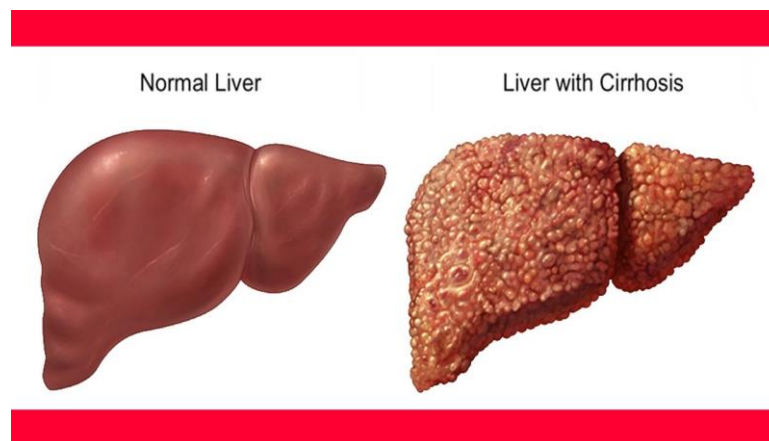


Cirrhosis and its management in primary care

Introduction

Cirrhosis of the liver is the common end-point response to prolonged liver insult arising from a range of causes. It represents an irreversible stage of liver disease and is most commonly associated with alcohol misuse, non-alcohol-related fatty liver disease (NAFLD) and chronic hepatitis B and C infections. It can also occur in a range of genetic, autoimmune and metabolic conditions including haemochromatosis and primary biliary cholangitis. It can develop in infancy and childhood, for example when prolonged neonatal jaundice resulting from biliary atresia is not diagnosed and surgical treatment is delayed. Most commonly in adults, cirrhosis develops over a period of years or decades of exposure to one or more risk factors, though not everyone exposed will develop cirrhosis.

To the naked eye, the cirrhotic liver is nodular rather than smooth and the liver feels firm. Histologically there may be evidence of liver cell death, inflammatory infiltration, replacement of liver tissue with fibrous scar tissue that disrupts the normal liver architecture including ducts and vascular tissue, together with regenerative nodules of hepatocytes.



When cirrhosis is mild the liver has enough reserve to maintain normal function. The patient may be asymptomatic and routine liver blood test panels (LFTs) are often completely normal. When cirrhosis is more advanced, patients may complain of malaise and fatigue, anorexia, weight loss and muscle wasting, nausea and vomiting and abdominal pain. If liver function is severely impaired there may be jaundice, abnormal bruising, peripheral oedema and ascites. Some patients remain asymptomatic and undiagnosed until they have serious complications of cirrhosis such as portal hypertension and bleeding oesophageal varices, coagulopathy, hepatic encephalopathy or hepatocellular carcinoma.

Risk factor modification and early diagnosis

Early recognition of risk factors and support for patients to resolve them can help prevent those at risk from developing cirrhosis, or can slow further development of established cirrhosis. The early diagnosis of cirrhosis and onward referral makes it possible for patients to access specialist supervision and monitoring to identify and manage the potential complications of cirrhosis early.

Identifying patients who are at increased risk of cirrhosis

NICE cirrhosis guidance identifies increased risk of cirrhosis in people who:

- have hepatitis B virus infection
- have hepatitis C virus infection
- misuse alcohol
- are obese (body mass index of 30 kg/m² or higher)

- have type 2 diabetes

The risk of cirrhosis is significantly increased if two or more of these risks are present. Though these are the most common causes of cirrhosis, patients with autoimmune, metabolic and genetic liver conditions are also at risk of cirrhosis.

Investigating patients at risk of liver fibrosis and cirrhosis

Blood tests are often normal in cirrhosis, though when synthetic liver function is significantly impaired there is likely to be raised bilirubin, reduced albumin, coagulation abnormalities and a low platelet count. Plasma sodium may be low in advanced cirrhosis and is a poor prognostic marker. Even in advanced cirrhosis, transaminases alanine amino transferase (ALT) and aspartate amino transferase (AST) may be normal.

The gold-standard diagnostic test for cirrhosis is liver biopsy, though this is not always clinically necessary.

Transient elastography (TE, commonly known by the trade name 'Fibroscan') is increasingly used to detect fibrosis and diagnose cirrhosis. It is a simple, non-invasive test, similar to ultrasound scan. Machines are available that are readily portable, and in some areas TE is available in community settings. There is no discomfort for the patient and no sedation, and the test is usually done in less than 10 minutes. It is significantly less expensive than liver biopsy, and has no unwanted effects. The results of the test are available instantly, and clinicians can share results with the patient and use them to make decisions during a routine clinic.

During TE a 50MHz sound wave is passed through the liver from a small transducer on the end of an ultrasound probe. The transducer measures the velocity of the wave as it passes through the liver. This velocity reading is then converted into a measure of liver 'stiffness', expressed in kilopascals. Liver stiffness is a proxy measure of liver fibrosis.

The NICE guidance on cirrhosis in over 16s suggests that GPs should use transient elastography to assess cirrhosis in the following:

- People with chronic hepatitis C virus infection;
- People who are drinking very heavily: men who drink over 50 units of alcohol per week and women who drink over 35 units of alcohol per week and have done so for several months;
- In people already known to have alcohol-related liver disease;
- Patients with NAFLD and advanced fibrosis (ELF score >10.51).

Further guidance on the assessment of fibrosis in those at risk from NAFLD is detailed in NICE NAFLD guidance. Further information on the identification of cirrhosis in patients with chronic hepatitis B infection can be found in NICE CG165 hepatitis B (chronic): diagnosis and management (2013).

However, a more recent NICE Medtech innovation briefing states that there are uncertainties around whether every primary care centre would be able to support a FibroScan clinic and comments that there is currently no evidence to support the contention that the use of FibroScan in primary care would reduce hospital waiting lists.

Acting on TE results in primary care

Normal TE

If a patient has risk factors for cirrhosis, but transient elastography is normal, the GP has an opportunity to offer interventions to reduce the risk of cirrhosis. Depending on the individual circumstances this may be through healthy eating, weight loss and activity advice in NAFLD, support to reduce alcohol consumption in alcohol misuse, referral to a hepatologist for those with chronic hepatitis B or C infection for consideration of antiviral treatment, or a combination of interventions.

For some people the risk of developing cirrhosis will remain, and NICE advises offering a re-test for cirrhosis every 2 years for:

- people diagnosed with alcohol-related liver disease;
- people with hepatitis C virus infection who have not shown a sustained virological response to antiviral therapy;
- people with NAFLD and advanced liver fibrosis.

The ongoing specialist management of patients with chronic hepatitis B infection is covered in NICE CG165 hepatitis B (chronic): diagnosis and management (2013).

Abnormal TE

If the TE result is abnormal, showing advanced liver fibrosis or cirrhosis. this needs specialist assessment; and people with abnormal elastography results should be referred to a specialist in hepatology along agreed referral guidelines.

Follow-up of patients with confirmed cirrhosis in secondary care

Once advanced fibrosis or cirrhosis is diagnosed, patients need specialist assessment and ongoing monitoring. This may include:

- using the Model for End-Stage Liver Disease (MELD) score to identify those at high risk of developing serious complications of cirrhosis;
- using ultrasound (with or without serum alpha-fetoprotein) every 6 months as surveillance for hepatocellular carcinoma;
- upper gastrointestinal endoscopy to detect oesophageal varices and provide surveillance;
- endoscopic variceal band ligation for the primary prevention of bleeding for people with cirrhosis with medium to large oesophageal varices;
- prophylactic intravenous antibiotics for people with cirrhosis who have upper gastrointestinal bleeding;
- transjugular intrahepatic portosystemic shunt for people with cirrhosis with refractory ascites;
- prophylactic oral ciprofloxacin or norfloxacin for selected people with cirrhosis and ascites.

End of life care in cirrhosis

Those with cirrhosis entering end of life (EOL) care may have specific areas of complexity for health care givers including palliative care teams, hospices and primary care clinicians.

Some with end-stage liver disease may choose to continue drug or alcohol use bringing challenges to inpatient resources together with the potential need for management of withdrawal symptoms if the patient becomes too ill to continue substance use. Others may face specific pharmacological challenges in palliation due to prescribing cautions in liver failure or the need to manage pain in the context of opioid dependence and tolerance. Relatives whose loved ones are dying as a consequence of alcohol or illicit substance misuse may have additional emotional burdens requiring support.

Links to documents and other useful resources are available via the toolkit

- NICE NG50 cirrhosis in over 16s guidance (2016)
- Toolkit resource: Top ten tips cirrhosis
- Toolkit resource: Clinical audit ideas: identifying and managing cirrhosis in primary care
- Toolkit resource: Personal learning reflection template
- Cirrhosis web link for patients
- Cirrhosis patient leaflet
- NICE advice: FibroScan for assessing liver fibrosis and cirrhosis in primary care