

DECISION-MAKING IN VIRAL HEPATITIS RELATED ADVANCED LIVER DISEASE

UNITED KINGDOM

STEP 1 - Could my patient have advanced liver disease?

Advanced Liver Disease is the term used for chronic liver disease that has progressed to near cirrhosis or cirrhosis.

Cirrhosis is caused by severe fibrosis (scarring). In **compensated cirrhosis**, the liver is still able to keep up with its major functions.

Decompensated cirrhosis typically refers to the presence of ascites/oedema, hepatic encephalopathy and other complications of portal hypertension.

What are the causes of advanced liver disease?

- Chronic viral hepatitis (hepatitis B and/or C)
- Hazardous alcohol consumption
- Obesity, type 2 diabetes and the metabolic syndrome
- Rarer liver diseases

Likelihood of advanced liver disease increases with:

Duration of liver disease, lifetime amount alcohol consumed, comorbid liver disease (e.g. obesity related liver-injury), increasing age, male gender, co-infection with HIV.

Why is diagnosis of advanced liver disease important?

To **prevent progression** to decompensation and hepatocellular carcinoma (HCC). Also impacts treatment choices for hepatitis C.

How to diagnose advanced liver disease

No single test can reliably diagnose all cases. Information from the clinical history, examination, blood tests, abdominal ultrasound and fibroscan results can provide clues.

When to suspect advanced liver disease

- **Physical findings:** ascites, oedema, muscle wasting, and hepatic encephalopathy
- **Laboratory abnormalities:** reversal of AST/ALT ratio (normal <1), falling albumin, rising INR and bilirubin, falling platelets (suggests portal hypertension)
- **Imaging:** irregular liver outline, enlarged portal vein, splenomegaly
- **Non invasive markers of fibrosis:** Fibroscan (Transient Elastography is a safe quick effective method to assess liver stiffness) >11.5 kpa, or blood test algorithms including APRI, ELF (Enhanced liver fibrosis) and Fibrotest

STEP 2 – Correction of underlying liver disease aetiology

Chronic hepatitis C virus (CHC) infection

All people with CHC infection and advanced liver disease should be encouraged to consider the benefits of HCV antiviral therapy, such as the potential to limit the progression of liver disease and assist regression of liver damage and the prevention of onward transmission.

Chronic hepatitis B virus (CHB) infection

All people with CHB and advanced liver disease should be on oral antiviral therapy. HBV therapy may lead to progressive recovery/regression of advanced liver disease.

It is important to manage associated causes of liver injury in advanced liver disease, including:

Alcohol

People with advanced liver disease should **NOT** consume any alcohol.

Non-Alcoholic Fatty Liver Disease (NAFLD)

- Suspect if obesity, T2DM, metabolic syndrome
- Management: lifestyle modification and weight loss by dietary, exercise and medical interventions

Other liver diseases

Screen for haemochromatosis (iron studies), autoimmune liver disease, alpha-1-antitrypsin deficiency, Wilson's disease, primary biliary cirrhosis, primary sclerosing cholangitis.

Vaccinations

Ensure the following vaccinations are undertaken when advanced liver disease is present:

- Pneumococcus and annual influenza
- Determine Hep B (HBsAg, anti-HBc, anti-HBs) & Hep A (anti-HAV IgG) status and vaccinate if not immune.

STEP 3 – When to refer to a Specialist

- **All patients with advanced liver disease**, as recognised by methods described in Step 1, should be referred to a specialist for treatment of known aetiology or further investigation if aetiology is unknown
 - especially if decompensated, untreated viral hepatitis, significant co-morbidities such as HIV or diabetes, focal abnormalities detected on scanning (do not biopsy without assessment in specialist centre)

Urgent referral to hospital if:

- Gastrointestinal bleeding
- Confusion/drowsiness (? possible encephalopathy)
- Unexplained fever or abdominal pain (? possible spontaneous bacterial peritonitis)
- New or progressive jaundice
- Marked shortness of breath with increased abdominal distension

Prognosis

- Median survival for compensated and decompensated cirrhosis are 12 and 2 years respectively.
- Severity and prognosis of liver disease can be estimated using the [Child-Pugh](#) score, the [MELD](#) score or the UK Model for End-Stage Liver Disease ([UKELD](#)) score. The UKELD is used in determining priority for liver transplantation.
- Complications of cirrhosis such as hepatorenal syndrome (development of renal failure), sepsis, variceal bleed and HCC are associated with a worse prognosis.

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STEP 4 – Management of compensated cirrhosis

Lifelong HCC surveillance is recommended for all patients with cirrhosis – see *HCC

Develop a chronic liver disease management plan and consider ongoing chronic disease management to:

- Minimise future liver damage
- Monitor for deterioration
- Screen for the complications, including HCC, osteoporosis, oesophageal varices, malnutrition and decompensation

Minimise future liver damage

- Treat HBV and/or HCV infection with antiviral therapy to prevent disease progression
- Encourage abstinence from alcohol, maintain a healthy diet and develop an exercise plan, especially if obese

Monitor for deterioration/decompensation

- Patients with compensated disease should have 6-monthly blood tests including FBC, EUC, LFT, INR/PT in conjunction with HCC screening and a clinical review especially monitoring nutritional status
- Gastroscopy surveillance for varices – see below for guidelines
- Watch for increasing INR, low albumin and rising bilirubin

Recommended surveillance for complications of cirrhosis

- ***HCC** – 6-monthly ultrasound
- **Osteoporosis** – 2-yearly DEXA scans and monitoring of serum Vitamin D
- **Varices** – once cirrhosis is diagnosed, all patients should have baseline endoscopic surveillance for varices
 - the intervals to next endoscopy depend on the severity of varices and liver disease

Liver transplantation

- Chronic viral hepatitis, particularly HCV, is one of the major indications for liver transplant in the UK
- Many patients have co-existent HCC
- A referral to the liver transplant unit from a specialist may be required

STEP 5 – Management of decompensated cirrhosis and complications of portal hypertension

General nutritional advice

- High protein diet; add protein supplements if albumin is low; regular exercise
- Multiple small snacks as supplements, including a night time snack
- Avoid raw seafood, unpasteurised dairy products and soft cheeses
- Vitamin D and Ca supplements if required for osteopaenia/ osteoporosis

Ascites

- NaCl restriction – 80mmol or 2000mg Na+ / day
- Fluid restriction is not necessary unless serum Na+ drops to ≤ 125 mmol/L
- Diuretics, if renal function allows. These are only effective with adequate Na+ restriction
 - Initially spironolactone 50-100 mg mane and titrate up every 3-5 days to combination of spironolactone and frusemide [starting at 100mg mane and 40mg mane respectively; to max 400mg mane and 80mg bd or 160mg once daily if compliance a concern]
 - Aim for 0.5kg/day weight loss (3kg per week) and monitor renal function
 - In patients who do not respond to aldosterone antagonists, as defined by a reduction of body weight of less than 2 kg/week, or in patients who develop hyperkalemia, frusemide should be added at an increasing stepwise dose from 40 mg/day to a maximum of 160 mg/day (in 40 mg steps)

Renal function

- Kidneys are sensitive to insults:
 - Avoid NSAIDs and other nephrotoxins
 - Any decompensation can contribute to renal impairment (Infection, bleeding)

Hepatic Encephalopathy (HE)

- Reversible neuropsychiatric changes: stereotypic asterix (hepatic flap), fetor (sweet breath), dyspraxia (difficulty with 5 point star), sleep pattern reversal
- Identify precipitants such as infection, GIT bleeding, medications (esp. sedatives)
- Titrate lactulose for 2-3 loose motions per day
- Non absorbable antibiotic Rifaximin if difficult to control HE
- Patients are likely unfit to drive, particularly if there are recurrent episodes

Hepatocellular carcinoma (HCC)

- Therapies dictated by tumour size and location, hepatic reserve and general health
- Treatment may be curative (surgery, percutaneous ablation and liver transplant) or palliative (chemoembolization, chemotherapy and support)
- Management should be in a centre of excellence with a multidisciplinary team to review treatment

Spontaneous Bacterial Peritonitis (SBP)

- May present with fever, change in mental status or pain
- Low threshold for referral to hospital
- Ascitic fluid WCC >250 cells/mm diagnostic
- Hospitalisation for IVI antibiotics and albumin infusion required
- Secondary prophylaxis with co-trimoxazole 160/800mg ("Bactrim DS") one daily or norfloxacin 400mg daily continuously is effective

Variceal bleeding

- Present with haematemesis and/or melaena
- Arrange urgent admission to hospital for endoscopic evaluation and therapy
- Secondary prophylaxis with propranolol reduces further bleeding (titrate dose to achieve a 25% reduction from usual baseline pulse rate)
- After discharge, further endoscopy therapies required to obliterate varices

Cardiopulmonary complications

- Breathlessness may be the first sign of cardiopulmonary complication such as hepatopulmonary syndrome, porto-pulmonary hypertension or cirrhotic cardiomyopathy