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British Society of Gastroenterology Best Practice Guidance: outpatient management of cirrhosis – part 1: compensated cirrhosis

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ABSTRACT

The prevalence of cirrhosis has risen significantly over recent decades and is predicted to rise further. Widespread use of non-invasive testing means cirrhosis is increasingly diagnosed at an earlier stage. Despite this, there are significant variations in outcomes in patients with cirrhosis across the UK, and patients in areas with higher levels of deprivation are more likely to die from their liver disease. This three-part best practice guidance aims to address outpatient management of cirrhosis, in order to standardise care and to reduce the risk of progression, decompensation and mortality from liver disease. Here, in part one, we focus on outpatient management of compensated cirrhosis, encompassing hepatocellular cancer surveillance, screening for varices and osteoporosis, vaccination and lifestyle measures. We also introduce a compensated cirrhosis care bundle for use in the outpatient setting. Part two concentrates on outpatient management of decompensated disease including management of ascites, encephalopathy, varices, nutrition as well as liver transplantation and palliative care. The third part of the guidance covers special circumstances encountered in managing people with cirrhosis: surgery, pregnancy, travel, managing bleeding risk for invasive procedures and portal vein thrombosis.

INTRODUCTION

Liver disease and liver cancer together caused 2.5% of deaths in England in 2018. Over half of these deaths occur in those of working age.¹ Liver-related deaths have increased by over 400% since 1970, and

the number of hospital admissions for liver disease has increased by half over the last decade.² Following the COVID-19 pandemic, premature mortality from all major causes of liver disease increased further in 2020,² with mortality highest in the most deprived areas.² Good outpatient management is crucial in preventing hospital admissions and keeping people living with cirrhosis well.

Cirrhosis is defined by widespread disruption of normal liver structure by fibrosis, caused by chronic progressive conditions affecting the liver; most commonly alcohol-related steatotic liver disease (ALD), followed by metabolic dysfunction associated steatotic liver disease (MASLD) (previously termed non-alcoholic fatty liver disease (NAFLD)). The diagnosis is generally made based on one, or a combination, of clinical findings, imaging, endoscopy, non-invasive tests (such as enhanced liver fibrosis test or transient elastography (TE)) and/or histology.

An asymptomatic compensated phase is followed, in the presence of ongoing liver damage, by a decompensated phase, marked by the development of overt clinical signs, most frequently ascites, bleeding, encephalopathy and jaundice. The Baveno group have developed a six-stage model of cirrhosis, reflecting the degree of portal hypertension (see [figure 1](#)). Mortality in the compensated phase (stages 0–2), a median of 10-year duration, is 1%, compared with 40%,



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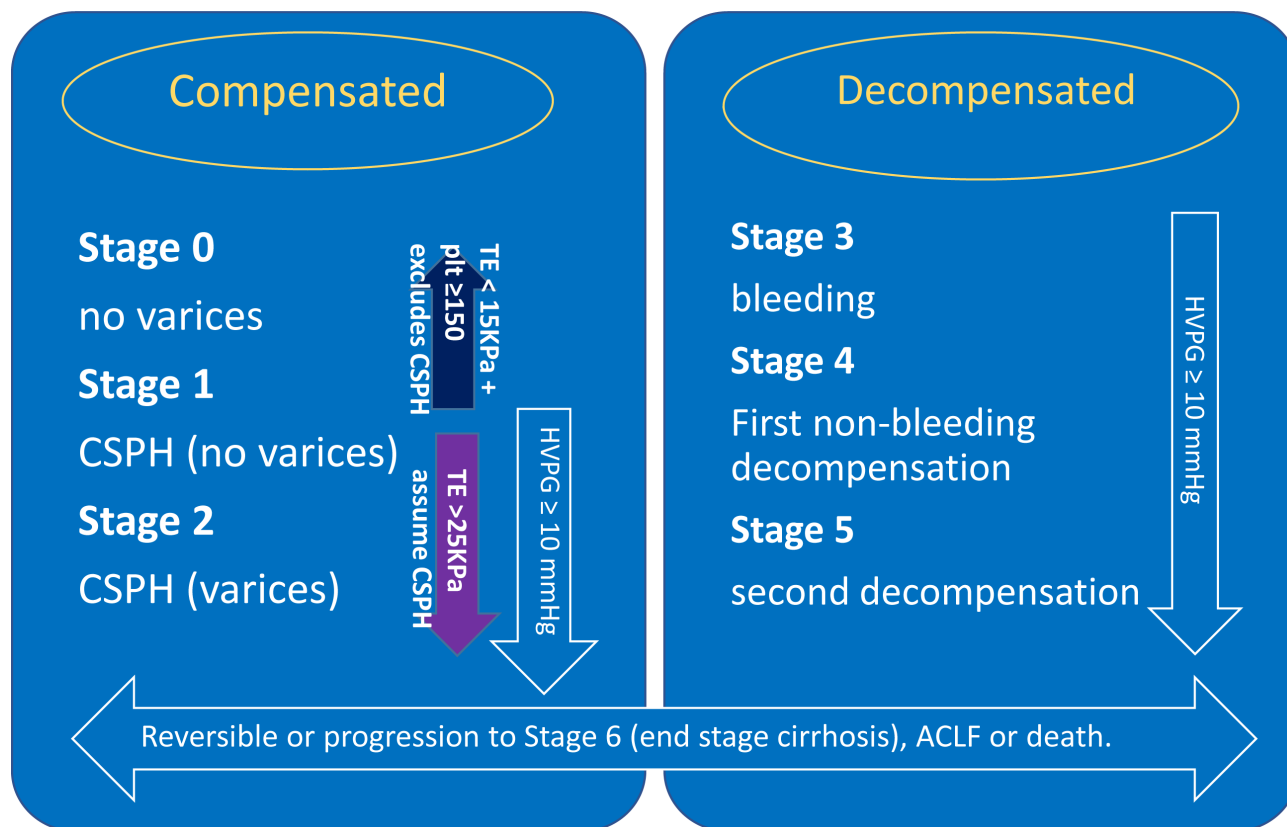


Figure 1 Stages of cirrhosis. ACLF, acute on chronic liver failure; CSPH, clinically significant portal hypertension; HVPG, hepatic venous pressure gradient; kPa, kilopascals; plt, platelet count; TE, transient elastography.

65% and 80% at 1, 2 and 5 years, respectively, for those progressing to decompensated cirrhosis.³ The Child-Pugh class (A–C)⁴ is referred to in parts of this guidance. While initially developed to estimate post-operative mortality, Child-Pugh score (5–15) and associated class are widely used to describe the severity of liver disease and are associated with prognosis. Child-Pugh class A and Child-Pugh class C indicate compensated and decompensated cirrhosis, respectively. Patients with Child-Pugh B cirrhosis may have compensated or decompensated disease. More recently developed scores such as the Model for End Stage Liver Disease (MELD)⁵ and UK Model for End Stage Liver Disease (UKELD)⁶ provide better prognostic value and so are used to predict mortality following a range of interventions in patients with cirrhosis, as well as eligibility for liver transplant (see part 2).

The Gastroenterology Getting It Right First Time Programme National Specialty Report,⁷ which analysed delivery of services across England, identified variation in how well hospital trusts managed patients with liver disease at risk, including the proportion of emergency admissions, proportion of patients having varices treated as an emergency (rather than at screening/surveillance) and outpatient management of ascites. The authors encouraged the use of cirrhosis care bundles as a way of ensuring patients are managed appropriately. This best practice guidance aims to

provide overarching guidance on the management of cirrhosis in the outpatient setting, to address variations in care, promote proactive outpatient management and improve outcomes.

The guidance is written in three parts, to cover the outpatient management of compensated (part 1), decompensated cirrhosis (part 2) and special circumstances, including surgery, pregnancy and travel in patients with cirrhosis (part 3). The aim of these documents is to provide a practical guide and service framework, including cirrhosis care bundles, for clinicians caring for patients with cirrhosis in secondary care, to promote best practice and multidisciplinary team working, and to identify areas for audit, quality improvement and research where there are gaps in the current evidence base. Aetiology-specific management, with the exception of alcohol use disorder (AUD), is outside the scope of this guidance. MASLD/NAFLD, viral hepatitis and autoimmune liver disease should be managed in accordance with the relevant published guidelines.

BACKGROUND AND METHODS

This guidance document was commissioned by the British Society of Gastroenterology (BSG) and endorsed by the British Association for the Study of the Liver (BASL) and British Liver Nurse Association (BLNA). A multidisciplinary working group, consisting of

hepatologists, specialist nurses, a surgeon, anaesthetist, pharmacist, dietitian and representative of the British Liver Trust, was formed, and subject areas agreed by the group. Allocated section leads were responsible for searching and summarising recent guidelines, updating with recent evidence where appropriate and drafting recommendations. These were appraised by the entire working group and consensus reached on the recommendations made, through a series of virtual meetings. These were then circulated to the BSG liver section committee, the BSG/BASL portal hypertension Special Interest Group and members of the BLNA for review prior to peer-reviewed publication.

Part 1 of the guidance covers management of compensated cirrhosis, including screening and surveillance for varices, osteoporosis and hepatocellular carcinoma (HCC) and vaccinations. Recommendations are collated into a care bundle to be used in outpatient clinics (figure 2). To avoid repetition, some areas are only covered in part 1 of the guidance (including HCC surveillance and management of AUD) and so reference is made to decompensated disease in these sections.

Information for people with cirrhosis

People diagnosed with cirrhosis should be followed up in clinic by a specialist with an expertise in the management of patients with liver disease.

At the time of diagnosis, patients should be provided with information on their condition in a way they are able to understand. This could include verbal information, tailored videos⁸ and information leaflets that patients can use to support self-care, bearing in mind that some patients may not be able to read or understand written information. They should also be signposted to patient support groups such as the British Liver Trust, where they can access a wide range of practical information and support.

Patients should be actively involved in decisions around the management of their cirrhosis. They should be made aware of red flag symptoms or complications to look out for and be given lifestyle advice on how to help prevent further liver damage. The rationale for screening, surveillance and primary prophylaxis of variceal bleeding (if applicable) should be discussed, including whether surveillance is appropriate. They should also be able to discuss the likely course of their disease and prognosis, if they wish, accepting that there is a degree of uncertainty.

Screening and surveillance of varices and primary prevention of variceal bleeding

In patients with cirrhosis, varices develop at a rate of 5% per year with a 10-year cumulative incidence of 44%.⁹ Variceal bleeding results in an inpatient mortality of 15% and 1-year mortality of up to 40%.⁹ Reducing the risk of the first variceal bleed (primary prevention) is an important clinical and economic goal.

Current UK guidelines recommend endoscopic screening in all patients with cirrhosis.^{9 10} Many units now use the Baveno VI criteria to circumvent the need for endoscopy in some patients with compensated disease. The Baveno VI criteria (liver stiffness measurement (LSM) <20 kPa on TE and platelet count >150×10⁹/L) were developed to identify patients with a low probability of high-risk varices, in whom endoscopy can be avoided.¹¹ These criteria have been increasingly used during the COVID-19 pandemic to prioritise those at highest risk, but their ongoing use remains controversial, and dependent on the circumstances of individual units and patient preference. If the Baveno VI criteria are used, TE and platelet count should be repeated annually in the presence of active liver disease (ongoing alcohol consumption, untreated viral hepatitis, cofactors such as obesity)—if LSM increases to >20 kPa or platelet count falls below 150×10⁹/L, screening endoscopy should be performed. Centres lacking the capacity to perform annual TE should continue to screen all patients endoscopically.

In patients undergoing endoscopic screening for varices, the frequency of surveillance and need for primary prophylaxis depend on the findings at endoscopy, and whether liver disease is active. Recommendations are detailed in figure 3.

There are two options for primary prevention of variceal bleeding: non-selective beta-blockers (NSBBs) and variceal band ligation (VBL). At present, we recommend NSBB or VBL in medium to large varices (>5 mm in diameter), considering comorbidities, tolerances and patient choice. Patients on NSBB for primary prevention do not need further surveillance. Those who have VBL should have banding approximately every 4 weeks until the varices are eradicated; in those who continue to have active liver disease (eg, still drinking alcohol), we would recommend rescope at 1 year (or if they develop decompensation) and then 1–2 yearly until abstinence is achieved and there is evidence that their liver disease is stable or improving.

A recent meta-analysis, including results from the PREDESCI trial,¹² suggests that NSBB such as carvedilol may reduce decompensation and mortality in patients with compensated cirrhosis, particularly in the presence of varices.¹³ Based on this evidence, carvedilol, where tolerated, could be preferred to VBL in patients with compensated cirrhosis and medium to large varices. In addition, carvedilol could be considered in patients with small varices (defined as varices <5 mm in diameter or varices which completely disappear on moderate insufflation of the oesophagus) and compensated cirrhosis in the presence of active liver disease. However, concerns of poor tolerance and concordance with NSBB (particularly in ARLD with ongoing alcohol use) could limit NSBB use in small varices and make VBL a preferable option in some patients with medium/large varices. We are currently awaiting the results of CALIBRE¹⁴

Patient details

Cirrhosis (compensated) Outpatient Clinic Care Bundle

1. Diagnosis						
Aetiology of liver disease						
Modality of diagnosis of cirrhosis		Biopsy	LSM	Imaging	Clinical	
Liver stiffness measurement		kPa	IQR/Med ratio			
2. Observations						
Weight (kg)	Height (m)	BMI	BP (mmHg)	Pulse		
3. Alcohol						
Record recent daily alcohol intake			 Units		
Thiamine 100mg BD (if potentially harmful alcohol consumption; >50u/week male or >35 U/week female)				Y	N	N/A
Advise controlled reduction in alcohol consumption to abstinence				Y	N	N/A
Refer to the alcohol team if not already under review				Y	N	N/A Decline
4. HCC surveillance						
Under active HCC surveillance				Y	N	Decline
Date of last imaging						
Result:						
AFP:						
Arrange follow up imaging (6 monthly ultrasound first line; those with significant comorbidities or poor performance status should be counselled against active monitoring)				Y	Stop	Decline
5. Portal Hypertension (see over)						
Varices	Y	N	Data of last assessment	OGD	LSM/pl	no-assess
Size of oesophageal varices		Small (grade 1)	Medium (grade 2)	Large (grade 3)		
Gastric varices				Y	N	
Previous variceal bleed				Y	N	
Treatment		Beta-blocker	Banding	N/A		
Beta-blocker dose optimised (aim HR 60/min with SBP >100 mmHg)				Y	N	N/A
Variceal assessment requested				Y	N	N/A decline
6. Fracture risk (see over)						
FRAX (+/-BMD)		Date	Low	intermediate	high	N/A
Treat if high FRAX or osteoporosis			Bisphosphonate	denosumab	decline	
7. Any features of hepatic decompensation						
Ascites	HE	Jaundice	UKELD			
If any features of decompensation and/or UKELD >49 then consider whether Liver transplantation may be indicated. Complete the decompensated cirrhosis outpatient bundle						
8. Vaccinations						
Advise patients to have relevant vaccinations (Influenza, COVID, Pneumococcal, Hep A & B)				Y	N	Decline
9. Provide information						
Patient relevant given written information about their liver disease				Y	N	previously

Figure 2 British Society of Gastroenterology/British Association for the Study of the Liver compensated cirrhosis outpatient care bundle. BD, two times per day; BMI, body mass index; BP, blood pressure; HCC, hepatocellular carcinoma; HE, hepatic encephalopathy; HR, heart rate; kPa, kilopascals; LSM, liver stiffness measurement; N, no; N/A, not applicable; OGD, oesophagogastroduodenoscopy; SBP, systolic BP; UKELD, UK Model for End Stage Liver Disease; Y, yes.

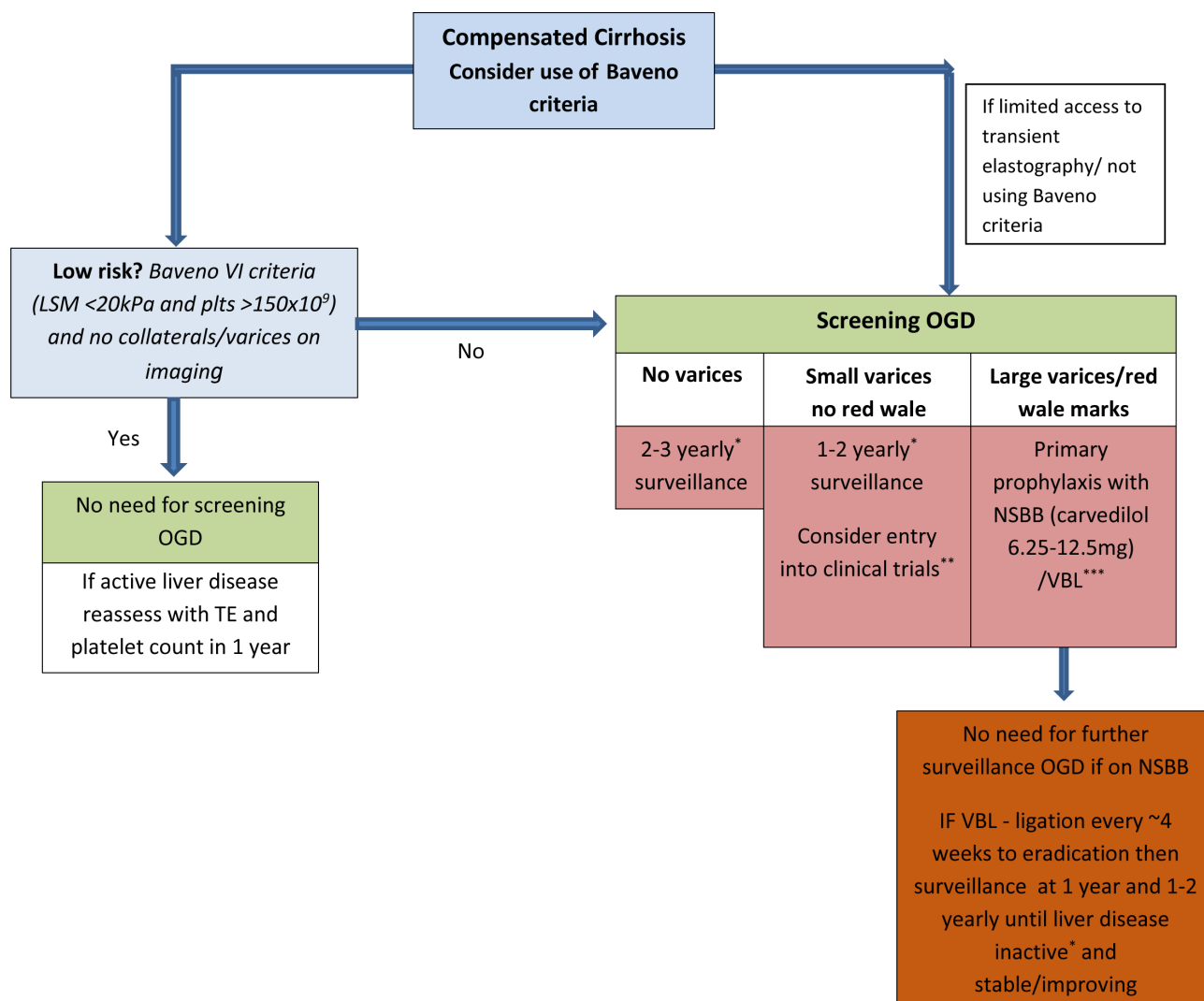


Figure 3 Screening, surveillance and primary prophylaxis in patients with compensated cirrhosis.

*Depending on whether liver disease is active (eg, continued alcohol consumption/untreated viral hepatitis or cofactors such as obesity/diabetes) or inactive (aetiological factor removed). **Outside of clinical trials, carvedilol may be considered in active disease after counselling patients on uncertainty of evidence and the side effects. Patient preference should be taken into account. If carvedilol started, no need for further surveillance OGD. ***On current evidence, carvedilol may be favoured after counselling patients on evidence and side effects. Patient preference should be taken into account. kPa, kilopascals; LSM, liver stiffness measurement; NSBB, non-selective beta-blocker; OGD, oesophagogastroduodenoscopy; plts, platelet counts; TE, transient elastography; VBL, variceal band ligation.

and BOPPP,¹⁵ two multicentre randomised controlled trials (RCTs) aimed at definitively addressing these issues.

Another area of active debate is the role of NSBB in preventing decompensation in clinically significant portal hypertension (CSPH), defined by the Baveno group as hepatic venous pressure gradient ≥ 10 mm Hg or LSM > 25 kPa. The recently published updated Baveno VII document includes a recommendation to use NSBB in all patients with CSPH¹⁶ regardless of the presence of varices. However, we believe further studies are required, and we do not currently advocate prescribing NSBB based on non-invasive markers (such as TE) alone, without endoscopic evidence of varices.

Osteoporosis screening

Patients with cirrhosis are at increased risk of fracture. A recent meta-analysis¹⁷ indicated an OR of 1.84 (for limb fracture) to 2.11 (for vertebral fracture) in patients with cirrhosis. National Institute for Health and Care Excellence (NICE)-accredited UK National Osteoporosis Guideline Group (NOGG) guidelines (<https://www.sheffield.ac.uk/NOGG/>) advocate use of the FRAX score or QFracture to assess fracture risk in people at increased risk of osteoporosis, which includes all patients with cirrhosis¹⁸ (figure 4). Although bone mineral density (BMD) scans are no longer mandatory for all patients, it is recommended in those with intermediate risk, and is useful for those at high risk

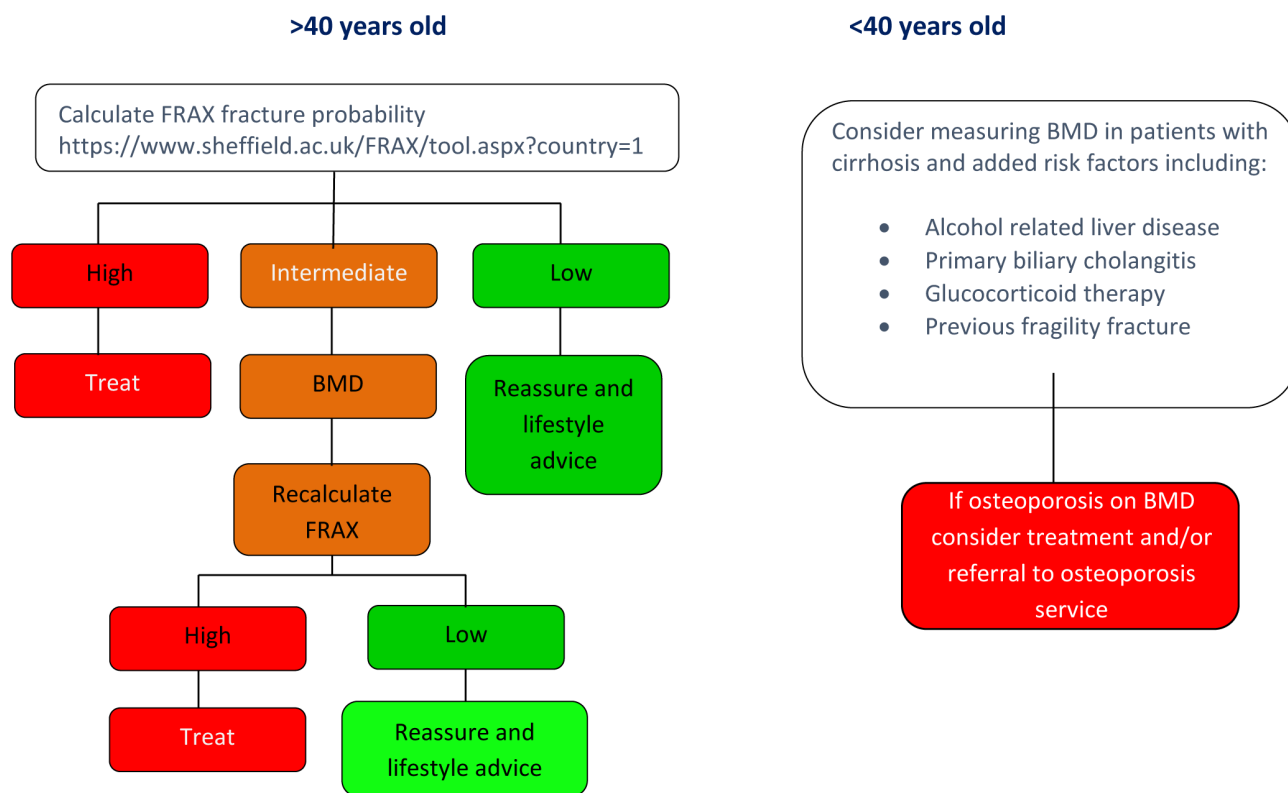


Figure 4 Screening for osteoporosis in patients with cirrhosis. BMD, bone mineral density.

in providing a baseline measurement for future monitoring.¹⁸

FRAX does not consider fracture site, recency or the number of fractures. In patients with a history of fragility fracture, particularly hip or vertebral fracture and those with multiple fragility fractures, NOGG recommends that treatment is usually indicated.¹⁸

For patients under 40 years with cirrhosis, BMD measurement should be considered in those with additional risk factors (high alcohol intake, cholestasis, glucocorticoid therapy or previous fragility fractures).¹⁸

All patients should be advised on adequate calcium intake, regular weight-bearing exercise, smoking cessation and ensuring adequate levels of vitamin D. Medications which may increase fracture risk such as proton pump inhibitors¹⁸ should be reviewed and stopped where possible. For those patients requiring active bone treatment, first-line therapy is oral bisphosphonate. Intravenous bisphosphonates or denosumab can be used as second line where there is concern about risk of gastrointestinal bleed (including medium/large varices or previous variceal bleed).¹⁸ Fracture risk should be reassessed after 3–5 years to determine whether treatment should be started, continued or paused.

Surveillance for HCC

The incidence of HCC in the UK, and the associated mortality, trebled between 1997 and 2017 to 5.5 per 100 000 and 4.0 per 100 000, respectively.¹⁹ Only one

in five patients receive curative treatment, and there are clear regional variations in the incidence, management and survival across England.²⁰ A UK-wide survey found that the provision of surveillance was poor overall, with many hospitals lacking the necessary mechanisms to make abnormal results known to referring clinicians, and the majority of HCCs being diagnosed at a very late stage.²¹ The aim of HCC surveillance is to identify tumours at an earlier stage, to provide the opportunity of curative treatment. However, potential physical and psychosocial harms of surveillance, including false-positive testing resulting in unnecessary and risk-associated procedures such as liver biopsy must also be considered, and surveillance should be targeted to those patients who are most likely to benefit.²²

NICE recommends six monthly ultrasound scans (USS) with or without alpha-fetoprotein (AFP) for patients with cirrhosis.¹⁰ Patients enrolled into a surveillance programme should have a good understanding of the purpose of surveillance, its aims and limitations. Patients with Child C cirrhosis, jaundice or ascites that is not controlled with diuretics who are not suitable for transplant would not be eligible for active HCC treatment and will not benefit from surveillance. Similarly, surveillance is not recommended in patients with significant comorbidities and poor performance status. If ultrasound views are inadequate, MRI of the liver should be considered to minimise radiation dose from multiple CT scans. If AFP is measured, and

is raised in the absence of abnormal imaging, appropriate action should be taken depending on individual context, for example, early repeat AFP and/or USS (eg, at 3 months) or further imaging. AFP can be raised for other reasons (such as pregnancy, testicular cancer and more rarely breast, stomach, colon, lung cancer or lymphoma), which should be considered if liver imaging is normal. There should be robust, reliable mechanisms for clinicians to be alerted to abnormal results, recall and follow-up, and access to specialist HCC multidisciplinary team. Trusts should have a means of recording and auditing surveillance rates.

ROUTINE VACCINATIONS

Patients should be counselled on the importance of vaccination. People with cirrhosis are immunosuppressed and are at higher risk of complications and serious morbidity and mortality from infectious diseases. The age-adjusted relative risk of death from influenza in patients with cirrhosis, for example, is 48.2 (compared with 47.3 for patients on immunosuppression), higher than all other risk groups.²³ The UK Health Security Agency recommends all individuals with chronic liver disease should receive the annual influenza vaccine, pneumococcal, hepatitis A and B vaccination, and SARS-CoV-2 vaccination in line with government guidelines for people at higher risk of COVID-19, in addition to all routine vaccinations.²³ Patients on mycophenolate, tacrolimus and high-dose azathioprine (>3 mg/kg) are advised to avoid live vaccines²³—where possible, vaccination should be administered prior to starting therapy.

ALCOHOL

Patients with cirrhosis should be routinely asked about alcohol intake as part of their clinical review. It is recommended that patients with cirrhosis from any cause should abstain from alcohol.¹⁸ Abstinence is a critical goal for people with ARLD, since it improves outcomes at all stages of disease.²⁴

Pharmacotherapy for relapse prevention should be considered for people with ARLD in combination with psychosocial/behavioural interventions. NICE recommends use of disulfiram, naltrexone or acamprosate to manage AUDs following successful alcohol withdrawal.²⁵ However, none of these medications have specifically been studied in patients with cirrhosis. Disulfiram and naltrexone undergo hepatic metabolism, increasing the risk of hepatotoxicity in those with hepatic dysfunction—they are therefore not recommended by the European Association for the Study of the Liver for use in patients with cirrhosis.²⁴ Acamprosate does not undergo hepatic metabolism, and based on limited data, is probably safe in Child-Pugh A and B cirrhosis.²⁶ To date, baclofen is the only pharmacotherapy for AUD for which there are RCT data in people with cirrhosis; a single RCT demonstrated the safety and efficacy of baclofen in promoting alcohol

abstinence in patients with ARLD and cirrhosis (including decompensated disease, but excluding patients with hepatic encephalopathy), but confirmatory studies are warranted as subsequent study results have been conflicting.^{24–28} The role of baclofen in the management of AUD is currently being evaluated in a further RCT.²⁹

Those who continue to drink alcohol, in a harmful or dependent pattern, are at risk of developing alcohol-related brain damage, in part due to thiamine deficiency. Prophylactic parenteral thiamine followed by oral thiamine (100 mg two times per day) should be given to those at risk who attend an emergency department or are admitted to hospital with an acute illness, including decompensated chronic liver disease.³⁰

People diagnosed with ongoing alcohol misuse or alcohol dependence (indicators of which include alcohol-withdrawal symptoms including seizures and the need for medically assisted withdrawal/detoxification) must be advised not to drive until after 6 (alcohol misuse) to 12 (alcohol dependence) months of controlled drinking or abstinence, and to notify the Driver and Vehicle Licensing Agency.³¹ This advice extends to those with any chronic cognitive impairment due to alcohol and those diagnosed with hepatic encephalopathy due to any cause of cirrhosis (see guidelines on decompensated cirrhosis).

NUTRITION

Malnutrition can be present in up to 20% of patients with compensated cirrhosis,³² and is associated with increased morbidity and mortality.³³ While more pronounced in decompensated cirrhosis, accelerated starvation and muscle breakdown can present in compensated cirrhosis with fatigue, reduced muscle mass, strength and function (sarcopenia) without overt weight loss. All patients with cirrhosis should be screened for malnutrition as part of routine outpatient review; screening tools such as the Malnutrition Universal Screening Tool may not be valid in patients with ascites or oedema. Alternative liver-specific tools such as the Royal Free Hospital Nutritional Prioritising tool³⁴ and the Liver Frailty Index,³⁵ which incorporates assessment of muscle strength and function, can be used in both compensated and decompensated cirrhosis. Those at high risk of malnutrition, including body mass index <18.5 or Child-Pugh C disease (see part 2), should have a full nutritional assessment by a dietitian.³⁶

Patients should be advised to eat a varied diet with three meals a day and be encouraged to include protein with each meal (aiming for 1.2–1.5 g/kg body weight/day). A protein and carbohydrate supper or evening snack minimises the overnight fast, reducing protein breakdown and muscle catabolism. Where oral intake is good, they should be encouraged to maintain or improve the quality of their diet with as many fruits and vegetables as they can manage.³⁷

Obesity is at least as frequent in cirrhosis as in the general population (20–35%³⁸) and affects most individuals with MASLD-related cirrhosis. Sarcopenia can be missed in the presence of obesity, and both obesity and sarcopenia can worsen the prognosis in cirrhosis.³⁸ Implementing nutritional and lifestyle changes (including moderate exercise) to achieve progressive weight loss (>5–10%) in obese patients with cirrhosis, and adopting a tailored, moderately hypocaloric (500–800 kcal/day deficit) diet, including adequate protein intake (>1.5 g proteins/kg ideal body weight/day) can be used to achieve weight loss without compromising muscle mass.³⁷ However, a slower sustained weight loss with calorie restriction of 250–500 kcal deficit is generally preferred to preserve muscle mass, particularly where exercise levels are low. Physical activity is often overlooked but is an important aspect of care in all patients with cirrhosis, irrespective of aetiology, and especially those with sarcopenic obesity. Patients should be encouraged to follow WHO advice of at least 150 min of moderate or 75 min of vigorous-intensity exercise per week with muscle strengthening exercises at least 2 days a week. However, any physical activity is better than none, and exercise can be built up slowly and gradually over time. Weight loss should be under dietetic supervision with regular checks on muscle mass and function.

MULTIDISCIPLINARY CARE

Patients with cirrhosis should be managed by a multidisciplinary team tailored to the holistic needs of the individual, including specialist nurses, dietitians and physiotherapists. Depending on the aetiology of the liver disease, other allied health practitioners, such as alcohol care teams, may be involved.

Specialist liver nurses, advanced clinical practitioners and specialist pharmacists can play a key role in monitoring patients with cirrhosis. Patients with compensated cirrhosis requiring 6-month review and surveillance can be managed with a combination of telephone, video and face-to-face appointments. Use of care bundles and objective scores (MELD/UKELD) can help to standardise outpatient care.³⁹ All patients should have an allocated consultant in overall charge of care and there should be an agreed referral pathway back to consultant if the clinical picture changes. Consultant support, adequate supervision and continuing professional development are also crucial in developing an effective nurse-led service.

Sustainability and service development

Efforts should be made to improve the sustainability of the service (for example, reducing the number of trips patients need to make to the hospital by linking outpatient appointments to ultrasound surveillance, avoiding unnecessary endoscopy, by treating patients closer to home and/or use of telephone and virtual clinics). Services should be flexible to deliver patient-centred

care, and strategies should be employed to manage more vulnerable patients (for example, frequent non-attenders with drug and alcohol problems) to optimise their engagement with the service.¹⁰

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