Palliative care in liver disease: what does good look like?

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ABSTRACT

The mortality rate from chronic liver disease in the UK is rising rapidly, and patients with advanced disease have a symptom burden comparable to or higher than that experienced in other life-limiting illnesses. While evidence is limited, there is growing recognition that care of patients with advanced disease needs to improve. Many factors limit widespread provision of good palliative care to these patients, including the unpredictable trajectory of chronic liver disease, the misconception that palliative care and end-of-life care are synonymous, lack of confidence in prescribing and lack of time and resources. Healthcare professionals managing these patients need to develop the skills to ensure effective delivery of core palliative care, with referral to specialist palliative care services reserved for those with complex needs. Core palliative care is best delivered by the hepatology team in parallel with active disease management. This includes ensuring that discussions about disease trajectory and advance care planning occur alongside active management of disease complications. Liver disease is strongly associated with significant social, psychological and financial hardships for patients and their carers; strategies that involve the wider multidisciplinary team at an early stage in the disease trajectory help ensure proactive management of such issues. This review summarises the evidence supporting palliative care for patients with advanced chronic liver disease, presents examples of current best practice and provides pragmatic suggestions for how palliative and disease-modifying care can be run in parallel, such that patients do not miss opportunities for interventions that improve their quality of life.

INTRODUCTION

The mortality rate from chronic liver disease (CLD) in the UK has risen by around 400% since 1970, in contrast to that of other life-limiting chronic diseases. Patients with compensated cirrhosis have a median survival of over 12 years; however, each year, 5%–7% progress to decompensated cirrhosis with a median survival of just 2 years. Over 70% of patients with liver disease in England die in hospital, around 25% higher than the average for all deaths. The cost to the National Health Service (NHS) of treating liver disease is high and rising, estimated at £2.1 billion per year in
2017. Physical symptom burden is high, comparable with that of patients with lung and colon cancer. A recently published systematic review found the most frequently reported symptoms in patients with end-stage liver disease (ESLD) were pain, breathlessness, muscle cramps, sleep disturbance, depression, anxiety and erectile dysfunction; however, these issues are seldom addressed by hepatologists.

The need for improvement in the care given to patients with ESLD towards the end of life (EOL) is increasingly recognised. Earlier institution of palliative care (PC) measures and advance care planning (ACP) discussions may allow patients and their carers to prepare better for disease progression and death. Unfortunately, changes in practice are slow, and many physicians will recognise the experience of Victoria Guy in 2006, as she witnessed her sister’s death from alcohol-related liver disease.

‘At last, I realized, with absolute certainty and for the first time, that we were no longer helping my sister. I refused to watch her whimper and cry in pain any longer. I decided to be her advocate. I requested palliative care, and morphine was ordered … With confidence, I told my sister we were trying to get her home, as she wished. This never happened. She died, in the hospital, 4 days later, at the age of 46.’

As a registered nurse Guy reflected poignantly on the perceived deficiencies in her sister’s care: the conflicting information given by healthcare professionals, the reluctance to admit how poor her sister’s prognosis really was, inadequate pain relief, and the realisation, too late, that her sister’s wishes had not been sought while she still had capacity to engage meaningfully in these conversations.

**Role of early palliative and supportive care**

In 2014, the World Health Assembly acknowledged the importance of PC, including it in the definition of universal health coverage and recommending its integration into the treatment of patients with any life-limiting condition. The WHO defines PC as:

’an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.’

While PC and EOL care are terms often used interchangeably, they are not synonymous. The official NHS definition of EOL care refers to care given to patients with a prognosis of 12 months or less. However, for many clinicians, EOL care refers to care given in the last days and weeks of life, where the trajectory of decline is predictable and ubiquitous. PC introduced at an early stage in the trajectory of advanced chronic disease has been shown to improve quality of life (QOL) and symptom management, often in conjunction with ongoing active and potentially curative therapy. National Health Service (NHS) England states ‘All professionals and staff in health and social care have a role in the effective provision of palliative and EOL care services across all care settings’. Professionals must acquire the skills to deliver ‘core level’, previously known as ‘generalist’, PC to their patients, referring only those with complex needs to specialist palliative care (SPC) services. The role of PC in ESLD remains poorly researched, with studies mainly focusing on SPC input in patients with hepatocellular carcinoma (HCC). A recent review concluded SPC input for patients with ESLD or HCC reduces costs, likelihood of death in hospital and encourages advance decision making, though evidence was heterogeneous and low quality. SPC referral rates for patients with ESLD remain low but are rising. In the USA, PC consultations for patients admitted with decompensated liver disease increased from just 0.97% in 2006 to 7.1% in 2012.

**Barriers to PC**

Potential barriers to discussing PC and to SPC referral include patient, physician and service-related factors. For patients, a poor understanding of illness trajectory and role of PC can lead to unrealistic expectations and unwillingness to engage early with ACP discussions and SPC services. The onset of hepatic encephalopathy (HE) can also leave patients lacking capacity and unable to participate in ACP discussions. Two recent surveys of gastroenterologists, hepatologists and SPC physicians identified multiple concerns, including unclear criteria for SPC referral, discomfort with the role of SPC physicians in joint care, the belief PC is synonymous with EOL care, insufficient time to engage in complex discussions and uncertainty about appropriate medication for symptom control. Despite this, the vast majority of gastroenterology and hepatology specialists (86%) recognised patients with ESLD benefit from earlier PC input and also felt initial discussions regarding ACP should be initiated by themselves, as the responsible clinician, rather than by SPC physicians.

The perception that PC is mutually exclusive to disease modifying treatments and transplantation has been recognised as a key barrier in the timely initiation of core PC measures. Although liver transplantation offers a potential cure, approximately 1000 transplants are carried out in the UK each year, while several thousand patients die from CLD annually. Around 15% of those listed will die or be removed from the waiting list each year. Evidence suggests patients active on the transplant list benefit from early SPC input, with a reduction in symptom burden and improved mood. Improving QOL for these patients, alongside those who are ineligible for transplant, is an important factor in delivering high-quality care.
LIVER

Table 1  Summary of prognostic screening tools

<table>
<thead>
<tr>
<th>Description</th>
<th>Supportive and Palliative Care Indicators Tool (SPICT)</th>
<th>Bristol Screening Tool</th>
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<tr>
<td>Tool to help identify people with deteriorating health due to one or multiple advanced conditions who may have unmet supportive and palliative care needs. Includes general indicators of poor or deteriorating health alongside condition-specific criteria. Suggested supportive care intervention is described for patients meeting criteria.</td>
<td>Prognostic screening tool used to identify patients admitted with decompensated cirrhosis at high risk of dying over the coming year. Suggested supportive care intervention is described for patients meeting criteria.</td>
<td></td>
</tr>
<tr>
<td>Criteria</td>
<td>Either: advanced cirrhosis with ≥1 complications in last year</td>
<td>Score of ≥2 from:</td>
</tr>
<tr>
<td></td>
<td>▶ Diuretic resistant ascites.</td>
<td>▶ Child-Pugh Grade C.</td>
</tr>
<tr>
<td></td>
<td>▶ Hepatic encephalopathy.</td>
<td>▶ Two liver-related admissions last 6 months.</td>
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<tr>
<td></td>
<td>▶ Hepatorenal syndrome.</td>
<td>▶ Ongoing alcohol use (alcohol-related liver disease patients).</td>
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<tr>
<td></td>
<td>▶ Bacterial peritonitis.</td>
<td>▶ Unsuitable for transplant work-up.</td>
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<tr>
<td></td>
<td>▶ Recurrent variceal bleeds or liver transplant contraindicated.</td>
<td>▶ WHO performance status 3–4.</td>
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PC IN ESLD: WHAT WORKS?

Parallel planning: early discussions about goals of care and ACP

The unpredictable nature of ESLD and the challenge of accurately predicting prognosis has led to the concept of a ‘parallel planning’ approach to care. This strategy recognises the frequent need to actively manage complications, such as screening for varices, while also preparing patients and their families for the possibility their health could rapidly and unexpectedly deteriorate.

Screening tools exist to help identify patients with CLD who have a particularly poor prognosis (see Table 1) and who may benefit from SPC input. However, while acting as a useful prompt, these tools may inadvertently perpetuate the idea that ACP discussions should be delayed until the patient’s condition has deteriorated significantly. Early conversations in clinic about prognosis and illness trajectory, even prior to the onset of decompensation, can ensure both patients and their relatives are better prepared if, or when, their disease progresses box 1. A recent literature review found patients and carers consistently wanted more information about their disease and management options. Brisebois et al advocate embedding ACP discussions into the routine care of patients with cirrhosis, explaining the uncertain disease trajectory and exploring patients’ changing priorities of care over time. They have produced a range of useful resources, including visual aids and question prompts, to help physicians initiate conversations at a pace that suits individual patients, acknowledging the poor health literacy of many patients by presenting information in various formats. Not all patients or their carers wish to engage in ACP discussions; however, information needs change over time and such discussions can be revisited, particularly as the illness progresses (Box 1). Crucially, PC should not be considered the sole responsibility of SPC teams. Patients state consistently that they prefer to have ACP discussions with a clinician they are familiar with, rather than someone unknown to them. With limited resources and growing demand, hepatologists must develop the skills required to provide core PC to their patients, allowing SPC practitioners to concentrate on complex cases where their skills and experience are most needed.

Symptom control

Improving QOL for patients and their families is the cornerstone of PC medicine. A recent review found improved management of HE, ascites and malnutrition have the greatest impact on patients’ QOL. Avoidance of hospital admissions has been identified by patients as an important goal, and educating and empowering patients and their carers to optimise symptom management themselves may help support this. For many patients, successful palliation involves both effective management of symptoms and relief of unnecessary burdens such as polypharmacy, and thus

Box 1  Advance care planning in action

A young homeless man with ongoing alcohol dependency and known cirrhosis with ascites, spontaneous bacterial peritonitis and recurrent variceal haemorrhage had over 15 admissions via the emergency department in the preceding 6 months. The case was discussed at an advanced liver disease MDT that resulted in a physiotherapy referral to help with breathlessness and referral to the community hospice team. Temporary housing was arranged by the hospice team, and the patient was given open access for day case paracentesis. An advance care plan was made with the patient during paracentesis sessions. He was clear that he did not want any further endoscopies and, in the case of further deterioration, he wished to die in hospital as he felt comfortable with the hepatology ward staff. An emergency treatment plan was written to clarify the limited plan for escalation of care, including use of midazolam in the event of a large gastrointestinal bleed. A Do Not Attempt Resuscitation form was completed and shared with the patient’s community team. The patient was subsequently admitted acutely with a variceal bleed, sepsis and hepatic encephalopathy. Bleeding settled spontaneously, but he deteriorated further with sepsis and worsening encephalopathy. End of life care was managed in a side room on the ward as per the patient’s wishes.
medications and interventions should be regularly reviewed to ensure they are still warranted.45

Hepatic encephalopathy

HE is distressing for patients and carers, especially as they are often unaware that it is a potential complication of CLD until it occurs for the first time.46 47 Treatment of both overt and covert HE has been found to significantly improve health-related QOL (HRQOL).48 49 Relatives are often best placed to notice subtle changes in personality and memory that indicate covert HE and should be empowered to both prevent and manage this condition. Unfortunately, one study found only 6% of patients and their carers knew they were on treatment for HE and understood how it worked.50 Encouraging patients and carers to adjust laxative and/or enema doses themselves may help improve QOL and avoid hospital admission.49

Recent studies examining the efficacy of rifaximin in clinical practice found, in combination with lactulose, it reduced both the frequency and length of hospital admissions,51 52 confirming previous clinical trial findings.53 Thus in patients with advanced disease, early use of rifaximin should be encouraged.54

Ascites

Approximately 60% of patients with cirrhosis develop ascites,55 which has a significant negative impact on HRQOL.56 57 Emergency admissions for paracentesis are distressing and costly. Day case paracentesis services in England reduce healthcare costs, days spent in hospital and lead to a lower probability of dying in hospital, when compared with patients receiving exclusively unplanned paracentesis.58 This study epitomises the benefits of parallel planning, clearly demonstrating optimal chronic disease management is an important component of PC.

Long-term abdominal drains offer another option for patients with refractory ascites, particularly those too frail to use outpatient paracentesis services, and early evidence suggests the safety profile is comparable with that of large volume paracentesis.59 60 Patients with refractory ascites have a median survival of less than 6 months,55 and frank conversations about the balance of burdens and benefits will help physicians focus on individual priorities of care (box 2). Although not yet widely available, the alfapump offers another alternative for out of hospital drainage, with recent data from a randomised controlled trial showing improved HRQOL scores at 3 months compared with those undergoing large volume paracentesis.61

Diuretic therapy has an important role, although concern regarding deteriorating renal function or electrolyte imbalance frequently limits use. However, in patients reaching the EOL, it may be appropriate to take a pragmatic view and limit blood monitoring as part of a shared decision-making approach.

Malnutrition

There is increasing recognition that frailty predicts poor outcomes in patients with cirrhosis, and sarcopenia is common in this group.62 63 An overnight fast in these patients has similar effects to a 72 hour fast in a healthy person.64 The European Association for the Study of the Liver (EASL) has produced comprehensive guidelines covering the management of nutrition and simple measures, such as encouraging patients to have a bedtime snack, have the potential to improve HRQOL.65 There is also evidence that optimising nutrition in patients with covert HE can improve cognition as well as HRQOL.43 Early dietitian referral is important, and all members of the healthcare team should emphasise the benefits of optimising nutrition to patients and carers.

Pain management

Concerns are often raised about metabolism and side effects of drugs, especially analgesics, in ESLD and advice regarding safe dosages is typically vague, encouraging caution. Despite a high pain and symptom burden, inadequate analgesic use is often reported by this group.67 68 If improving QOL is the priority of care, then patients and carers need to discuss the relative merits of analgesics versus potential side effects, such as worsening HE. In order to improve consistency and confidence in prescribing, the BASL EOL Special Interest Group has recently published pragmatic guidelines for symptom control in advanced CLD (https://www.basl.org.uk/index.cfm/content/page/cid/33).

Box 2 Parallel planning in action

A middle-aged man with alcohol-related chronic liver disease, abstinent for several years but not suitable for liver transplant due to frailty. Patient had resistant ascites requiring paracentesis every 10–14 days but was mobile and expressed a wish to avoid spending time in hospital. After further discussion, a shared decision was made to insert a long-term abdominal drain (LTAD). A joint consultation with a hepatology consultant and specialist palliative care consultant took place to discuss prognosis and ACP and patient reiterated desire to remain at home if possible, avoiding further admissions to hospital. After successful insertion, patient was eventually admitted when community blood tests demonstrated acute renal impairment. Initially, the amount of fluid removed via the LTAD was decreased but, after discussion with hepatology team, patient requested discontinuation of blood testing and removal of enough fluid to ensure comfort. Family was keen to care for patient at home therefore patient was discharged with anticipatory medications and community PC input. Patient survived a further 2 months at home and managed to go on a short holiday in the UK. He was cared for by family with support from district nurses and community PC team and moved to hospice for last few days of life as hepatic encephalopathy made care at home difficult. He died peacefully in the hospice.
Coordinating care

General practitioners (GPs) are keen to be closely involved in the care of patients with ESLD, although providing community-based care can be difficult where social circumstances are challenging. A recent qualitative study of GPs highlighted lack of expertise in hepatology, limited confidence with prognostication and a desire for ongoing support from secondary care as concerns. To bridge the gap between primary and secondary care, a recent feasibility study based in Edinburgh employed a Supportive Care Liver Nurse to improve care coordination, ACP and QOL for people with ESLD and their carers. The intervention was acceptable, effective in improving ACP and resulted in several potential financial benefits, including a reduction in unplanned admissions, shorter stays in hospital and fewer primary care consultations. Case studies (boxes 3–6) highlight other UK centres that have established models to improve integration of primary and secondary care.

Place of death

There is growing evidence that, although patients and carers may state a preference for death at home, location is much less of a priority than comfort. In fact, death in hospital may be the preferred option for some patients with ESLD, especially those with unstable social situations. However, the stark discrepancy between the proportion of patients with CLD who die in hospital (78%) and those with HCC (39%) suggests early conversations about priorities of care and place of death occur less frequently in patients with a non-malignant diagnosis. Unfortunately, many patients with ESLD have no carer, which can be a source of concern as their disease progresses; exploring ways to offer alternative support early is important and these conversations should be part of core PC delivery.
Financial needs
In the UK, the incidence of CLD is strongly associated with increasing socioeconomic deprivation. Furthermore, patients are typically of working age and often have dependants.33 When interviewed, both patients and carers acknowledge the financial strain that results from the disease.34 44 The majority of carers of patients with CLD are partners or spouses and a significant number report having to give up or cut down the number of hours worked as a result of the demands of caring.72 73 Some hospitals have teams available to help patients with benefits applications but, where these services are not available, it is important for physicians to be aware of local services or charitable organisations that can assist patients with this complex process.

Do not forget the carers
A report published by Carers UK in 2015 found the economic contribution made by unpaid carers is £132 billion per year, almost double its value in 2001.74 Although positive aspects of caring are reported, it is an extremely challenging role, with multiple competing demands placed on people who, in most cases, do not have formal training.75 Factors that increase caregiver burden in ESLD include multiple hospitalisations, a history of HE, active alcohol use, additional dependents in the household and low household income.73 Ensuring carers are aware of local support services, as well as financial assistance they may be eligible for, acknowledges the importance and difficulty of their role. Patients often want carers to be involved in ACP discussions, recognising that if they lose capacity it is reassuring to know their carer is aware of their prior wishes and can be an effective advocate.24 Evidence suggests carers cope better with bereavement if their loved one received prolonged PC input prior to death.76 Table 2 summarises recommendations.

WHERE DO WE GO FROM HERE?
Many departments have acknowledged the complex needs of this group and designed novel models of care.
Table 2  Achievable changes

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<th>Achievable changes</th>
<th>Details</th>
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| **Early, open discussions around prognosis and advance care planning**               | Discuss disease progression, potential complications and management options early with patients and carers.41  
Provide patients and carers with opportunities to express preferences around future place and type of care.  
British Liver Trust’s ‘Thinking Ahead’ leaflet is available to support discussions (https://www.britishlivertrust.org.uk/liver-information/thinking-ahead-planning-for-your-future-when-you-have-advanced-liver-disease/). |
| **Advanced liver disease MDT**                                                     | Encourage discussion of patients with unstable disease.  
Clarify optimal medical management, discuss emergency treatment plans and establish reasonable ceilings of care.  
Ensure clear, consistent communication between primary and secondary care as well as patients and carers. |
| **Prognostic scoring**                                                             | Use SPICT or Bristol Screening Tool to identify patients with ESLD who may benefit from SPC input.38 39 |
| **Hepatic encephalopathy**                                                         | Education of patients and carers about recognition, avoidance and management of HE.  
Encourage patients and carers to adjust laxative doses themselves to control symptoms and reduce hospital admissions.  
Proactive use of rifaximin – second episode of HE. |
| **Ascites**                                                                        | Access to day case paracentesis service.  
Consider use of LTAD or alfapump  
Pragmatic approach to diuretic use at EOL. |
| **Malnutrition**                                                                  | Early referral to dietitian.  
Education of patients and carers on good nutrition in liver disease – encourage bedtime snack.  
Use liver frailty index (https://liverfrailtyindex.ucsf.edu/). |
| **Pain management**                                                                | Assess for pain and advise patients, carers and GPs on safe analgesic use in advanced CLD.  
Use BASL guidelines for prescribing in advanced CLD (https://www.basl.org.uk/index.cfm/content/page/cid/33). |
| **Financial assistance**                                                           | Provide information about local services and charities that can assist patients with applications for financial assistance. |
| **Carer support**                                                                 | Early referral to carer support services, for example, respite care.  
Support to access financial assistance if eligible. |

CLD, chronic liver disease; EOL, end of life; ESLD, end-stage liver disease; HE, hepatic encephalopathy; LTAD, long-term abdominal drain; SPC, specialist palliative care; SPICT, Supportive and Palliative Care Indicators Tool.
to address them; examples are summarised in the case studies. A key element of these approaches is recognition that conversations about prognosis and ACP take time, and adequate resources need to be allocated for these services to be effective. Unfortunately, without more evidence showing financial benefit, departments may struggle to secure funding for similar models. Trusts providing these services must monitor impact, audit actively and share findings widely to provide data to help other departments compile business cases. The Improving Quality in Liver Services scheme offers a useful ‘choice architecture’ to encourage widespread practice improvement. Inclusion of metrics that recognise the importance of high-quality coordinated care, early ACP discussions and PC input will enable impact to be evaluated.

For departments with constrained resources, an advanced liver disease MDT is an achievable goal. Liver disease is ‘multi-dimensional’, affecting people socially, psychologically and financially, as well as physically. Such MDTs encourage discussion of patients with unstable disease, for example, those with decompensated cirrhosis and should ideally comprise a hepatology consultant, liver specialist nurse, palliative medicine specialist, alcohol liaison nurse, pharmacist, dietitian, physiotherapist and social worker. The MDT aims to clarify optimal chronic medical management for patients, discuss emergency treatment plans, establish reasonable ceilings of care and consider holistically other factors that might improve QOL. MDT outcomes can guide future conversations with patients. A key part of effective working is ensuring good, consistent communication; plans can be shared with community teams (GP, district nurses, paramedics and hospice) as well as patients and their families to improve continuity of care.

Improved communication with patients and carers about disease trajectory, prognosis and management options is essential. Unfortunately, limitations on clinician time make this difficult to deliver in practice, and alternative methods for providing information are needed. Communication aids, such as question prompt lists, help to focus conversations onto patients’ specific needs. Multimedia resources may also help, as limited literacy levels among many patients with CLD mean written resources are not always helpful.

Unfortunately, while interest in the role of PC among all healthcare workers is vital, and dispelling the myth that PC is synonymous with EOL care underpins this, PC should be viewed as a means of optimising QOL for patients and carers in parallel with active management of CLD. Limited SPC resources mean hepatologists need to take responsibility for core PC provision as they are best placed to identify and support patients who may benefit from ACP discussions. Gastroenterology trainees and specialist nurses need to receive robust practical training in the principles of PC to help achieve this. A proactive and methodical approach to parallel planning, with early ACP discussions can do much to avoid the experiences of Victoria Guy and her sister, which epitomise many failings of the current approach. We must recognise and seize all opportunities to improve our patients’ quality of living as well as dying.

Acknowledgements Dr Suzanne Ford-Dunn from St Barnabas House Hospice, Virginia Campbell from St Luke’s Hospice and Catherine Carroll from the Royal Free Hospital for their assistance in providing information for the case studies. Dr Katrina Curtis for her assistance with proofreading.

Contributors MW conceived the original idea for the review. HW performed the literature search, wrote the manuscript and is the guarantor for the article. MW, BH, AM and KF all read and edited early and final drafts of the review and contributed specialist clinical knowledge.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Commissioned; externally peer reviewed.

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