosis on ascites-related parameters such as the decreased need for paracentesis, weight loss, and decreased abdominal circumference measurement were examined.

S: Studies that used a randomized controlled trial design, published in the English language, and whose full text could be accessed were included in the study.

For this systematic review, a literature review was carried out between June and August 2019 with no year limitation on Scopus, Web of Science, CINAHL, Science-Direct, PubMed, Medline, Ulakbim National Database, and Cochrane Library databases using “ascites, refractory ascites, liver cirrhosis, intervention, prophylaxis, treatment, nursing management, prevention, ascites management, randomized controlled trials” as keywords and their Turkish translations. As a result of the review, 2447 articles were found. The number of studies found as a result of the review was

categorized according to databases and shown in the PRISMA-P flow chart (Figure 1). Repetitive studies were sorted out with the EndNote X7 (v. X7; Clarivate, 22 Thomson Place, 36T3 Boston, MA 02210), the titles and abstracts of the studies were examined, and studies that met the inclusion criteria were independently evaluated by the researchers. A total of 11 randomized controlled trials (RCTs) were included in the systematic review. The bias risk assessment of the studies was made, and were found to be low.

Inclusion Criteria

The inclusion criteria of this systematic review targeted studies

- with sample groups consisting of patients aged more than 18 years with liver cirrhosis, regardless of sex, race, socioeconomic status, and etiology;
- in which anti-ascitic and therapeutic interventions were administered to patients with ascites associated with liver cirrhosis;
- in which results related to ascites, such as ascites development, need for paracentesis, decrease in weight and abdominal circumference, as a result of interventions were evaluated, and that used a randomized controlled trial method and were published in Turkish and English languages, with no year limitation.

Evaluation of Studies

The quality evaluation of the studies included in a systematic review should be done with valid and reliable tools to reach high evidence results. The studies included in this systematic review were evaluated using the “bias assessment tool for RCTs” proposed by the Cochrane Library. In this assessment tool, studies are evaluated using criteria, such as the type of the randomization method, hiding randomization information, participant and practitioner blinding, blinding in the evaluation of results, incomplete results data, and elective reporting criteria. According to these criteria, the studies are judged as low risk, high risk, or vague. In the assessment tool, low-risk judgment is denoted with a ‘+,’ high-risk judgment with a ‘-,’ and situations that are not fully explained in the study are shown with a ‘?’ A high number of low-risk situations indicates that the study has a low bias (Higgins et al., 2011). The bias evaluation of the studies included in this systematic review is given in Figure 2. The bias risks of the studies included in this systematic review were found to be low.

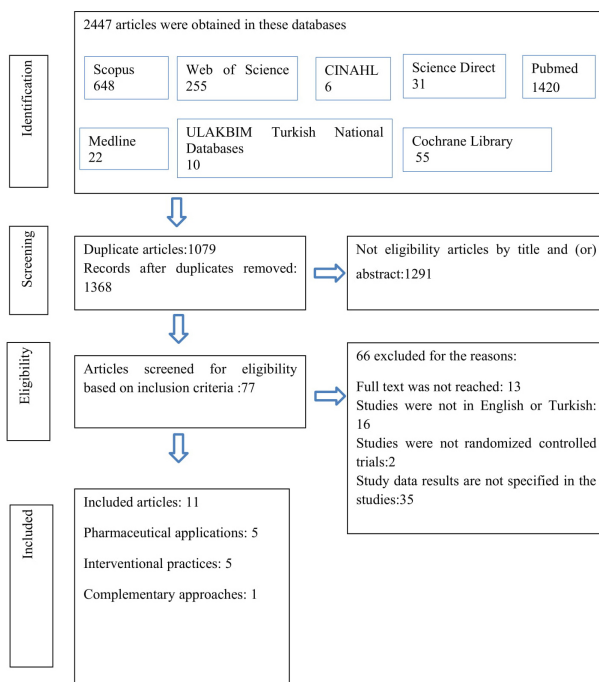


Figure 1
Flowchart of Study Identification (PRISMA-P Flow Diagram)

STUDIES	RISK OF BIAS SUMMARY					
	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personel (performance bias)	Blinding of outcome assesment (detection bias)	Selective reporting (reporting bias)	Other bias
Xing et al. 2012	+	+	+	+	+	+
Wong et al. 2010	+	+	+	+	+	+
Bureau et al. 2017	+	+	-	-	+	+
Rössle et al. 2000	+	+	?	?	+	+
Bureau et al. 2016	+	+	?	?	+	+
Narahara et al. 2011	+	+	?	?	+	+
Gine`s et al. 2002	+	+	?	?	+	+
Raza et al., 2010	+	-	+	+	?	+
Caraceni et al. 2018	+	+	-	-	+	+
Bari et al. 2012	+	+	+	-	+	+
Hanafya and Hassaneenb, 2016	+	+	+	?	+	+

“+”: low risk “-“ : high risk “?”: unclear risk

Figure 2
Risk of Bias Summary

Results

A total of 11 RCTs were included in this systematic review that was carried out to evaluate the effectiveness of preventive and therapeutic approaches in the management of abdominal ascites in patients with liver cirrhosis. The studies were conducted between June 2000 and June 2018. All the studies were found to evaluate therapeutic approaches to ascites, but did not include preventive approaches. This systematic study focused on the evaluation of the effectiveness of preventive and therapeutic approaches in ascites management in individuals with liver cirrhosis, and the keywords for the database search had been chosen accordingly. Although no studies evaluating preventive approaches could be included in the systematic review, we decided to include the phrase “preventive ap-

proaches” in the title of the study so that we would not take sides and could emphasize the lack of preventive approaches in practice. The therapeutic approaches in this systematic review were grouped under the following titles: pharmaceutical applications, interventional practices, and complementary approaches. Summaries of the studies are presented in Table 1.

Pharmaceutical Applications

Features of the Studies

Of the studies included in the systematic review, 5 evaluated the efficiency of drugs used in ascites treatment in patients with liver cirrhosis. Albumin, diuretics, midodrine, and satavaptan were used for ascites management. The studies covered the period between August 2010 and June 2018.

Table 1

Results of Studies Including Therapeutic Approaches Used in Ascites Management in Patients with Liver Cirrhosis

Pharmaceutical Applications

Article	Sample (n)	Method	Application Format	Examined Parameters	Results
Caraceni et al. (2018)	IG:176 CG:172	IG: Albumin was administered in addition to routine treatment CG: Routine treatment administered	Albumin administration was applied as 40 g twice a week for two weeks, then 40 g per week.	Number of paracentesis	The need for paracentesis was found to be lower in the intervention group.
Hanafy and Hassaneen, (2016)	IG:370 CG:85	IG: Midodrine and rifaximin were used in addition to diuretic treatment CG: Diuretic treatment administered	Midodrine 3×5 mg, rifaximin 2×550 mg administered. All of the patients consumed 2 gr/day salt in their diets.	Diuresis Check of ascites weight	Diuresis, weight loss, and need for paracentesis were lower in the intervention group.
Bari et al. (2012)	IG1:35 IG2:35	IG1:Octreotide and Midodrine administered IG2:Albumin administered	Midodrine 3×10 mg/day oral, octreotide 20 mcg intramuscular injection	Ascites formation time	Ascites formation occurred earlier in the octreotide and midodrine group.
Raza et al. (2011)	IG:30 CG:30	IG: Mannitol administered	20% mannitol was administered intravenously as 30 g.	Natriuresis, urine volume, weight, abdominal circumference	In the intervention group, natriuresis, increased urine volume, weight, and abdominal circumference decreased.
Wong et al. (2010)	IG1:19 IG2:27 IG3:28 PG:20	IG1:Sativaptan 5 mg administered IG2: Satavaptan 12.5 mg administered IG3: Satavaptan 25 mg administered	5, 12.5, and 25 mg satavaptan administered.	Paracentesis frequency The increasing amount of ascites	Paracentesis frequency decreased in all groups using Satavaptan. The increase in the number of ascites in the placebo group was greater than in the other groups.

Interventional Practices

Bureau et al. (2017a)	IG1:27 CG:31	IG1: Automated low-flow ascites pump administered CG: Large-volume paracentesis administered	IG1: Using of diuretic discontinued IG2: Diuretic protocol continued.	Large-volume paracentesis time Paracentesis requirement	The need for paracentesis and the number of paracentesis performed were less in the group treated with an automatic low-flow ascites pump.
Bureau et al. (2017b)	IG1:29 IG2:33	IG1:TIPS administered IG2: Large-volume paracentesis administered	When 3 L or more of acid liquid was removed, 8 g/L of albumin group were applied.	Ascites formation Admission to the hospital	The number of required paracentesis was 32 in the TIPS group, whereas it was 320 in the large-volume paracentesis group. The number of admissions to the hospital was 17 days in the TIPS group and 35 days in the paracentesis group.

Table 1*Results of Studies Including Therapeutic Approaches Used in Ascites Management in Patients with Liver Cirrhosis (Continued)***Pharmaceutical Applications**

Article	Sample (n)	Method	Application Format	Examined Parameters	Results
Interventional Practices					
Narahara et al. (2011)	IG1:30 IG2:30	IG1:TIPS administered IG2: Albumin and large-volume paracentesis administered	In case of withdrawal of 4 L or more in large-volume paracentesis application, 6 g of albumin was applied for each liter of withdrawn fluid.	Check of ascites	Control of ascites was better in the TIPS group.
Ginès et al. (2002)	IG1:35 IG2:35	IG1:TIPS administered IG2: Large-volume paracentesis group with albumin administered	Albumin 8 g/L of fluid drawn administered with large-volume paracentesis application.	Formation of ascites	Ascites and hepatorenal syndrome development is lower in the TIPS group.
Rössle et al. (2000)	IG1:29 IG2:31	IG1:TIPS administered IG2: Large-volume paracentesis	GG1: TIPS administered. GG2: The group that continues diuretic therapy as long as it can tolerate, when 4 L or more of ascites fluid is removed, 8 g of albumin per liter are administered.	Response to treatment	The need for paracentesis was found to be less in the TIPS group. The daily dose of spironolactone was decreased in the TIPS group.
Complementary Approaches					
Xing et al. (2012)	IG: 47 PG: 45	Xiaozhang Tie cataplastic patch administered to umbilicus	Compression of 7×7 cm long patches to the umbilicus.	Ascites, urine volume, abdominal circumference, weight Liver function	In the intervention group, there was a greater reduction in ascites, abdominal circumference, and weight measurements, and a greater increase in urine volume. In the intervention group, there was a decrease in bilirubin value and an increase in albumin value.

Note. *IG = intervention group; IG1 = intervention group 1; IG2 = intervention group 2; IG3 = intervention group 3; CG = control group; PG = placebo group.

Results of the Studies

The study in which albumin infusion was administered to the intervention group, paracentesis was required in 71 of the 176 patients in the intervention group and in 116 of 172 patients in the control group ($p < .001$) (Caraceni et al., 2018). The study in which the effects of the use of midodrine and rifaximin together with diuretic treatment on diuresis, ascites control, and weight loss was compared with diuretic use alone found that although diuresis and weight loss were higher in the intervention group, the need for paracentesis was low ($p < .001$) (Hanafya & Hassaneen, 2016). In the study evaluating the effect of

octreotide and midodrine use on ascites formation after large-volume paracentesis intervention, compared with albumin use, ascites was observed to form earlier in the octreotide and midodrine group (Bari et al., 2012). In the study evaluating the effect of mannitol use on natriuresis, urine volume, weight, and abdominal circumference, it was observed that the amount of sodium excreted in urine ($p < .001$), weight loss ($p < .05$), and the decrease in abdominal circumference ($p < .001$) were higher in the intervention group (Raza et al., 2011). In the study evaluating the efficiency of satavaptan in ascites management, the sample had been divided into 4 study groups, of

which 3 groups were administered 5 mg, 12.5 mg, and 25 mg satavaptan, and the fourth group was administered a placebo. The mean increase in the volume of ascites was higher in the placebo group than in the other groups. The mean increase in ascites was $2.82 \pm .48$ /week in the placebo group, whereas it was $2.12 \pm .40$, $2.14 \pm .33$, $2.06 \pm .40$ /week in the groups using 5, 12.5, and 25 mg satavaptan, respectively. The frequency of paracentesis was found to decrease in all groups using satavaptan ($p < .05$) (Wong et al., 2010).

Interventional Practices

Features of the studies

Of the studies included in the systematic review, 5 evaluated the efficiency of interventional treatments used for ascites treatment in patients with liver cirrhosis. Paracentesis, automated low-flow ascites pump, and TIPS application were among the interventional methods used. The studies were conducted between June 2000 and January 2017.

Results of the Studies

In the study evaluating the efficiency of the automated low-flow ascites pump, the need for the large-volume paracentesis emerged later in the intervention group ($p < .001$) (Bureau et al., 2017a). Bureau et al. have compared the TIPS with large-volume paracentesis and found that the number of paracenteses required during the study was 32 in the TIPS group and 320 in the large-volume paracentesis group (Bureau et al., 2017b). The number of hospital presentations of patients in the large-volume paracentesis group was twice that of the TIPS group ($p < .05$). In another study that compared the efficiency of the TIPS application with the large-volume paracentesis application, it was stated that the TIPS application was more effective than the large-volume paracentesis application in the control of ascites ($p < .01$). However, the rate of hepatic encephalopathy development was higher in the TIPS group (Narahara et al., 2011). In another study, the development of ascites and hepatorenal syndrome was less in the group treated with TIPS than in the group treated with paracentesis, whereas the development of hepatic encephalopathy was higher in the group treated with TIPS (Ginès et al., 2002). In a study by Rössle et al. (2000) although patients in the TIPS group needed paracentesis 21 times during the study, patients in the paracentesis group required paracentesis 280 times. The daily dose of spirono-

lactone decreased in the TIPS group ($p < .05$) (Rössle et al., 2000).

Complementary Approaches

Features of the Studies

Of the studies included in the systematic review, 1 examined the effect of plaster compression applied on the umbilicus for ascites management. The study was conducted in January 2012 (Xing et al., 2012).

Results of the Study

In the placebo-controlled study, in which a cataplast plaster application called Xiaozhang Tie was applied to the umbilicus, the compression was applied to the umbilicus using 7×7 cm long plasters. When change in the volume of ascites was evaluated with ultrasound in the intervention group, it was found that ascites fluid was not detected in 17 patients, it was eliminated in 14 patients, it was partially reduced in 15 patients, and there was only a slight decrease in 1 patient. In the placebo group, however, ascites could not be detected in 9 patients, it was eliminated in 10 patients, partially reduced in 16 patients, and a very slight decrease was observed in 10 patients. In the intervention group, the decrease in weight and abdominal circumference measurements ($p < .01$) and the increase in urine volume were found to be higher ($p < .05$). Although there was a decrease in bilirubin value ($p < .05$) and an increase in albumin value ($p < .01$) in the intervention group, there was statistically no significant change in the alanine aminotransferase (ALT) value. In the control group, although there was no statistically significant change in the bilirubin value, the ALT value was found to decrease ($p < .05$), and the albumin value increased ($p < .01$) (Xing et al., 2012).

Discussion

Although chronic liver diseases are among the major global health problems, not much attention is paid by nurses to it compared with other chronic diseases, such as diabetes, chronic lung diseases, cardiovascular diseases, and neurological diseases. It is recommended that the education and training of nurses in the field of hepatology should be improved, and the number of nurses providing care to patients with chronic liver diseases in primary healthcare services and hospitals should be increased (Fabrellas et al., 2018). As health professionals, nurses play an important role in providing holistic care to patients

with chronic liver diseases, providing pretreatment training, increasing the treatment compliance of patients, and providing control and evaluation during the treatment process (Shah & Abu-Amara, 2013).

In this systematic review, which evaluated the effectiveness of preventive and therapeutic approaches to the management of ascites in patients with liver cirrhosis, a literature review was conducted without a year limitation. The review revealed that although many studies were found, and there were keywords to detect studies on preventive approaches, none of the studies included in the study were found to address ascites-preventive approaches. However, it was stated that the rate of repeated hospitalizations owing to ascites varied between 13.8% (Tapper et al., 2016) and 26.9% within 30 days (Pate et al., 2019) and between 21% (Tapper et al., 2016) and 56% within 90 days (Shaheen et al., 2019). Reasons for repeated hospitalizations for ascites were reported as insufficient training on salt restriction and inadequate paracentesis administration before discharge (Tapper & Volk, 2017; Volk et al., 2012). Although salt consumption is one of the keystones in ascites management, a study reported that 48% of the participants thought that sea salt had less sodium than table salt (Volk et al., 2013). In the 2018 guidelines of the EASL, it was stated that the provision of training about salt consumption to patients with ascites would prevent hospitalizations caused by noncompliance with salt restriction (European Association for the Study of the Liver, 2018; Tapper & Volk, 2017). The primary role of nurses in the ascites management of patients with cirrhosis includes preventing ascites formation. Patient education provided by the nurse has an important place in the prevention of ascites formation. The content of patient education includes topics, such as eating a sodium-restricted diet, avoiding alcohol, ensuring compliance with medical treatment, maintaining fluid-electrolyte balance, and gaining skills that can provide ascites management outside the hospital (Fullwood & Purushothaman, 2014; Thomson et al., 2015). Nurses should inform patients that no salt should be added to foods and that daily salt consumption should be planned as 4.6–6.9 g (European Association for the Study of the Liver, 2010). The positive effect of avoiding alcohol on liver health should be explained, and patients should be guided to seek specialist support, if necessary, to stop alcohol use. Appropriate interventions should be planned for substance use disorder (Carpenito-Moyet, 2005). To maintain as-

cites management outside the hospital, the patients should gain the ability to follow intake and excretion, monitor weight with the same clothes at the same hour every day, and make abdominal circumference measurements (Thomson et al., 2015).

In the initial phase of ascites formation, nurses have responsibilities for the identification of ascites. The abdomen should be observed continuously, and a physical examination should be done. The patient should be evaluated in terms of enlargement, tension, and dryness of the skin, cracks, and umbilical hernia around the abdomen by inspection. Appropriate nursing interventions should be planned, according to nursing diagnosis, for impaired tissue integrity. The effects of change in physical appearance on the patient should be evaluated, and psychological support should be provided when necessary. Appropriate nursing interventions should be planned for body image discomfort per the nursing diagnosis (Bulechek et al., 2017). Symptoms, such as sensitivity and pain in the abdominal area, should be evaluated with palpation (Fullwood & Purushothaman, 2014). Appropriate nursing interventions should be planned for pain management per the nursing diagnosis. With fluid accumulation in the abdominal cavity, the space required for expansion of the lungs decreases, and the patients may experience dyspnea, especially in the supine position. Patients may restrict their physical activity owing to dyspnea and the feeling of weight created by the ascites fluid. The pressure of the fluid in the abdomen to the stomach may cause early satiety in patients; and therefore, they may eat less than they need. The compression of ascitic fluid on the intestines can reduce the blood flow to the abdominal organs, leading to a decrease in intestinal and renal functions, which can accelerate the development of hepatic encephalopathy (with decreased intestinal function) and hepatorenal syndrome (with decreased renal function) (Werner & Perez, 2012). The patients' quality of life may decrease with the development of liver cirrhosis complications such as hepatic encephalopathy and hepatorenal syndrome in the pathogenesis of dyspnea, decreased mobility, decreased nutrition, body appearance, and ascites formation (Cox-North et al., 2013). Nurses should be sensitive to patients, patient education should be sustainable, and appropriate interventions should be planned by evaluating the psychological needs of patients. The patients should also be supported in activities that will help increase their comfort, such as listening to music, reading books, and meditation

(Fullwood & Purushothaman, 2014). Appropriate nursing interventions should be planned according to the nursing diagnoses of ineffective breathing patterns, activity intolerance, inadequate nutrition, constipation, and excess fluid volume (Bulechek et al., 2017; Carpenito-Moyet, 2005).

The most effective method in patients with ascites is liver transplantation. However, the impossibility of liver transplantation in all patients necessitates focusing on new approaches to treating ascites with the high success levels and minimal complications. The first of these approaches is drug therapy. Drug therapies used in the management of ascites include midodrine (European Association for the Study of the Liver, 2018) and satavaptan as well as diuretics and albumin (Wong et al., 2010). In their study comparing the use of midodrine together with octreotide with the use of albumin, Bari et al. (2012) have found that ascites formation occurred later in the group using albumin. In a study of Caraceni et al. (2018), it was reported that albumin infusion reduced the need for paracentesis. It has been stated that mannitol, a diuretic drug, helps ascites management by contributing to weight loss, decrease in abdominal circumference, and urinary sodium excretion (Raza et al., 2011). It has been found that some antibiotic drugs used in ascites treatment (European Association for the Study of the Liver, 2018), and the combination of rifaximin, an antibiotic used in liver diseases, with midodrine increases diuresis and weight loss and reduces the need for paracentesis (Hanafy & Hassaneen, 2016). In addition, the use of 5–25 mg of satavaptan may be beneficial in reducing ascites formation following the large-volume paracentesis (Wong et al., 2010).

When RCTs are examined, it is seen that various drug groups are used in ascites management. The nurses should know of the drug therapies used in ascites management and their effects and side effects. During drug treatment for ascites management, the patients should be informed by the nurses of the follow-up of daily weights and laboratory values. Daily weight loss should be targeted at 0.5 kg in patients without peripheral edema and 1 kg in patients with peripheral edema. Diuretic treatments should be reviewed if the weight loss is less than 2 kg a week (European Association for the Study of the Liver, 2010). The patients should be informed and followed up for the side effects of diuretic use, such as renal failure, electrolyte imbalances, muscle cramps, gynecomas-

tia, and hepatic encephalopathy. Albumin, sodium, and potassium values should be followed up from laboratory values (Hampel et al., 2001). Appropriate nursing interventions regarding electrolyte management should be planned (Bulechek et al., 2017). The positive effect of albumin infusion on paracentesis requirement necessitates the storage, administration, and monitoring of the efficiency of albumin. The high efficiency of some drugs used in treatment, their positive effects on diuresis, weight loss, and paracentesis need along with salt restriction show the importance and necessity of nurses using this information for care and patient education. During the evaluation of the effectiveness of drug use in ascites treatment in patients with liver cirrhosis, the absence of RCTs on preventive measures and nursing interventions for the use and side effects of these drugs indicates that more studies are needed in this area.

Interventional methods are required when repeated formation of ascites cannot be prevented despite drug treatments. In large-volume paracentesis application, which is one of the interventional methods, albumin infusion is administered to prevent circulatory shock after paracentesis (European Association for the Study of the Liver, 2018). The cost of albumin infusion; the inability to use the paracentesis procedure in patients who are not collaborative, have an abdominal infection, are pregnant, and have severe coagulopathy or intestinal distension; the inability to prevent recurrent ascites formation despite paracentesis application; and the necessity that patients should present to the hospital every 1–3 weeks require alternative methods to the paracentesis procedure (Arroyo, 2013; European Association for the Study of the Liver, 2018; Stirnimann et al., 2017). Therefore, TIPS application is recommended if paracentesis cannot be tolerated after 4 or more paracentesis applications or if there is a contraindication (Zhao et al., 2018). In large-volume paracentesis administration, nurses should ensure that the procedure is carried out in line with aseptic principles. Before the procedure, the pain assessment of the patient should be made, and the pain level should be questioned after the procedure. The vital signs of the patient must be evaluated before the procedure, their general condition must be observed during the procedure, and cardiac stability must be evaluated every 15–30 minutes. The patient should be in a comfortable position and calm during the procedure. Conditions, such as bleeding, circulatory shock,

and infection that may develop after paracentesis, should be evaluated; and necessary interventions should be performed (European Association for the Study of the Liver, 2010). After the drainage catheter is removed, the intervention area should be covered with a clean and dry sponge and observed for bleeding. To prevent cardiovascular complications, appropriate fluid replacement and albumin infusion should be done when necessary (Bernardi et al., 2012). Renal functions should be checked to follow the development of hepatorenal syndrome. To prevent the recurrence of ascites after the procedure, the appropriate medication should be maintained, and electrolyte values and renal functions should be monitored. The patient should be encouraged to inform the healthcare staff if they have problems such as abdominal discomfort and/or bleeding at the site of the procedure area following the intervention (Werner & Perez, 2012).

Studies have shown that the use of TIPS reduces the need for paracentesis. In the study by Bureau et al., (2017b) the number of paracenteses required was 32 in the TIPS group, whereas it was 320 in the large-volume paracentesis group. It was reported that the paracentesis requirement of the large-volume paracentesis group was 10 times greater than in the TIPS group. In the study of Rössle et al. (2000) patients in the TIPS group required paracentesis 21 times in total, whereas the patients in the paracentesis group required paracentesis 280 times, which was more than 10 times of what the TIPS group required. Narahara et al. (2011) have stated that the TIPS application was more effective than the large-volume paracentesis application in ascites management. Because recurrent ascites development was high in the group in which large-volume paracentesis was applied, complications such as bleeding owing to increased portal pressure, increase in hospital admissions, and umbilical hernia because of the pressure and tension created by abdominal ascites were observed (Bureau et al., 2017b). TIPS is an effective method in ascites management, and it reduces hospitalizations owing to ascites; however, hepatic encephalopathy was found to be higher in patients who underwent TIPS. Ascites development was less in the group that was administered TIPS, whereas the rate of hepatic encephalopathy development of was observed to be high (Narahara et al., 2011). Nurses should evaluate patients who have undergone TIPS in terms of complications that may develop because of the interventional proce-

dures and especially hepatic encephalopathy that can develop after the procedure. Although TIPS reduces hospital admissions, there is a need for different effective treatment options that increase patient comfort because of the inability to apply it in some patients, the complications related to the procedure, and the prevalence of hepatic encephalopathy. It has been stated that an automated low-flow ascites pump, which is a new method in the treatment of ascites, increases the quality of life of patients and reduces the need for paracentesis and hospital admissions (Bureau et al., 2017a). This pump automatically removes ascites fluid from the abdominal cavity in small amounts. Thus, albumin infusion is not required to prevent circulatory shock as in the large-volume paracentesis. This method is reported to reduce the cost and increase the comfort of the patient (Stirnemann et al., 2017). Results of RCTs on interventional applications show that the effectiveness of automated low-flow ascites pump and TIPS applications in ascites treatment is high. The automated low-flow ascites pump improves the quality of life by allowing patients to adjust the speed and amount of ascites fluid removal according to clinical and social requirements. However, it has some complications. Nurses should inform the patients about interventional problems that may arise during the insertion of the pump and complications such as infection, and catheter dislocation that may occur after the procedure. Nurses should evaluate patients in terms of these symptoms (Bellot et al., 2013). Positive contributions can be made to patient outcomes when nurses caring for patients with liver cirrhosis are aware of the results of RCTs regarding interventional practices, patient follow-up, patient education, and increase their knowledge.

Complementary approaches are also used for ascites management in the studies reviewed. In a study evaluating umbilical band application, it was found that weight and abdominal circumference measurements decreased and urine volume increased in the group in which the band was applied. Although this is effective in ascites management, caution should be exercised when using complementary approaches (Xing et al., 2012). Nurses should be informed that the patients should avoid the use of drugs or supplements that may cause a decrease in kidney function or sodium retention and that may interact with the drugs used (Hampel et al., 2001). Nurses can contribute positively to patient care and education and patient outcomes when they

have enough knowledge in this field. They should question the complementary approaches used by patients with liver disease, be careful about the negative effects of these approaches, and inform the patients and their families.

There are many different methods used to manage ascites in the abdomen. However, these methods can have positive and negative effects. Liver transplantation, which is stated to be the most effective method in ascites treatment, cannot be applied to all patients. Nurses should inform patients about liver transplantation as soon as ascites starts to form. The introduction of stem cell therapies for liver diseases and positive results show that there is hope for treatment without the need for liver transplantation in the future (Liang et al., 2012).

When the results of therapeutic approaches are examined, it is seen that the interest in innovative methods with low complications in ascites management, which will reduce hospital dependence and improve patient comfort, is increasing. However, despite these advances in treatment, the limited number of RCTs on the nursing care of patients with ascites is seen as an important deficiency. It is thought that studies that examine or compare the effectiveness of nursing interventions, such as preventing ascites in the abdomen, detecting it earlier, daily weight monitoring, abdominal circumference measurement, salt restriction, and medication management should be conducted and that nursing practices including effective patient monitoring systems should be expanded. Expected patient outcomes after nursing interventions for ascites management include prevention of ascites recurrence; increasing quality of life by maintaining adequate nutrition, respiratory functions, and mobility; prolonging survival until transplantation; prevention of ascites complications, such as spontaneous bacterial peritonitis, renal failure, and hepatic encephalopathy; and reducing the length of hospital stay and the frequency of readmissions because of the treatment and complications of ascites (Fitzpatrick, 2010).

Conclusion and Recommendations

In this systematic review, preventive and therapeutic approaches to ascites were evaluated based on the results of RCTs with no year limitation. Although keywords related to preventive approaches were

used in the literature review, no studies evaluating preventive approaches according to the inclusion criteria were found. The need for repetitive paracentesis in patients with abdominal ascites and repeat hospitalizations is quite common. It is thought that ascites-preventive nursing approaches, such as weight control, salt restriction, diet and medication compliance, and follow-up of drug side effects will contribute to the prevention of ascites formation. Contrary to preventive studies, it was observed that there were various studies on therapeutic approaches. Currently, the focus is on stem cell studies for liver diseases. It is expected that there will be a cure for liver diseases without the need for liver transplantation in the future.

Nurses who care for patients with cirrhosis have an important role before and during the formation of ascites and in every step of ascites treatment before, during, and after the procedure. Therefore, these nurses are recommended to plan their interventions under the guidance of nursing diagnoses, such as substance use disorder, excess fluid volume, pain, ineffective breathing pattern, activity intolerance, inadequate nutrition, constipation, electrolyte management, impaired tissue integrity, body image discomfort, or infection risk. We believe that this systematic review will contribute to the education of nurses who care for patients with cirrhosis and the nursing instructors about effective ascites management approaches. The nurses are recommended to follow evidence-based information in outpatient and clinical follow-ups of patients with cirrhosis, to conduct RCTs to prevent ascites in the abdomen, to follow up-to-date treatment methods and their effects, and to plan nursing interventions according to patient requirements for treatment methods to prevent complications and repeated hospitalizations.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – F.C., H.B.; Design – F.C., H.B.; Supervision – H.B.; Resources – F.C., H.B.; Materials – F.C., H.B.; Data Collection and/or Processing – F.C., H.B.; Analysis and/or Interpretation – F.C., H.B.; Literature Search – F.C., H.B.; Writing Manuscript – F.C., H.B.; Critical Review – H.B.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

References

- Arroyo, V. (2013). A new method for therapeutic paracentesis: The automated low flow pump system. Comments in the context of the history of paracentesis. *Journal of Hepatology*, *58*(5), 850-852. [Crossref]
- Bari, K., Miñano, C., Shea, M., Inayat, I. B., Hashem, H. J., Gilles, H., Heuman, D., & Garcia-Tsao, G. (2012). The combination of octreotide and midodrine is not superior to albumin in preventing recurrence of ascites after large-volume paracentesis. *Clinical Gastroenterology and Hepatology*, *10*(10), 1169-1175. [Crossref]
- Bellot, P., Welker, M. W., Soriano, G., von Schaewen, M., Appenrodt, B., Wiest, R., Whittaker, S., Tzonev, R., Handshiev, S., Verslype, C., Moench, C., Zeuzem, S., Sauerbruch, T., Guarner, C., Schott, E., Johnson, N., Petrov, A., Katzarov, K., Nevens, F., ... Such, J. (2013). Automated low flow pump system for the treatment of refractory ascites: A multi-center safety and efficacy study. *Journal of Hepatology*, *58*, 5, 922-927. [Crossref]
- Bernardi, M., Caraceni, P., Navickis, R. J., & Wilkes, M. M. (2012). Albumin infusion in patients undergoing large-volume paracentesis: A meta-analysis of randomized trials. *Hepatology*, *55*(4), 1172-1181. [Crossref]
- Biecker, E. (2011). Diagnosis and therapy of ascites in liver cirrhosis. *World Journal of Gastroenterology*, *17*(10), 1237-1248. [Crossref]
- Bulechek, G. M., Butcher, H. K., Dochterman, J. M., & Wagner, C. M., 2017. Nursing Interventions Classification (NIC). (Eds: Erdemir, F., Kav, S., Akman Yilmaz, A.). Istanbul, Turkey: Nobel Medical Bookstores, pp:337-339.
- Bureau, C., Adebayo, D., de Rieu, M. C., Elkrief, L., Valla, D., Peck-Radosavljevic, M., McCune, A., Vargas, V., Simon-Talero, M., Cordoba, J., Angeli, P., Rosi, S., MacDonald, S., Malago, M., Stepanova, M., Younossi, Z.M., Trepte, C., Watson, R., Borisenko, O., ... Jalan, R. (2017a). Alfapump® system vs. large volume paracentesis for refractory ascites: A multicenter randomized controlled study. *Journal of Hepatology*, *67*(5), 940-949. [Crossref]
- Bureau, C., Thabut, D., Oberti, F., Dharancy, S., Carbonell, N., Bouvier, A., Mathurin, P., Otal, P., Cabarrou, P., Péron, J.M., & Vinel, J.P. (2017b). Transjugular intrahepatic portosystemic shunts with covered stents increase transplant-free survival of patients with cirrhosis and recurrent ascites. *Gastroenterology*, *152*(1), 157-163. [Crossref]
- Caraceni, P., Riggio, O., Angeli, P., Alessandria, C., Neri, S., Foschi, F.G., Levantesi, F., Airoldi, A., Boccia, S., Svegliati-Baroni, G., Fagioli, S., Romanelli, R.G., Cozzolongo, R., Di Marco, V., Sangiovanni, V., Morisco, F., Toniutto, P., Tortora, A., De Marco, R., G., ... Bernardi, M. (2018). Long-term albumin administration in decompensated cirrhosis (ANSWER): An open-label randomised trial. *The Lancet*, *391*(10138), 2417-2429. [Crossref]
- Carpenito-Moyet, L. (2005). Nursing Diagnostics Handbook (Ed. Erdemir, F.). Istanbul, Turkey: Nobel Medical Bookstores, pp:335-342.
- Cox-North, P., Doorebus, A., Shannon, S. E., Scott, J., & Curtis, J. R. (2013). The transition to end-of-life care in end-stage liver disease. *Journal of Hospice and Palliative Nursing*, *15*(4), 209-215. [Crossref]
- European Association for the Study of the Liver (EASL), (2010). EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. *Journal of Hepatology*, *53*(3), 397-417.
- European Association for the Study of the Liver (EASL), (2018). EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. *Journal of Hepatology*, *69*(2), 406-460. [Crossref]
- Fabrellas, N., Carol, M., Torradadella, F., & De Prada, G. (2018). Nursing care of patients with chronic liver diseases: Time for action. *Journal of Advanced Nursing*, *74*, 498-500. [Crossref]
- Fitzpatrick, E., (2010). Assessment and management of patients with hepatic disorders. In S. Smeltzer, B. Bare (Eds.), *Brunner&Suddarth's Textbook of Medical Surgical Nursing* (pp. 1153-1158). China: Wolters Kluwer.
- Fullwood, D., & Purushothaman, A. (2014). Managing ascites in patients with chronic liver disease. *Nursing Standard*, *28*(23), 51-58. [Crossref]
- Gimenes, F. R. E., Motta, A. P. G., Silva, P. C. S., Gobbo, A. F. F., Atila, E., & Carvalho, E. C. (2017). Identifying nursing interventions associated with the accuracy used nursing diagnoses for patients with liver cirrhosis. *Revista Latino-Americana de Enfermagem*, *25*, e2933. [Crossref]
- Ginès, P., Uriz, J., Calahorra, B., Garcia-Tsao, G., Kamath, P. S., Del Arbol, L. R., Planas, R., Bosch, J., Arroyo, V., & Rodés J. (2002). Transjugular intrahepatic portosystemic shunting versus paracentesis plus albumin for refractory ascites in cirrhosis. *Gastroenterology*, *123*(6), 1839-1847. [Crossref]
- Hampel, H., Bynum, G. D., Zamora, E., & El-Serag, H. B. (2001). Risk factors for the development of renal dysfunction in hospitalized patients with cirrhosis. *American Journal of Gastroenterology*, *96*(7), 2206-2010. [Crossref]
- Hanafy, A. S., & Hassaneen, A. M. (2016). Rifaximin and midodrine improve clinical outcome in refractory ascites including renal function, weight loss, and short-term survival. *European Journal of Gastroenterology & Hepatology*, *28*(12), 1455-1461. [Crossref]
- Higgins, J. P. T., Altman, G., Gøtzsche, P. C., Jüni, P., Moher, D., Oxman, A. D., Savovic, J., Schulz, K. F., Weeks, L., & Sterne, J. A. C. (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*, *343*, d5928. [Crossref]
- Liang, J., Zhang, H., Zhao, C., Wang, D., Ma, X., Zhao, S., Wang, S., Niu, L., & Sun, L. (2017). Effects of allogeneic mesenchymal stem cell transplantation in the treatment of liver cirrhosis caused by autoimmune diseases. *International Journal of Rheumatic Diseases*, *20*, 1219-1226. [Crossref]
- Moher, D., Shamseer, L., & Clarke, M. (2015). Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews*, *4*(1), 1. [Crossref]
- Moore, K.P., Wong, F., Gines, P, Bernardi, M., Ochs, A., Salerno, F., Angeli, P., Porayko, M., Moreau, R., Garcia-Tsao, G., Jimenez, W., Planas, R., & Arroyo, V. (2003). The management of ascites in cirrhosis: Report on the consensus conference of the International Ascites Club. *Hepatology*, *38*, 258-266. [Crossref]
- Narahara, Y., Kanazawa, H., Fukuda, T., Matsushita, Y., Harimoto, H., Kidokoro, H., Katakura, T., Atsukawa, M., Taki,

- Y., Kimura, Y., Nakatsuka, K., & Sakamoto, C. (2011). Transjugular intrahepatic portosystemic shunt versus paracentesis plus albumin in patients with refractory ascites who have good hepatic and renal function: A prospective randomized trial. *Journal of Gastroenterology*, 46(1), 78-85. [\[Crossref\]](#)
- Patel, R., Poddar, P., Choksi, D., Pandey, V., Ingle, M., Khairnar, H., & Sawant, P. (2019). Predictors of 1-month and 3-months hospital readmissions in decompensated cirrhosis: A prospective study in a large Asian cohort. *Annals of Hepatology*, 18(1), 30-39. [\[Crossref\]](#)
- Raza, M. A., Qureshi, U. F., Humayoun, M. A., Waseem, T., & Akram, J. (2011). Effect of intravenous mannitol in mobilization of resistant cirrhotic ascites. *European Journal of Gastroenterology & Hepatology*, 23(2), 184-188. [\[Crossref\]](#)
- Rössle, M., & Gerbes, A. L. (2010). TIPS for the treatment of refractory ascites, hepatorenal syndrome and hepatic hydrothorax: A critical update. *Gut*, 59, 988-1000. [\[Crossref\]](#)
- Rössle, M., Ochs, A., Gülberg, V., Siegerstetter, V., Holl, J., Deibert, P., Olschewski, M., Reiser, M., & Gerbes, A. L. (2000). A comparison of paracentesis and transjugular intrahepatic portosystemic shunting in patients with ascites. *New England Journal of Medicine*, 342(23), 1701-1707. [\[Crossref\]](#)
- Shah, H. A., & Abu-Amara, M. (2013). Education provides significant benefits to patients with hepatitis B virus or hepatitis C virus infection: A systematic review. *Clinical Gastroenterology and Hepatology*, 11, 922-933. [\[Crossref\]](#)
- Shaheen, A. A., Nguyen, H. H., Congly, S. E., Kaplan, G. G., & Swain, M. G. (2019). Nationwide estimates and risk factors of hospital readmission in patients with cirrhosis in the United States. *Liver International*, 39(5), 878-884. [\[Crossref\]](#)
- Stirnemann, G., Banz, V., Storni, F., & De Gottardi, A. (2017). Automated low-flow ascites pump for the treatment of cirrhotic patients with refractory ascites. *Therapeutic Advances in Gastroenterology*, 10(2), 283-292. [\[Crossref\]](#)
- Tapper, E. B., Halbert, B., & Mellinger, J. (2016). Rates of and reasons for hospital readmissions in patients with cirrhosis: A multistate population-based cohort study. *Clinical Gastroenterology and Hepatology*, 14(8), 1181-1188. [\[Crossref\]](#)
- Tapper, E. B., & Volk, M. (2017). Strategies to reduce 30-day readmissions in patients with cirrhosis. *Current Gastroenterology Reports*, 19(1), 1. [\[Crossref\]](#)
- The Joanna Briggs Institute, (2014). *Chapter eight; The protocol design for reviews of economic evidence, inclusion criteria. In The Joanna Briggs Institute Reviewers' Manual: 2014 edition* (pp. 88-91). Australia: The Joanna Briggs Institute.
- Thomson, M., Volk, M., Kim, H. M., & Piette, J. D. (2015). An automated telephone monitoring system to identify patients with cirrhosis at risk of re-hospitalization. *Digestive Diseases and Sciences*, 60(12), 3563-3569. [\[Crossref\]](#)
- Volk, M. L., Fisher, N., & Fontana, R. J. (2013). Patient knowledge about disease self-management in cirrhosis. *The American Journal of Gastroenterology*, 108(3), 302. [\[Crossref\]](#)
- Volk, M. L., Tocco, R. S., Bazick, J., Rakoski, M. O., & Lok, A. S. (2012). Hospital readmissions among patients with decompensated cirrhosis. *American Journal of Gastroenterology*, 107(2), 247-252. [\[Crossref\]](#)
- Werner, K. T., & Perez, S. T. (2012). Role of nurse practitioners in the management of cirrhotic patients. *The Journal for Nurse Practitioners*, 8(10), 816-821. [\[Crossref\]](#)
- Wong, F., Gines, P., Watson, H., Horsmans, Y., Angeli, P., Gow, P., Wong, F., Gines, P., Watson, H., Horsmans, Y., Angeli, P., Gow, P., Minini, P., & Bernardi, M. (2010). Effects of a selective vasopressin V2 receptor antagonist, satavaptan, on ascites recurrence after paracentesis in patients with cirrhosis. *Journal of Hepatology*, 53(2), 283-290. [\[Crossref\]](#)
- Xing, F., Tan, Y., Yan, G. J., Zhang, J. J., Shi, Z. H., Tan, S. Z., Feng, N. P., & Liu, C. H. (2012). Effects of Chinese herbal cataplasm Xiaozhang Tie on cirrhotic ascites. *Journal of Ethnopharmacology*, 139(2), 343-349. [\[Crossref\]](#)
- Zhao, R., Lu, J., Shi, Y., Zhao, H., Xu, K., & Sheng, J. (2018). Current management of refractory ascites in patients with cirrhosis. *Journal of International Medical Research*, 46(3), 1138-1145. [\[Crossref\]](#)