REVIEW



# Understanding the Role of Palliative Care Within Routine Care of Advanced Liver Disease

Simone A. Jarrett<sup>1</sup> · Edward Bley<sup>1</sup> · Richard S. Kalman<sup>2</sup>

Accepted: 31 January 2024 © The Author(s) 2024

#### Abstract

**Purpose of Review** This paper aims to investigate the crucial role of palliative care in the management of chronic liver disease (CLD) and cirrhosis. Faced with a global surge in liver-related morbidity and mortality, our goal is to understand the impact of early engagement with palliative care specialists on symptom management, quality of life, and the overall trajectory of advanced liver disease.

**Recent Findings** While strides have been made in preventing and treating specific etiologies of CLD, such as viral infections, the escalating rates of alcohol use and obesity present new challenges for physicians. Despite advancements, liver transplantation unfortunately remains an elusive solution for many due to various constraints. Our review underscores the underutilization of palliative care in this context, emphasizing its potential to mitigate symptoms and enhance the overall well-being of patients and their caregivers.

**Summary** Implementing palliative care early during CLD proves instrumental in reducing symptoms, hospitalizations, and resource utilization. This not only improves the quality of life for patients but also signifies a paradigm shift in approaching the uncertainties surrounding advanced liver disease. Urging further research and global initiatives, our findings advocate for a comprehensive integration of palliative care in the holistic management of patients with advanced liver disease.

Keywords Liver failure · Cirrhosis · Liver transplant · End-stage liver disease · Palliative care · End-of-life care

# Introduction

Chronic liver disease (CLD) and cirrhosis have emerged as a common health challenge faced by clinicians worldwide and with it comes a myriad of complications. Approximately 44,000 deaths in the United States and 2 million deaths globally are because of underlying liver disease which portrays the increased morbidity and mortality associated with the condition [1]. With rising rates of obesity and alcohol use globally these findings are not entirely surprising.

Simone A. Jarrett simone.jarrett@jefferson.edu

> Edward Bley Edward.Bley@jefferson.edu

Richard S. Kalman Richard.Kalman@jefferson.edu

<sup>1</sup> Department of Internal Medicine, Jefferson Einstein Hospital , 5501 Old York Road, Philadelphia, PA 19141, USA

<sup>2</sup> Department of Gastroenterology and Hepatology, Jefferson Einstein Hospital, Philadelphia, PA 19141, USA The most common etiologies of chronic liver disease and cirrhosis include alcohol use disorder (ALD), metabolic dysfunction-associated steatotic liver disease (MASLD), and viral hepatitis including hepatitis B and C [2]. Other less common causes of CLD include genetic conditions such as Wilsons disease, hemochromatosis, and alpha 1 antitrypsin deficiency, as well as immunemediated causes such as autoimmune hepatitis. Congestive hepatopathy and Budd Chiari syndrome may also lead to CLD and cirrhosis.

Despite recent developments in the prevention and treatment of some of these underlying etiologies particularly viral infections with hepatitis B vaccinations and curative medications for hepatitis C, the rising incidence of alcohol use and the obesity epidemic are changing the global framework. Unfortunately, with more cases of advanced liver disease, there is an increasing incidence of associated complications that lead to multiorgan involvement including but not limited to hepatic encephalopathy, ascites, hepatorenal syndrome, variceal bleeding, and protein malnutrition. These patients' ultimate hope for long-term survival relies on liver transplantation, which is not attainable for most patients due to a variety of reasons beyond the scope of this article.

The uncertainty of transplantation in this group of patients highlights the importance of engaging palliative care clinicians in the initial stages of management of these patients who face a long road of healthcare challenges fraught with multiple complications and setbacks. Furthermore, symptoms from CLD have been shown to negatively impact the quality of life for patients, which can be ameliorated through early engagement with a palliative care specialist or team. Considering this, the aim of our review is to explore the use of palliative care for patients with CLD and explore why early implementation of these services is essential in helping manage symptoms and providing a better understanding of the severity of illness with CLD and cirrhosis. These patients' ultimate hope for long-term survival relies on liver transplantation, which is not attainable for most patients due to a variety of reasons beyond the scope of this article.

# **History of Palliative Care**

Palliative care as characterized by the World Health Organization (WHO) is a subspecialized field of medicine that aims to optimize the quality of life and alleviate the suffering of patients with serious illnesses [3]. Palliative care usually comprises a group of professionals who work in synchrony to provide comprehensive care to patients. These professionals include but are not limited to palliative care physicians, nurses, social workers, chaplains, and other religious bodies, pharmacists, and care managers.

Hospice care, on the other hand, is care that is provided to patients with life-limiting illnesses, typically 6 months or less, who are essentially at the end of life and are suffering from terminal diseases. The origins of palliative care stem from focusing on the care of patients with terminal illnesses, which has unfortunately led to its underutilization. This underutilization is due to the underlying myth and misconception that palliative care is only for patients actively dying. However, palliative care encompasses a multitude of services, where hospice care falls under this umbrella. Still, it is undoubtedly only a tiny percent of the critical utility of palliative care in patients suffering from chronic diseases [4].

## **End-stage Liver Disease**

CLD is typically defined as a progressive deterioration of liver function for 6 months, which includes the synthesis of clotting functions and proteins, detoxification of harmful products of metabolism, and the excretion of bile [5]. This deterioration coincides with a continuous process of inflammation, destruction, and regeneration of the liver parenchyma, ultimately leading to fibrosis and cirrhosis. While the transition point between reversible and irreversible fibrosis is still not wholly understood, mortality rises significantly once cirrhosis has developed and further rises with each complication such that patients with cirrhosis, bleeding varices, and ascites have a 1-year mortality rate of more than 50% [6]. Patients with hepatorenal syndrome have a 2-month mortality rate of over 90% without transplant [7].

Classifying the stage of cirrhosis remains paramount to realizing the severity of the disease at a particular time, as well as understanding the prognosis and predicting mortality. Several scoring systems have been developed with this objective in mind. One of these scoring systems is the Child-Pugh score, based on total bilirubin, albumin, PT/INR, and presence/absence of hepatic encephalopathy and ascites. This scoring system requires a subjective assessment, recognized as a system limitation. It is categorized into three classes: A, B, and C. Compensated cirrhosis is defined as Child-Pugh A in which patients are asymptomatic and have no clinical stigmata of the disease. The median survival rate of these patients can be approximately 12 years [8]. Meanwhile, decompensated cirrhosis is Child–Pugh B/C, typically characterized by the onset of ascites, hepatic encephalopathy, spontaneous bacterial peritonitis, or variceal bleeding and is associated with high mortality within the short-term period compared to compensated disease [6].

Another scoring system developed after the Child–Pugh score was the Model for end-stage liver disease (MELD). This score initially included four variables: creatinine, bilirubin, INR, and the presence of hemodialysis at least twice in the last week. MELD offered better mortality prediction by including an assessment of renal function while limiting subjective evaluation of clinical status. This score was later updated to include the serum sodium, known as the MELD-Na, and updated again in 2022. The most recent version, called MELD 3.0, added variables of sex and albumin [9]. This has allowed for a more accurate mortality assessment seeking to reduce gender disparities on the liver transplant wait list, which has long favored male candidates for a variety of reasons.

Although these scoring systems are helpful when discussing prognosis, the trajectory of these patients can change rapidly with patients undergoing sudden decompensation even after a period of compensated disease. It is estimated that approximately 5 to 7% of patients per year will devolve from compensated to decompensated, and with this comes increased morbidity and mortality [10]. These findings and the uncertainty surrounding when and how long a patient may remain decompensated further emphasize why it is essential to utilize the services of palliative care from initial consultation for these patients

as they face a long, unpredictable road ahead. Many of these patients without transplantation have a median survival of approximately 2 years [11].

# The Role of Palliative Care

Advanced liver disease is not just associated with significant health-related issues but is also associated with major social, psychological, and financial hardships for not just the patients but their loved ones and caregivers [12]. Early integration of palliative care into treating patients with chronic diseases has long been studied and has shown positive findings [13]. While the evidence is limited, a growing body of work shows that early palliative intervention results in a better quality of life for both patients and caretakers. For example, patients with advanced heart failure referred to palliative care were found to have fewer readmissions and less mechanical ventilation, reducing health care utilization and improving quality of life [14].

Similarly, with CLD, data from ongoing research has shown that early initiation of palliative care and advanced care planning in all patients, even those with compensated disease, dramatically improves long-term outcomes in the inpatient and outpatient setting [15]. Patients with CLD suffer from a variety of symptoms, which may range from pain, shortness of breath, anxiety, and depression and can significantly affect their quality of life [16]. The palliative approach to the patient should involve palliative care providers and the primary team of hepatologists, gastroenterologists, general physicians, and caretakers who provide care to these patients. Timely recognition and intervention and a multidisciplinary approach are crucial to ensure the best outcome for these patients.

Studies have shown that early utilization of palliative care contributed to a decrease in symptom burden such as depression and improvement in other areas such as fatigue, well-being, appetite, itching, and anxiety [17]. Families also reported that time spent with their family members increased due to early palliative care. Lamba et al. found that in patients with early intervention, hospital length of stay decreased significantly by almost 9 days, as well as a decrease in ICU length of stay. They also showed that goals-of-care discussions with physicians on rounds increased from 2 to 38% [18]. DNR statuses were instituted earlier, and DNR to-death time increased. These interventions resulted in earlier consensus around goals of care for dying patients, and families felt they had more "time to say goodbye." These findings suggest that these changes can result in better outcomes for patients, patient families, and providers.

Patients with advanced liver disease may face a tumultuous course with multiple periods of decompensation

and recovery, which makes it increasingly difficult for the patient and their families to make decisions regarding longterm care, especially when the prospect of a possible liver remains in sight. Considering this, palliative care physicians are essential as they can provide emotional support and education early in the disease process to allow for informed decisions and prepare a practical plan regarding advanced care [19].

# **Advanced Care Planning**

Advanced care planning (ACP) is a process that involves multiple conversations between the healthcare team and the patient and their family to guarantee that the values and wishes of the patient are respected when it comes to endof-life care and interventions [20]. While ACP should be addressed with the patient and their primary team, palliative care physicians play a key role.

The stigma behind ACP due to the concern that these conversations indicate that physicians may be giving up on the patient or suggesting that death is near has led many physicians to shy away from these conversations until the patient is near the end of their life. Studies have shown that despite patients being open to some of these conversations, few have had these discussions with the transplant team even when they are deemed not a candidate for transplant [21]. ACP is an important opportunity to explore goals and values for these patients and should be addressed not just at the end of life. Therefore, the best way to modify this pattern, supported by the literature, is to have healthcare systems with intentional planning and documentation. Palliative care teams are essential to help achieve this goal.

A recent study in Edinburgh showed that after implementing a supportive care liver nurse to help bridge the gap between care and improve coordination between services such as palliative care and patients, there was an improvement in advanced care planning, which resulted in a reduction in unplanned admissions, shorter hospital stays and fewer consultations [21]. There is also less grief as family members have had time to come to terms with the decision that the patient wanted.

# **Barriers to Palliative Care**

Unfortunately, there remains a significant number of barriers to patients accessing palliative care services, whether these are patient factors or healthcare-related. Some of the obstacles, which may be patient-driven, include a lack of education with a poor underlying understanding of their disease as well as decompensation with hepatic encephalopathy, leading to a lack of capacity and difficulty engaging with the palliative care team [21]. There is also a common misconception regarding the role of palliative care and its association with end-of-life and death, thereby leading to an unwillingness to engage. Other barriers that exist that hinder the use of palliative care services in patients with advanced liver disease include physiciandriven causes such as overestimation of the duration of illness, misconceptions associated with palliative care, discomfort in having these types of conversations, and focus laid only on life-saving interventions.

In the literature, there is evidence to suggest that the time from transplant denial to palliative care consult is almost a month, with median survival after consult being 15 days [22]. Another study showed that only 33.9% of patients are referred to palliative care, with almost 91% of these consults being in the inpatient setting. Those who are transplant-listed had significantly lower odds of being referred to palliative despite the benefits of consulting the service due to increased hospitalization due to symptom management and decompensation [23]. Evidence also shows those patients denied transplants still receive intensive care despite a very poor prognosis and no likelihood of cure and reflects delayed advance care planning conversations. Up to 88% of non-listed patients were full code during their terminal hospitalization [23]. Integrating palliative care with the standard of care in diagnosing severe illness improves several patient and system-related factors. These include quality of life, satisfaction, symptom burden, and advanced care planning documentation, while emergency room utilization and costs of care decline [22]. Studies have also shown a significant survival benefit in patients who engage with palliative care early in treatment vs. at the end of life, where their involvement did not have this same benefit. This may be because earlier in the course of illness, patients are more receptive and able to have these types of conversations.

#### **Impact on Caregivers**

The impact on caregivers is often missed in patients who are suffering from critical or terminal illness who rely heavily on the support of family members, close friends, and their community. Caregivers must be taken into consideration, particularly those caring for patients with advanced liver disease, considering the chronic and unpredictable nature of the disease and its impact psychologically and financially on caregivers.

Studies have shown that caregivers often experience depression, anxiety, and decreased quality of life when compared to the general population, even when a patient undergoes a liver transplant [24]. A systematic review on the health-related quality of life in liver transplant (HRQL) patients suggests that patients impacted the caregiver and vice versa, which may be linked to patient outcomes. This data reinforces the need for further studies on the effects of advanced liver disease and liver transplant on the patient's families and caregivers. This will help us to understand the importance of caregiver support to maximize outcomes for these patients and their caregivers [24].

In this scenario, palliative care can provide not only resources and support for the patient but also for the family and caregivers, which will help in the long term, especially in those cases where patients are not transplant candidates. There is data to suggest that the bereavement period is less as patients and families have a proper understanding of what is to come and how to address it when it does.

# Symptom Management for Patients with ESLD

As mentioned earlier, patients with CLD suffer from a variety of symptoms [16]. In addition to the high symptom burden in patients with cirrhosis, there are physiological changes associated with cirrhosis that impact the metabolism of many medications, thereby creating challenges in treatment. Symptoms may be liver specific but also generalized, as seen in Table 1 [25].

Based on a recent systematic review, the most frequently reported symptoms are pain (prevalence range, 30–79%); breathlessness (20–88%); muscle cramps (56–68%); sleep disturbance (insomnia, 26–77%; daytime sleepiness, 29.5–71.0%); psychological symptoms (depression, 4.5–64.0%; anxiety, 14–45%); and sexual dysfunction (53–93%). Common management steps utilized are further described in Table 2.

#### **Hospice Care in ESLD**

In hospice care for patients with advanced and terminal diseases, the focus is on allowing patients to live as comfortably as possible. It differs from palliative care, focusing exclusively on comfort rather than disease-directed curative treatment. It is a service reserved for persons with life expectancy measured in months.

Evidence suggests that patients placed in hospice in the United States have more coverage of certain symptomrelieving therapies, such as liberalized coverage of oxygen in the home [38].

Hospice is associated with improved control of physical and psychological symptoms, quality of life, and caregiver

Symptom	Pathophysiology
Ascites	Peripheral arterial vasodilation leading to underfilling of circulatory volume. This triggers the baroreceptor-mediated activation of the renin–angiotensin–aldosterone system, sympathetic nervous system, and nonosmotic release of vasopressin to restore circulatory integrity. The result is an avid sodium and water retention, identified as a preascitic state. This condition will evolve in overt fluid retention and ascites, as the liver disease progresses. Once ascites is present, most therapeutic modalities are directed on maintaining negative sodium balance, including salt restriction, bed rest, and diuretics [26]
Muscle cramping	Precise etiology of muscle cramps is unclear, alterations in nerve function, energy metabolism, plasma volume, and electrolytes may contribute. Often spontaneous, intermittent, and nocturnal [27]
Insomnia	Likely multifactorial in these patients. They may experience decreased sleep latency, frequent awakenings, reduced total sleep time, decreased sleep efficiency, lower amounts of slow-wave sleep, and REM sleep. Additionally, poorly timed medications, such as diuretics in the late afternoon or lactulose in the evening, could lead to frequent awakenings to use the bathroom [28]
Pruritus	Common symptom in patients with cirrhosis of all etiologies, although it disproportionately affects patients with chole- static liver disease. The pathophysiology is not well understood, but bile acids, lysophosphatidic acid, and autotaxin have been implicated [25]
Appetite changes	This is a significant predictor of morbidity and mortality in patients with cirrhosis and tends to worsen with the increasing severity of liver disease. It may be attributed to a variety of liver-specific factors, including early satiety from ascites, hepatic encephalopathy, gastroparesis, autonomic dysfunction, taste change, and restricted diets (e.g., low-sodium diet) [25]
Pain	Etiology of pain in persons with cirrhosis can be divided into liver-associated mechanical pain, inflammatory pain, and non-liver-associated pain. Cirrhosis can directly lead to somatic or nociceptive pain through splenomegaly, ascites, and hepatic capsular stretch or indirectly because of elevation of proinflammatory cytokines [29]. Nonhepatic etiologies of pain can range widely, but the most common are neuropathic (e.g., diabetic neuropathy) and musculoskeletal (e.g., osteoarthritis) [30]
Sexual dysfunction	Results from cirrhosis because of associated hypogonadism, low testosterone, and altered circulation [31]
Depression and anxiety	Multifactorial in etiology and should be addressed early as studies have shown an increased rate of suicide in these patients [32]
Dyspnea	Typically, a subjective experience of breathlessness is experienced by 47–88% of persons with cirrhosis and can be attributed to multiple causes, including ascites, volume overload, hepatic hydrothorax, hepatopulmonary syndrome, portopulmonary syndrome, and infection [33]

Table 1 Table demonstrating some of the common symptoms experienced by patients with chronic liver disease and cirrhosis

bereavement. It has been provided very close to the end of life in patients with decompensated cirrhosis and is not often utilized due to delayed discussions about end of life, the unpredictability of decompensating events, and clinician discomfort with end-of-life conversations [39].

#### Palliative Care for Advanced Liver Disease

Palliative care for advanced liver disease patients is important for a myriad of reasons. Not only does it support the patient's psychological well-being as well as caregivers, but it is also vital in symptom management. Patients suffer from a multitude of complications ranging from hepatic encephalopathy to pruritus to malnutrition to chronic pain. Palliative specialists can decrease this burden by managing patient expectations and controlling symptoms. This will lead to not only reduced hospitalization but also utilization of hospital resources.

Providing physicians with education as to when and why to reach out to palliative care and to develop a close partnership with hepatology is the most crucial step in improving the utilization rate of palliative care in managing these patients. More research is needed; however, a study done by Soo Yung Kim reviewing palliative care in ESLD showed that the effectiveness of palliative care has been validated using the E sass scale and psychosocial measurements based on medical records such as DNR orders, consultation of palliative care, days of hospitalization and days from palliative care consultation to death [17].

As we advance in managing these patients, we need to learn how to align practical palliative care programs with ESLD patients in the healthcare system across the country while respecting various cultures and backgrounds.

#### **Our Experiences**

In our clinical practice in a large community health hospital with a strong liver transplant program in an underserved area, palliative care services remain grossly underutilized in not only advanced liver disease patients but also all critically ill patients. Barriers to care that Table 2 Table summarizing management steps for patients with symptoms of chronic liver disease and cirrhosis

Symptom	Common management steps		
	First steps	Second steps	
Ascites	<ul> <li>A combination of diuretics and sodium restriction</li> <li>The diuretic choice usually includes a combination of loop diuretics and aldostrone antagonists</li> <li>Generally, this includes spironolactone and furosemide in a 5:2 ratio [25]</li> </ul>	<ul> <li>Refractory ascites normally involve a large volume paracentesis. Administration of albumin with large volumes (&gt; 5 L) of ascites removed helps to prevent post-paracentesis circulatory dysfunction that can result from large fluid shifts</li> <li>Frequent paracentesis, however, can be burdensome for patients, increase the risk of spontaneous bacterial peritonitis, and act as an irritant to the surrounding skin [25]</li> </ul>	<ul> <li>If the MELD score is &lt; 18, an a trans jugular intrahepatic po (TIPS)</li> <li>Because of the shunting that oplacement, patients are more sencephalopathy (HE). The risi placement is about 25%,</li> <li>Risk factors for HE, higher ME oplacement for a drain placement for ascites who were not transplat of a drain was both effective a health resource utilization but infection and is often reserved [25, 34]</li> </ul>
Muscle cramping	<ul> <li>Restoration of effective circulating blood volume with albumin has been shown to result in improve- ment in cramping</li> <li>Correction of electrolytes repleting potassium, magnesium, and zinc [25]</li> </ul>	• Taurine (2–3 g daily), vitamin E (200 mg three times a day), and baclofen (5–10 mg three times a day) have preliminary supportive data and can be considered in patients with cirrhosis and significant muscle cramps [33]	• The PICCLES trial showed th safely reduce cramp severity i However, effective therapies t cramps for patients with cirth- need [35]
Insomnia	• Evaluate and treat underlying causes for insomnia such as HE, pruritus, obstructive sleep apnea, and restless leg syndrome [33]	<ul> <li>Non-pharmacological methods such as meditation and cognitive behavioral therapy should be consid- ered prior to beginning pharmacotherapy [36]</li> </ul>	<ul> <li>When pharmacological measu best to avoid benzodiazepines</li> <li>25 mg and melatonin 3 mg ard doses of zolpidem should be t with caution</li> </ul>
Pruritus	<ul> <li>Topical therapy such as emollients with aqueous cream with menthol followed, cool humidified air, and avoidance of frequent bathing, hot water, and harsh soaps or detergents are initially tried</li> </ul>	• Bile acid sequestrants cholestyramine (4 g/d with titration to 16 g/d) or colestipol are the next step	• If the patient is not jaundiced, followed by naltrexone and th considered [36]
Appetite changes	<ul> <li>Evaluate for any potential etiologies and reverse them. (e.g., LVP for large volume ascites and treatment of gastroparesis)</li> <li>Protein supplement shakes</li> <li>Nutrition consultation [25]</li> </ul>	<ul> <li>For patients who cannot achieve adequate oral intake, temporary enteral nutrition</li> <li>Given their known deficiency in cirrhosis, supplementation of zinc and magnesium [25]</li> </ul>	<ul> <li>Parenteral nutrition should be which even enteral nutrition is are other contraindications to</li> <li>Appetite stimulants can be co mirtazapine</li> </ul>
Pain	<ul> <li>Assess and treat reversible causes (e.g., tense ascites, local infection, and musculoskeletal injury) [33]</li> <li>Multimodal pain management approaches: personcentered holistic, multidisciplinary approach, engaging a combination of expertise from across several specialties (e.g., palliative care, psychiatry, pain management, pharmacy, physical and occupational therapy, or social work)</li> </ul>	<ul> <li>Acetaminophen, 500 mg every 6 h, up to a maximum dose of 2 g/d, is the preferred first-line pharmacotherapy for the management of pain in patients with cirrhosis</li> <li>Systemic NSAIDs should be avoided in patients with cirrhosis due to risk of bleeding and kidney failure [29]</li> </ul>	<ul> <li>Avoid opioids, when possible However, when necessary, op approached with caution and with patients and caregivers</li> <li>Low-dose oxycodone or hydr started in select cases on an a titrated to effect, often in cons agement experts [33]</li> </ul>

- other option is to place rtosystemic shunt
- susceptible to hepatic k of HE after TIPS occurs with TIPS
- S placement include sar-
- nt candidates, placement LD, and advanced age r those with refractory und safe and reduced carries a high risk of for hospice patients
  - at sips of pickle juice osis remain an unmet n a short-term trial. o prevent muscle
- ss [36]. Hydroxyzine re acceptable. Small used for short terms and rres are required, it is
  - en sertraline can be then rifampicin
- s not sufficient, or there reserved for cases in enteral feeding [25] nsidered, such as
- with careful discussion , for chronic pain. ioid use should be
- romorphone can be as-needed basis and sultation with pain man-

Table 2 (continued)			
Symptom	Common management steps		
	First steps	Second steps	
Sexual dysfunction	• Medications (e.g., beta-blockers) and substances (e.g., alcohol, tobacco) that can cause sexual dys- function should be assessed for and removed where appropriate [33]	<ul> <li>Underlying conditions that contribute to sexual dysfunction, such as depression and diabetes, should be medically managed</li> </ul>	• Phosphodiesterase inhibitors. One small study of tadalafil in 25 men with cirrhosis, erectile dysfunction, and a mean MELD of $13\pm4$ found that 10 mg over a 4-week period was a safe and efficacious approach [37]
Depression and anxiety	<ul> <li>Evaluating for and treating contributors, such as vitamin B12, iron, or folate deficiency, sleep disorders, and encephalopathy</li> <li>Cognitive behavioral therapy [33]</li> </ul>	<ul> <li>Pharmacotherapy including SSRIs</li> <li>Selection requires consideration of other symptoms, and the presence of sexual dysfunction, somnolence, and/or weight loss should guide the selection of specific SSRIs [33]</li> </ul>	
Dyspnea	<ul> <li>Manage reversible causes (e.g., volume overload, asthma, sleep apnea)</li> <li>Bedside fans</li> <li>Supplemental oxygen therapy even for nonhypoxic patients</li> <li>Mindfulness, meditation, guided imagery [33]</li> </ul>	• Paracentesis • Thoracentesis	<ul> <li>Opioids and anxiolytics can be used cautiously in select cases, typically at the end of life (e.g., starting dose i.v. hydromorphone 0.2 mg every 3 h as needed, titrated to symptom relief)</li> <li>Placement of drains (usually in the setting of hospice care) [33]</li> </ul>

have been identified specifically in CLD include shortage of providers, lack of evidence-based referrals, stigma surrounding palliative care, lack of clarity on the role of palliative care, lack of provider training, lack of prognostic certainty, and prognostic certainty [33]. At our institution, prior studies demonstrate that during the COVID-19 pandemic, there was limited use of palliative care services, and among those having severe disease, only 40% had palliative care involvement [40]. Of those who received palliative care, they were noted to be older age, on vasopressors, needed intubation, or were near death. As we begin to move to a post-pandemic world, it is crucial that we start to re-evaluate the role of palliative care in the care of these patients. For many patients with CLD, the standard of care is to wait until a patient is deemed not a transplant candidate to involve the palliative care team. However, a growing body of data is showing that this practice is missing a huge opportunity to help patients in their journey to either transplant or end-of-life. Changing this practice is vital and will likely require re-education of the entire staff to understand better the role of palliative care in these patients. Our institution is the sponsoring site for the PCORI (patient-centered outcomes research institute) PAL-Liver study serving to introduce palliative care within the treatment of end-stage liver disease in a randomized fashion ClinicalTrials.gov ID: NCT03540771[41]. As such, our approach has been evolving rapidly to involve palliative care specialists much earlier in the CLD disease course, much to the benefit of our patient population. Our team is even involving palliative care for patients active on the transplant list. We have also found our surgical colleagues and transplant team members to be quite receptive to this change in practice. In fact, many of our patients continue to see palliative care specialists even after their study participation has concluded.

# Conclusion

Palliative care remains underutilized in the care of patients with advanced liver disease. Understanding the role of these specialists and implementing their care early in the onset of the disease process will not only lead to a decrease in symptoms, hospitalizations, and resource utilization but also improve the quality of life for these patients and their caregivers. Further research is needed on this topic, and universal initiatives should be set in place to ensure palliative care providers are engaged early for all patients with advanced liver disease, considering the chronicity and uncertainty surrounding the disease process and prospects of liver transplantation. Author Contribution S.A.J.: data collection, drafting, writing, and revision of the manuscript. E.B.: study design, data collection, and drafting of the abstract. R.K.: study design, drafting of the manuscript, and critical revision of the manuscript.

#### Declarations

Competing interests The authors declare no competing interests.

**Conflict of Interest** The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

**Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

## References

- Moon AM, Singal AG, Tapper EB. Contemporary epidemiology of chronic liver disease and cirrhosis. Clin Gastroenterol Hepatol. 2020;18:2650–66. https://doi.org/10.1016/J.CGH.2019.07.060.
- Smith A, Baumgartner K, Bositis C. Cirrhosis: diagnosis and management. Am Fam Physician. 2019;100:759–70.
- Teoli D, Schoo C, Kalish VB. Palliative Care. [Updated 2023 Feb 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/ books/NBK537113/
- Loscalzo MJ. Palliative care: an historical perspective. Hematology. 2008;2008:465–465. https://doi.org/10.1182/ASHEDUCATI ON-2008.1.465.
- Sharma A, Nagalli S. Chronic Liver Disease. [Updated 2023 Jul 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. Available from: https://www.ncbi.nlm.nih.gov/ books/NBK554597/
- D'Amico G, Garcia-Tsao G, Pagliaro L. Natural history and prognostic indicators of survival in cirrhosis: a systematic review of 118 studies. J Hepatol. 2006;44:217–31. https://doi.org/10.1016/J. JHEP.2005.10.013.
- Velez JCQ. Patients with hepatorenal syndrome should be dialyzed? PRO Kidney. 2021;360(2):406. https://doi.org/10.34067/ KID.0006952020.
- Zipprich A, Garcia-Tsao G, Rogowski S, Fleig WE, Seufferlein T, Dollinger MM. Prognostic indicators of survival in patients with compensated and decompensated cirrhosis. Liver Int. 2012;32:1407–14. https://doi.org/10.1111/J.1478-3231.2012. 02830.X.
- 9. Kim WR, Mannalithara A, Heimbach JK, Kamath PS, Asrani SK, Biggins SW, et al. MELD 3.0: The model for end-stage

liver disease updated for the modern era. Gastroenterology. 2021;161:1887. https://doi.org/10.1053/J.GASTRO.2021.08.050.

- Kumar R, Kumar S, Prakash SS. Compensated liver cirrhosis: natural course and disease-modifying strategies. World J Methodol. 2023;13:179. https://doi.org/10.5662/WJM.V13.I4.179.
- Fleming KM, Aithal GP, Card TR, West J. All-cause mortality in people with cirrhosis compared with the general population: a population-based cohort study. Liver Int. 2012;32:79–84. https:// doi.org/10.1111/J.1478-3231.2011.02517.X.
- Woodland H, Hudson B, Forbes K, Mccune A. Palliative care in liver disease: what does good look like? Gastroenterology. 2020;11:218–27. https://doi.org/10.1136/figastro-2019-101180.
- Kircher C, Hanna T, Tranmer J, Goldie C, Ross-White A, Goldie C. Defining and implementing early palliative care for persons diagnosed with a life-limiting chronic illness: a scoping review protocol. JBI Evid Synth. 2020;18:2335–41. https://doi.org/10. 11124/JBISRIR-D-19-00377.
- Diop MS, Bowen GS, Jiang L, Wu WC, Cornell PY, Gozalo P, et al. Palliative care consultation reduces heart failure transitions: a matched analysis. J Am Heart Assoc. 2020;9:13989. https://doi. org/10.1161/JAHA.119.013989.
- Quinn KL, Stukel T, Stall NM, Huang A, Isenberg S, Tanuseputro P, Goldman R, Cram P, Kavalieratos D, Detsky AS, Bell CM. Association between palliative care and healthcare outcomes among adults with terminal non-cancer illness: population based matched cohort study. BMJ. 2020;370:m2257. https://doi.org/10. 1136/bmj.m2257
- Peng JK, Hepgul N, Higginson IJ, Gao W. Symptom prevalence and quality of life of patients with end-stage liver disease: a systematic review and meta-analysis. Palliat Med. 2019;33:24–36. https://doi.org/10.1177/0269216318807051.
- Kim S, Lee K, Kim C, Choi J, Kim S. How do we start palliative care for patients with end-stage liver disease? Gastroenterol Nurs. 2022;45:101. https://doi.org/10.1097/SGA.000000000000611.
- Lamba S, Murphy P, McVicker S, Smith JH, Mosenthal AC. Changing end-of-life care practice for liver transplant service patients: structured palliative care intervention in the surgical intensive care unit. J Pain Symptom Manage. 2012;44:508–19. https://doi.org/10.1016/J.JPAINSYMMAN.2011.10.018.
- Hansen L, Press N, Rosenkranz SJ, Baggs JG, Kendall J, Kerber A, et al. Life-sustaining treatment decisions in the ICU for patients with ESLD: a prospective investigation. Res Nurs Health. 2012;35:518. https://doi.org/10.1002/NUR.21488.
- 20 Sedini C, Biotto M, CrespiBel'skij LM, MoroniGrandini RE, Cesari M. Advance care planning and advance directives: an overview of the main critical issues. Aging Clin Exp Res. 2020;34:325–30. https://doi.org/10.1007/S40520-021-02001-Y.
- 21. Carbonneau M, Davyduke T, Spiers J, Brisebois A, Ismond K, Tandon P. Patient views on advance care planning in cirrhosis: a qualitative analysis. Can J Gastroenterol Hepatol 2018:4040518. https://doi.org/10.1155/2018/4040518
- 22. Kelly SG, Campbell TC, Hillman L, Said A, Lucey MR, Agarwal PD. The utilization of palliative care services in patients with cirrhosis who have been denied liver transplantation: a single center retrospective review. Ann Hepatol. 2017;16:395–401. https://doi.org/10.5604/16652681.1235482.
- Ufere NN, Halford JL, Caldwell J, Jang MY, Bhatt S, Donlan J, et al. Health care utilization and end-of-life care outcomes for patients with decompensated cirrhosis based on transplant candidacy. J Pain Symptom Manage. 2020;59:590–8. https://doi.org/ 10.1016/J.JPAINSYMMAN.2019.10.016.
- Young AL, Rowe IA, Absolom K, Jones RL, Downing A, Meader N, et al. The effect of Liver Transplantation on the quality of life of the recipient's main caregiver-a systematic review. Liver Int. 2017;37:794–801. https://doi.org/10.1111/LIV.13333.

- Kaplan A, Rosenblatt R. Symptom management in patients with cirrhosis: a practical guide. Curr Treat Options Gastroenterol. 2022;20:144. https://doi.org/10.1007/S11938-022-00377-Y.
- 26 Kashani A, Landaverde C, Medici V, Rossaro L. Fluid retention in cirrhosis: pathophysiology and management. QJM: An Int J Med. 2008;101:71–85. https://doi.org/10.1093/QJMED/HCM121.
- Mehta SS, Fallon MB. Muscle cramps in liver disease. Clin Gastroenterol Hepatol. 2013;11:1385–91. https://doi.org/10.1016/J. CGH.2013.03.017.
- Bruyneel M, Sersté T. Sleep disturbances in patients with liver cirrhosis: prevalence, impact, and management challenges. Nat Sci Sleep. 2018;10:369–75. https://doi.org/10.2147/NSS.S186665.
- Chandok N, Watt KDS. Pain management in the cirrhotic patient: the clinical challenge. Mayo Clin Proc. 2010;85:451–8. https:// doi.org/10.4065/MCP.2009.0534.
- Rogal SS, Bielefeldt K, Wasan AD, Lotrich FE, Zickmund S, Szigethy E, et al. Inflammation, psychiatric symptoms, and opioid use are associated with pain and disability in patients with cirrhosis. Clin Gastroenterol Hepatol. 2015;13:1009–16. https:// doi.org/10.1016/J.CGH.2014.10.029.
- Chiang HC, Chien YC, Lin PY, Lee HL, Chen YL. Assessing men with erectile dysfunction before and after living donor liver transplantation in real-world practice: integrating laboratories into clinical settings. PLoS ONE. 2018;13:e0206438. https://doi.org/ 10.1371/JOURNAL.PONE.0206438.
- Jang SY, Rou WS, Kim SH, Lee BS, Eun HS. Association between new-onset liver cirrhosis and suicide risk in South Korea: a nationwide cohort study. Clin Mol Hepatol. 2021;27:283. https://doi.org/ 10.3350/CMH.2020.0227.
- Rogal SS, Hansen L, Patel A, Ufere NN, Verma M, Christopher , et al. AASLD Practice Guidance: palliative care and symptom- based management in decompensated cirrhosis VA HSR&D Center for Innovations in Quality, Effectiveness, and Safety (IQuESt) and. Hepatology. 2022;00:1–35. https://doi.org/10.1002/hep.32378.
- Boike JR, Thornburg BG, Asrani SK, Fallon MB, Fortune BE, Izzy MJ, et al. North American practice-based recommendations for transjugular intrahepatic portosystemic shunts in portal hypertension. Clin Gastroenterol Hepatol. 2022;20:1636-1662. e36. https://doi.org/10.1016/J.CGH.2021.07.018.
- 35 Tapper EB, Salim N, Baki J, Zhao Z, Sundaram V, Patwardhan V, et al. Pickle juice intervention for cirrhotic cramps reduction:

the PICCLES randomized controlled trial. Am J Gastroenterol. 2022;117:895–901. https://doi.org/10.14309/AJG.000000000 001781.

- Wright M, Woodland H, Hudson B. Symptom control in advanced chronic liver disease: integrating anticipatory palliative and supportive care. Frontline Gastroenterol. 2022;13:e109–15. https:// doi.org/10.1136/FLGASTRO-2022-102114.
- Thakur J, Rathi S, Grover S, Chopra M, Agrawal S, Taneja S, et al. Tadalafil, a phosphodiesterase-5 inhibitor, improves erectile dysfunction in patients with liver cirrhosis. J Clin Exp Hepatol. 2019;9:312–7. https://doi.org/10.1016/J.JCEH.2018.07.007.
- Davidson, John H. Choices in Palliative Care: Issues in Health Care Delivery Mayo Clinic Proceedings, 82(9),1147
- Ufere NN, Donlan J, Waldman L, Dienstag JL, Friedman LS, Corey KE, et al. Barriers to use of palliative care and advance care planning discussions for patients with end-stage liver disease. Clin Gastroenterol Hepatol. 2019;17:2592–9. https://doi.org/10.1016/J. CGH.2019.03.022.
- 40. Haydar A, Bryan Lo K, Goyal A, Gul F, Peterson E, Bhargav R, et al. Journal pre-proof palliative care utilization among patients with COVID-19 in an underserved population: a single-center retrospective study. J Pain Symptom Manage. 2020. https://doi. org/10.1016/j.jpainsymman.2020.05.022.
- 41. Verma M, Kosinski AS, Volk ML, Taddei T, Ramchandran K, Bakitas M, et al. Introducing palliative care within the treatment of end-stage liver disease: the study protocol of a cluster randomized controlled trial. J Palliat Med. 2019;22:S-34-S-43. https://doi.org/10.1089/jpm.2019.0121.

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Guarantor of the article: Simone A. Jarrett, MD.

The article has not been published previously in abstract form or by a nonprofit, recognized preprint server. .