NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

SCOPE

1 Guideline title

Cirrhosis: assessment and management of cirrhosis

1.1 Short title

Cirrhosis

2 The remit

The Department of Health has asked NICE to develop a clinical guideline on the 'assessment and management of cirrhosis'.

3 Clinical need for the guideline

3.1 Epidemiology

a) Cirrhosis is condition that occurs as a response to liver damage. It is characterised at a cellular level by fibrosis and the distortion of the normal liver structure into abnormal nodules. It usually takes several years for liver damage to develop into cirrhosis but in some cases it may take an accelerated course over weeks.

b) Cirrhosis interferes with the normal functions of the liver, reducing its ability to produce proteins (reduced hepatic synthetic function). This can lead to problems such as coagulopathy (problems with blood clotting), low albumin and raised bilirubin.

c) The most common causes of cirrhosis include alcohol, chronic hepatitis C virus infection and non-alcoholic fatty liver disease. Less common causes include autoimmune liver diseases (autoimmune hepatitis, primary biliary cirrhosis or primary sclerosing cholangitis), genetic conditions, hepatitis B with or without hepatitis D, chronic

infection with hepatitis E virus in people who are immunosuppressed, secondary biliary cirrhosis, Budd–Chiari syndrome or veno-occlusive disease, prolonged exposure to certain chemicals or medications (such as amiodarone or methotrexate), sarcoidosis, chronic right-sided heart failure, and type IV glycogen storage disease.

d) At least 7000 new cases of cirrhosis were diagnosed each year between 1992 and 2001, based on an incidence study using the UK General Practice Research Database. The study estimated that the incidence of cirrhosis rose by 45% between 1992 and 2001.

e) In 2010 there were 5631 deaths in England recorded with an underlying diagnosis of cirrhosis of the liver. The British Society of Gastroenterology reported that mortality from cirrhosis in the UK increased from 6 per 100,000 population in 1993 to 12.7 per 100,000 population in 2000.

f) In patients admitted to hospital in England in 2012, the mortality rate was higher in patients admitted with liver disease (1 in 11 or 8.8 per cent) than in overall admissions (1 in 72 admissions or 1.4 per cent). Nearly half of liver disease admissions were for alcohol-related liver disease (47.7%), and approximately 1 in 8 of these resulted in a hospital death (12.3%). Men accounted for more than two-thirds of admissions for alcohol-related liver disease. Patients aged 50 to 69 had the greatest number of hospital deaths due to liver disease, but patients aged 70 or older had the highest mortality rate.

g) The NHS Atlas of Variation in Healthcare for People with Liver Disease revealed widespread geographical variation in the prevalence of risk factors for cirrhosis, such as hepatitis infection, obesity and alcohol abuse. Admission rates to hospital for end-stage liver disease due to chronic hepatitis C virus also showed widespread geographical variation, with the highest rates

found in central London and North West England. The North West region also had the highest rate of admissions for alcohol-related liver disease, but the North East region had the highest rate of admissions for all liver diseases.

h) The prevalence of cirrhosis varies according to level of deprivation; for both men and women the highest prevalence occurs in the most deprived quintile in England and lowest among the least deprived quintile. Consequently, the most deprived 20% of the population have significantly more admissions for cirrhosis than the rest of the population.

i) The aetiologies of cirrhosis in children and young people are generally different to those in adults (for example, biliary atresia), and the assessment (including the scoring systems for children for referral for transplantation) and management of these aetiologies will be different. However, it is acknowledged that although the guideline will be focused on adults, the recommendations may be useful to clinicians who are caring for young people who transition into this care pathway when they reach 16 years.

3.2 Current practice

a) Cirrhosis is often asymptomatic (40% of cases) and may be revealed by abnormal results from liver tests performed for other reasons or patients may present to their GPwith non-specific symptoms (for example, fatigue). People may also present with signs and symptoms of complications of cirrhosis such as portal hypertension (for example, ascites and variceal bleeding), increased risk of infection (for example, spontaneous bacterial peritonitis), decreased detoxification capacity (for example, hepatic encephalopathy) or hepatocellular carcinoma. This also impacts significantly on quality of life.

b) There are no standard criteria for identifying cirrhosis or referring a person with suspected cirrhosis from primary care for assessment

in secondary care. A study of referral practice in Liverpool PCT found that primary care practices had different criteria and standards for referral within the same PCT.

c) There is currently variation in practice across England and Wales for diagnostic tests for cirrhosis, for example, which liver tests are carried out and whether ultrasound is undertaken.

d) Liver biopsy, performed in secondary care, is the definitive diagnostic method for confirming cirrhosis. As well as revealing the extent of the fibrosis it helps determine the cause of the liver damage, and consequently may inform treatment options. The effectiveness, cost and patient acceptability of liver biopsy compared with non-invasive assessment of fibrosis are important factors to consider, and there is widespread variation in the use of non-invasive tests to assess liver fibrosis.

e) Guidelines are needed in primary care to standardise both the investigation of patients with suspected cirrhosis and the criteria for referral to secondary care in order to avoid delaying treatment.

f) Guidelines are needed in secondary care to standardise the methods used to diagnose cirrhosis and assess severity of liver dysfunction and also to standardise the investigation and treatment of complications of cirrhosis.

g) Guidelines are needed to standardise referral criteria to tertiary care for specialist liver treatments (for example, liver transplant assessment).

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, ‘Further information’).

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

a) Adults with cirrhosis that is suspected or confirmed when they are 16 years or older.

b) No patient subgroups have been identified as needing specific consideration.

4.1.2 Groups that will not be covered

a) People whose cirrhosis is diagnosed before the age of 16 years.

4.2 Setting

a) Primary and secondary NHS-commissioned care including referral to tertiary care.

4.3 Assessment and management

4.3.1 Key issues that will be covered

Assessment

a) Identification of people who may have cirrhosis.

b) Assessment of suspected cirrhosis including:

- Liver blood tests (for example, bilirubin).
- Non-invasive surrogate markers of cirrhosis (for example, transient elastography).
- Liver biopsy.

c) Tools to assess severity of cirrhosis (for example Child–Pugh score and Model for End-stage Liver Disease).

Management

d) Monitoring people with cirrhosis to detect complications early (for example, hepatocellular carcinoma).

e) Managing the complications of cirrhosis (for example, ascites, prevention of spontaneous bacterial peritonitis and hepatorenal syndrome)

Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

f) Referral criteria for tertiary care (including criteria for referral for assessment for liver transplant).

4.3.2 Issues that will not be covered

a) Diagnosis, investigation and management of the underlying cause of cirrhosis.

b) Complications specific to the underlying cause of cirrhosis.

c) Liver transplantation (other than the criteria for referral for assessment for liver transplantation).

d) Management of hepatocellular carcinoma.

e) Management of variceal haemorrhage.

4.4 Main outcomes

a) Health-related quality of life.

b) Mortality (with or without later transplantation).

c) Adverse effects.

d) Length of hospital stay.

e) Re-admission rates.

4.5 Review questions

Review questions guide a systematic review of the literature. They address only the key issues covered in the scope, and usually relate to interventions, diagnosis, prognosis, service delivery or patient experience. Please note that these background review questions are draft versions and will be finalised with the Guideline Development Group.

4.5.1 Assessment

a) In whom should cirrhosis be suspected?

b) What is the usefulness of different tests in the diagnosis of cirrhosis?

c) What is the usefulness of different tools to assess the severity of cirrhosis?

4.5.2 Management

d) How should people with cirrhosis be monitored?

e) What are effective management strategies for complications related to cirrhosis?

f) What are the most important criteria for referring people with cirrhosis to tertiary care?

4.6 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and

analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in The guidelines manual.

4.7 Status

4.7.1 Scope

This is the final scope.

4.7.2 Timing

The development of the guideline recommendations will begin in June 2014.

5 Related NICE guidance

5.1 Published guidance

- Subcutaneous implantation of a battery-operated catheter drainage system for managing refractory and recurrent ascites. NICE interventional procedure guidance 479 (2014).
- Hepatitis B and C – ways to promote and offer testing. NICE public health guidance 43 (2013).
- Hepatitis B (chronic). NICE clinical guideline 165 (2013).
- Acute upper gastrointestinal bleeding. NICE clinical guideline 141 (2012).
- SonoVue (sulphur hexafluoride microbubbles) – contrast agent for contrast-enhanced ultrasound imaging of the liver. NICE diagnostics guidance 5 (2012).
- Alcohol dependence and harmful alcohol use. NICE clinical guideline 115 (2011).
- Stent insertion for bleeding oesophageal varices. NICE interventional procedure guidance 392 (2011).
- Alcohol-use disorders: preventing harmful drinking. NICE public health guidance 24 (2010).
- Alcohol-use disorders: physical complications. NICE clinical guideline 100 (2010).

- Extracorporeal albumin dialysis for acute liver failure. NICE interventional procedure guidance 316 (2009).

5.2 Guidance under development

NICE is currently developing the following related guidance (details available from the NICE website):

- Virtual Touch Quantification to diagnose and monitor liver fibrosis. NICE medical technology guidance. Publication expected February 2015.
- Suspected cancer. NICE clinical guideline. Publication expected May 2015.
- Liver disease (non-alcoholic). NICE clinical guideline. Publication date to be confirmed.
- Hepatitis C. NICE clinical guideline. Publication date to be confirmed.
- Rifaximin for the maintenance treatment of hepatic encephalopathy. NICE technology appraisal. Publication date to be confirmed.

6 Further information

Information on the guideline development process is provided in the following documents, available from the NICE website:

- How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS: 5th edition.
- The guidelines manual.

Information on the progress of the guideline will also be available from the NICE website.