

METHODS FOR DETECTING CIRRHOSIS IN PHC AND THE MOST IMPORTANT GUIDELINES

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Abstract

Common causes of chronic liver disease include alcohol, non-alcoholic fatty liver disease and chronic viral hepatitis. Nearly half of patients with cirrhosis are symptoms the discovery of patients with cirrhosis in primary care usually depends on identifying common risk factors. The gold standard test for the diagnosis of cirrhosis remains a liver biopsy Staging of cirrhosis is an important indicator of prognosis and is necessary to guide administration. patients present with signs and symptoms of liver cirrhosis complications such as jaundice, ascites, varicose veins, hepatic encephalopathy or liver cancer or unspecified symptoms of chronic diseases such as fatigue or weight loss may.

Keyword: Cirrhosis, Chronic, Liver, Alcohol, Viral hepatitis

Introduction

Cirrhosis is a condition that arises as a result of chronic liver damage and is usually over many years. It is characterized by fibrosis in the liver. Cirrhosis interferes with the normal functions of the liver, which reduces its ability to produce proteins, which can lead to coagulation, decreased blood spirals and bilirubin triggered. The high incidence of cirrhosis in the UK, this can be attributed primarily to increased levels of alcohol consumption and obesity. Deaths from cirrhosis are also on the rise. Common causes of chronic liver disease include alcohol, non-alcoholic fatty liver disease and chronic viral hepatitis. Nearly half of patients with cirrhosis are symptoms. As a result, the condition can only be detected accidentally as a result of abnormalities in liver function tests or abdominal imaging performed for other reasons. (1)

Instead, patients may present with signs and symptoms of liver cirrhosis complications such as jaundice, ascites, varicose veins bleeding, hepatic encephalopathy or liver cancer. The discovery of patients with cirrhosis in primary care usually depends on identifying common risk factors. Currently, there are no standard standards for investigating patients with suspected cirrhosis. If the patient suspects the presence of cirrhosis, most General Practitioners will

arrange for blood tests and ultrasound of the liver to be performed. The gold standard test for the diagnosis of cirrhosis remains a liver biopsy. Staging of cirrhosis is an important indicator of prognosis and is necessary to guide administration. (1)

Materials and Methods:

A web-based search utilizing the advanced characteristics of different databases like PubMed, Google Scholar, Embase, Scopus, and Cochrane electronic databases was carried out. The MeSH and other keywords like; Cirrhosis, Chronic, Liver, Alcohol, Viral hepatitis and etc., were used to search the databases. The search included the latest studies published, and the search was limited to studies published in English

Discussion:

Cirrhosis is a condition that arises as a result of chronic liver damage, usually over many years. It is characterized by fibrosis in the liver. Cirrhosis interferes with the normal functions of the liver, reducing its ability to produce proteins (reduced synthetic liver function), which in turn can lead to coagulation, low serum albumin and raising bilirubin levels. Chronic liver disease affects 30,000 people in the UK with 7,000 new diagnoses made each year. The incidence is

increasing sharply, between 1992 and 2001, there was a 45 per cent increase in cirrhosis cases in the United Kingdom.¹ This was primarily due to increased levels of alcohol consumption and obesity.² Deaths from cirrhosis are also on the rise; between 1993 and 2000, the British Society reported that the mortality rate from cirrhosis doubled to 12.7 per 100,000 in 2000. In 2010, there were 5,631 deaths from cirrhosis. During this period, deaths from cirrhosis in women also increased sharply (an increase of 46 per cent in Scotland and 44 per cent in England and Wales)³ and the prevalence of cirrhosis is also more common in the most disadvantaged populations in England and Wales. This is believed to be due to the high prevalence of risk factors for cirrhosis in this category (excess alcohol consumption, obesity, and chronic viral hepatitis

. The largest cases of inequality were in the 25-44 age group, with relative risks of 4.73 (95 per cent 0.4-5.59) and 4.24 (95 per cent 0.3:5.0-5.13) for men and women, respectively, when compared with those in the disadvantaged group. Alcohol-related mortality rates in urban areas are higher than in rural areas. (2)

Common causes of chronic liver disease

The causes of chronic liver disease in adults are widespread. Common causes include alcohol, non-alcoholic fatty liver disease and chronic viral hepatitis (B and C). Less common causes include autoimmune liver diseases such as autoimmune hepatitis, primary biliary cirrhosis or primary cleft colloidal infections, genetic conditions such as antitrypsin A-1, Wilson's disease, secondary biliary cirrhosis, pod-cheri syndrome or veno-occlusive disease,

prolonged exposure to certain toxins or medications such as amiodarone, ionocide, methotrexate, and chronic heart failure on the right side. (3)

Presentation

Nearly half of patients with cirrhosis are symptoms . As a result the condition can only be detected by accident as a result of abnormalities in liver function tests or abdominal imaging, performed for other reasons. Alternatively, patients present with signs and symptoms of liver cirrhosis complications such as jaundice, ascites, varicose veins, hepatic encephalopathy or liver cancer or unspecified symptoms of chronic diseases such as fatigue or weight loss may.

The discovery of patients with cirrhosis in primary care usually depends on identifying common risk factors associated with the development of cirrhosis. In the UK, the most common risk factors include over-the-top. Alcohol consumption and obesity.² Worldwide, most cases of cirrhosis occur due to chronic viral hepatitis (B or C). (4)

Liver function tests correlate poorly with the presence of liver fibrosis or cirrhosis

There is a marked geographical variation in the frequency of risk factors for cirrhosis in the UK. The NHS Atlas of The Variation in Healthcare for People with Liver Disease found that the highest rates of hospitalization for terminal hepatitis C disease were in central London and north-west England. Admissions to alcohol-related liver diseases were more common in the Northwest (5)

Table 1: Common non-invasive serum markers of fibrosis

Common non-invasive serum markers of fibrosis				
Serum marker panels of fibrosis	Test components	Conditions in which test has been applied	Sensitivity (> F2)	Specificity (> F2)
Enhanced liver fibrosis (ELF) test ^{39,40}	Hyaluronic acid, N-terminal propeptide of type III collagen, tissue inhibitors of matrix metalloproteinase-1	HCV, HBV ALD, NAFLD PBC	87-90%	27-77%
FIBROSpect II ¹⁴	Hyaluronic acid, tissue inhibitors of matrix metalloproteinase-1, alpha 2-macroglobulin	HCV NAFLD	70-83%	66-79%
FibroTest/FibroSure ⁴¹	γ 2-macroglobulin, γ 2-globulin, γ -globulin, apolipoprotein A1, γ glutamyl transferase, total bilirubin	HCV	75%	85%
Fib-4 ⁴²	$(\text{Age} \times \text{AST}) / ((\text{platelet count}) \times (\text{ALT})^2)$	NAFLD, HCV \pm HIV	70%	97%
Serum hyaluronic acid level, serum AST and albumin level (SHASTA) index ¹⁵	Hyaluronic acid, AST, albumin	HCV HIV+HCV	100%	52%
Aspartate aminotransferase to platelet ratio index (APRI) ⁴³	$(\text{AST elevation} / \text{platelet count}) \times 100$	HCV, HCV+HIV NAFLD	76%	72%
NAFLD fibrosis score ^{44,45}	Age, body mass index, blood glucose levels, aminotransferase levels, platelet count, and albumin	NAFLD	77%	71%
Hepascore ⁴⁶	Age, gender, bilirubin, GGT, hyaluronic acid, γ 2-macroglobulin	HCV ALD	63%	89%
BARD score ⁴⁷	BMI, AST:ALT ratio, type 2 diabetes	NAFLD	85%	67%

Key: HCV = hepatitis C virus; HBV = hepatitis B virus; ALD = alcoholic liver disease; NAFLD = non-alcoholic fatty liver disease; PBC = primary biliary cirrhosis; HIV = human immunodeficiency virus; F2 = fibrosis \pm septal growth of most portal areas on liver biopsy (see table 5, p18)

Assessment

There are currently no standard standards for investigating patients suspected of cirrhosis, and there is considerable variation between different clinical commissioning groups and individual practices.⁸ Primary care guidelines are currently being developed to standardize the investigation of suspected cirrhosis patients and to identify criteria for referral to secondary care.⁹ The guidelines will also attempt to standardize methods used in secondary care to diagnose and assess the severity of cirrhosis and to determine the criteria for referral to third care, for example to assess liver transplantation.⁹ If there is any doubt about the patient's cirrhosis. Liver, most GPs will order blood tests and ultrasound of the liver to be performed. (5)

Table 2: risk factors for the development of hepatocellular carcinoma

Risk factors for the development of hepatocellular carcinoma	
Age	> 60 ⁴⁸
Sex	Male sex ⁴⁸
Chronic viral hepatitis (B and C)	Worldwide approximately half of cases of HCC are attributed to hepatitis B and a third to hepatitis C ⁴⁸ Co-infection with HIV further increases the risk of HCC ⁴⁹
Cirrhosis	One third of cirrhotic patients will develop HCC during their lifetime ⁵⁰
Alcohol	Excessive alcohol consumption is a risk factor for HCC independent of cirrhosis ^{48,51}
Metabolic syndrome	Diabetes, obesity and fatty liver ^{51,52}
Smoking	Smoking ^{51,53}
Haemochromatosis	Up to half of patients with untreated iron overload will develop HCC in their lifetime, although most patients will be non-cirrhotic at diagnosis ⁵⁴
Toxins	Aflatoxin B, ⁵⁵ anabolic steroids ⁵⁶
Genetic predisposition	BRCA1/BRCA2/EGF gene ^{57,58}

Blood tests

Abnormal liver function tests (LFTs) are common to find in primary care. However, it can be elevated for many reasons and is badly associated with the presence of cirrhosis or cirrhosis for example, aspartate aminotransferase (ALT) is only high in 1-4% of patients with cirrhosis.¹⁰ In 2001, a national review was conducted to manage patients with abnormal LFTs (twice the upper limit of the normal reference range) in primary care in the UK 10 10 : (6• 62% and patients were diagnosed with a condition requiring hospitalization or follow-up • 18% of patients were not properly followed up • 11% had the main undetected liver disease which would have benefited from a specialized review. (6)

Ultrasound

Ultrasound is an excellent first-line investigation in patients with suspected liver disease. It can detect more than 90% of gallstones.¹¹ It can also differentiate between solid and cystic lesions within the liver parenchyma. IV contrast (microbubble agents) and/or Doppler can further improve

overall sensitivity. Ultrasound also has high sensitivity (91%) and specificity (94%) to detect cirrhosis. Non-invasive markers of cirrhosis

The gold standard test for the diagnosis of cirrhosis remains a liver biopsy, but this is only available in secondary care and is associated with complications such as bleeding without capsular in up to 1% of cases. Non-invasive serum signs of cirrhosis are currently being investigated as an alternative means of identifying referrals to secondary care. (7)

Ultrasound has a high sensitivity and specificity for the detection of cirrhosis

Currently, if any combination of these preliminary investigations suggests chronic liver disease, referral to secondary care is recommended. Referral should be arranged promptly if the patient displays clinical signs, for example, varicose bleeding, jaundice, significant ascites, hepatic encephalopathy. For patients with a stable disease waiting for a routine appointment, many GPs will begin investigating the cause of liver disease by sending a non-invasive liver examination in addition to the above investigations, as this may be useful for a specific treatment. (7)

Grading the severity of chronic liver disease

The severity of chronic liver disease can be assessed clinically or satisfactorily. Staging of cirrhosis is an important indicator of prognosis and is necessary to guide administration. (8)

Clinical scoring systems

Commonly used grades include a baby bo degree, see table 4, left, or a model of end-stage liver disease (MELD) result.

Biopsy:

Liver biopsy is still investigating the gold standard for diagnosing and evaluating the severity of chronic liver disease. Chronic liver disease is characterized by cirrhosis and the formation of nodules. The severity of chronic liver disease is satisfactorily classified by metavir or isaac staging systems, see table 5, above. Liver biopsy samples less than 1/50,000 of liver parenchyma,¹³ so sampling errors are possible. In addition, liver biopsy is not amused by patients and is relatively expensive, making serial measurements difficult. (9)

Table 3: (Child-Pugh score)

Child-Pugh score			
Score	1	2	3
Bilirubin (mg/dl)	< 2	2-3	>3
Prothrombin time (INR)	< 4s (<1.7)	4-6s (1.7-2.3)	> 6s (>2.3)
Albumin (g/dl)	> 3.5	2.8-3.5	< 2.8
Ascites	Absent	Mild	Severe
Encephalopathy	Absent	Mild	Severe

The Child-Pugh score ranks the severity of cirrhosis into three classes. A score of ≤ 6 defines the patient as class A, 7 to 9 as class B, and ≥ 10 as class C. Class A is associated with a 3-year survival of 73%, Class B 59% and Class C 46%.³⁸

Novel non-invasive markers

Due to the limitations of liver biopsy, there has been a growing interest in developing non-invasive markers to diagnose cirrhosis and assess severity. Most of these tests have been developed in the past decade and are undergoing ongoing verification studies, but have begun to be incorporated into routine diagnostic algorithms and clinical guidelines for the management of chronic liver diseases. (10)

Serum markers:

Non-invasive serum signs of fibrosis are divided into direct and indirect signs. Direct biomarkers such as fibrous vipromesect II, 14SHASTA Index, 15 and GF panell16 include products of extracellular matrix synthesis or degradation, or cytokines and chemokines associated with fibroids for example first and third procollagen types, hyaluronic acid and tissue inhibitors of metalloproteinase. Indirect signs for example APRI, 17 FibroTest/FibroSure, 18 and Hepascore 19 use modifications in liver function markers rather than fibroids such as serum aminotransferase levels, platelet count, INR, GGT, bilirubin, alpha-2-macroglobine, and alpha-2-globulin (hepatolpene).

Many tests within indirect algorithms are routine blood tests and are therefore easier to integrate into daily clinical practice. More complex algorithms are becoming increasingly available through online calculators. When interpreting these tests, it is recognized that they may be falsely elevated due to inflammatory activity outside the liver. Alternatively important fibroids may go undetected if there is minimal hepatitis. Generally, these signs have become increasingly reliable in detecting fibrosis although they are poorly associated with the fibrosis stage. (11)

Transient ultrasound elastography

Transient ultrasound (fibrosis test) measures fibrosis by placing an ultrasound probe on the liver. The pulse generator inside the probe produces the shear wave that spreads through the liver tissue and is detected by pulse wave ultrasound. The speed of the shear wave is measured and is associated with the level of fibrosis. The measurement of > 7 kPa indicates a large fibrosis (Metavir grade F2-F4) $> 11-14$ kPa is consistent with cirrhosis, see Table 5, left. Compared to a standard biopsy, a fibroid will assess a much higher proportion of the liver and therefore be associated with fewer sampling errors. Measurements are painless, rapid and as a result of serial measurement to monitor treatment response such as chronic viral hepatitis, are feasible and acceptable to patients. Although the susceptibility to cloning is generally very good, the difference between the numberer is still present, and its sensitivity is reduced in patients who are obese or with significant ascites. Acoustic Pulse Radiation Force (ARFI) 21 is another ultrasonic-based tool, similar to fibroids that can also be used to measure liver stiffness. (11) [Figure1]

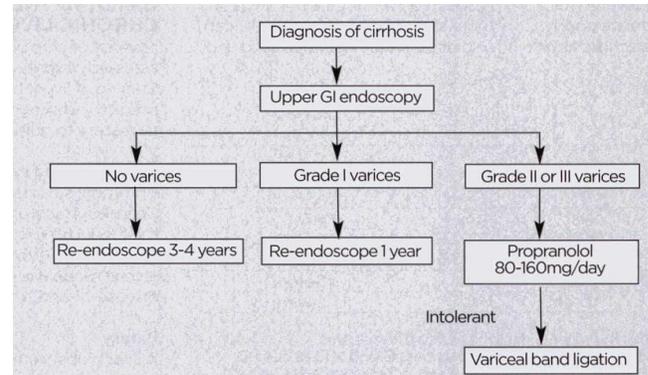


Figure 4:

Causes:

A wide range of diseases and conditions can lead to liver damage and liver cirrhosis.

Some of the reasons include:

Chronic alcohol abuse

- Chronic viral hepatitis (hepatitis B, C and D)
- Accumulation of fat in the liver (non-alcoholic fatty liver disease)
- Accumulation of iron in the body (puppet disease)
- Cystic
- Accumulated copper in the liver (Wilson's disease)
- Non-problem bile ducts
- Alpha-1 antitrypsin deficiency
- Disorders inherited from sugar metabolism
- Genetic disorder (Alagille syndrome)
- Liver diseases caused by the body's immune system (autoimmune hepatitis)
- Destruction of bile ducts (primary biliary cirrhosis)
- Hardening and scarring of bile ducts (major cholangitis)
- Infections, such as syphilis or brucellosis
- Medications, including methotrexate or elysyniazid

Cirrhosis has different causes. In the United States, heavy alcohol consumption and chronic hepatitis C were the most common causes of cirrhosis. Obesity has become a common cause of cirrhosis, either as a single cause or in combination with alcohol, hepatitis C, or both. Many people with cirrhosis have more than one cause of cirrhosis not caused by liver trauma or other acute causes, or short-term, damage. Normally, years of chronic injury are needed to cause cirrhosis.

Alcohol-related liver diseases

Most people who consume alcohol do not suffer from liver damage. But heavy alcohol use over several years can cause chronic liver injury. The amount of alcohol required by liver damage varies greatly from person to person. For women, two to three drinks — including beer and wine — per day, and for men, three to four drinks per day can lead to liver damage and cirrhosis. In the past, alcohol-related cirrhosis has led to more deaths than cirrhosis due to any

other cause. Deaths from obesity-related cirrhosis are on the rise.

Chronic C

Hepatitis C virus is a liver infection that spreads through contact with the blood of the infected person. Chronic hepatitis C causes inflammation and liver damage over time that can lead to cirrhosis

Chronic hepatitis B and D

Hepatitis B virus is a liver infection that is spread through contact with the blood of the infected person, semen, or other body fluids. Hepatitis B, such as hepatitis C, causes hepatitis and injury that can lead to cirrhosis. The hepatitis B vaccine is given to all infants and many adults to prevent the virus. Hepatitis is another virus that affects the liver and can lead to cirrhosis, but it occurs only in people who already suffer from hepatitis B.

Non-alcoholic fatty liver disease (NAFLD)

In NAFLD, fat accumulates in the liver and eventually causes cirrhosis. This common hepatic disease is increasingly associated with obesity, diabetes, protein malnutrition, coronary artery disease and corticosteroid medications..

Autoimmune hepatitis

This type of hepatitis occurs because the body's immune system attacks liver cells and causes inflammation, damage, and eventual cirrhosis. Researchers believe that genetic factors may make some people more susceptible to autoimmunediseases. About 70 percent of people with autoimmune hepatitis are female

Diseases that damage or destroy bile ducts

Many different diseases can damage or destroy the bile ducts of the liver, causing bile to appear back up in the liver and lead to cirrhosis. In adults, the most common condition in this group is primary biliary cirrhosis, a disease in which the bile ducts become inflamed and damaged, and eventually disappear. Secondary biliary cirrhosis can occur if the ducts are accidentally connected or injured during gallbladdersurgery. Major collages is another condition that causes damage and scarring of the bile ducts. In infants, they are usually caused by Alagille syndrome or gallbladder, a condition where the ducts are absent or infected

Inherited diseases

Cystic fibrosis, alpha-1 antitrypsin deficiency, hematology, Wilson'sdisease , galactosemia, and glycogen storage diseases are inherited diseases that interfere with how the liver is produced, processes, and stores enzymes, proteins, minerals, and other substances that the body needs to function properly. Cirrhosis can result from these conditions.

Drugs, toxins and infections

Other causes of cirrhosis include drug interactions, prolonged exposure to toxic chemicals, parasitic infections, and frequent episodes of heart failure with liver congestion

Risk factors

- Drink ing a lot of alcohol. Excessive alcohol consumption is a risk factor for cirrhosis.

- Weightgain. Exposure to ghee increases the risk of diseases that may lead to cirrhosis, such as non-alcoholic fatty liver disease and non-alcoholic fatty liver disease.

- The presence of viralhepatitis. Not everyone with chronic hepatitis will develop cirrhosis, but it is one of the leading causes of liver disease in the world.

Complications (12)

Complications of cirrhosis can include:

- High blood pressure in the veins that supply the liver (high blood pressure portal). Cirrhosis slows the normal flow of blood through the liver, thereby increasing the pressure in the vein that brings blood to the liver from the intestines and spleen.

- Cellular liver cancer

Table 4 (risk factors to develop Hepatocellular carcinoma)

Risk factors for the development of hepatocellular carcinoma	
Age	> 60 ⁴⁸
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Toxins	Aflatoxin B, ⁵⁵ anabolic steroids ⁵⁶
Genetic predisposition	BRCA1/BRCA2/EGF gene ^{57,58}

- Swelling of the legs andabdomen. Increased pressure in the enterocaral vein can cause fluid buildup in the legs (edema) and abdomen (ascites). Edema and ascites may also be caused by the liver's inability to make enough blood proteins, such as synovial.

- Expansion of the spleen (splenomegaly). High entrance hypertension can also cause changes in spleen swelling, trapping white blood cells and platelets. Low white blood cells and platelets in the blood can be the first sign of cirrhosis.

- The bleeding. High blood pressure input can cause blood to be redirected to smallveins. These small veins may be strained by additional pressure, causing seriousbleeding. Enteroidal hypertension may cause enlarged veins (varicose veins) in the esophagus (varicose esophagus) or stomach (varicose veins) and lead to life-threateningbleeding. If the liver can't make enough clotting factors, it can also contribute to continued bleeding..

- Infections. If you have cirrhosis,your body may have difficulty fightinginfection. Ascites can lead to bacterial peritonitis, a serious infection.

- Poornutrition. Cirrhosis may make it difficult for the body to process nutrients, leading to weakness and weight loss.
- Accumulation of toxins in the brain (hepatic encephalopathy). The damaged liver of cirrhosis is unable to detoxify the blood as well as the healthy liver. These toxins can then accumulate in the brain and cause mental confusion and difficulty concentrating. Over time, hepatic encephalopathy can develop into a lack of response or coma.
- Jaundice. Jaundice occurs when the liver does not remove the caffeine bilirubin, a blood waste product, from the blood. Jaundice causes yellowing of the skin, eyes and urine sheaths.
- Bone disease. Some people with cirrhosis lose bone strength and are more likely to have fractures.
- Increased risk of liver cancer. A large percentage of people who develop liver cancer have pre-existing cirrhosis.
- Severe cirrhosis on chronic. Some people end up experiencing multiorgan failure. Researchers now believe that this is a obvious complication in some people with cirrhosis, but they do not fully understand its causes.

Prevention

Reduce your risk of cirrhosis by taking these steps to take care of the liver:

- Do not drink alcohol if you have cirrhosis. If you have liver disease, you should avoid alcohol.
- A healthy diet. Choose a vegetarian diet full of fruits and vegetables. Identify whole grains and lean sources of protein. Reduce the amount of fatty and fried foods you eat.
- Maintaining a healthy weight. An excessive amount of body fat can damage the liver. Talk to your doctor about a weight loss plan if you are obese or overweight.
- Reduce your risk of hepatitis. Sharing needles and having unprotected sex can increase your risk of hepatitis B and C. Ask your doctor about hepatitis vaccines.
- If you're worried about the risk of cirrhosis, talk to your doctor about ways you can reduce your risk. (13)

Conclusion:

There are currently no standard standards for investigating patients suspected of cirrhosis, and there is considerable variation between different clinical commissioning groups and individual practices. Primary care guidelines are currently being developed to standardize the investigation of suspected cirrhosis patients and to identify criteria for referral to secondary care. The guidelines will also attempt to standardize methods used in secondary care to diagnose and assess the severity of cirrhosis and to determine the criteria for referral to third care, for example to assess liver transplantation.

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