Cystic Fibrosis our focus

Cystic fibrosis-related liver disease

Factsheet – April 2017

Fighting for a Life Unlimited

Cystic fibrosis-related liver disease

Cystic fibrosis-related liver disease

Introduction

Around 40% of people with cystic fibrosis (CF) will have some liver abnormalities, although only around 5–10% of the CF population will experience problems with their health as a result. In recent years an increase in prevalence of cystic fibrosis-related liver disease (CFLD) has been noted and is most likely related to CF patients being screened for liver disease from a young age.

This factsheet provides general information about CF related liver disease; it is not intended to replace any advice you may receive from your specialist CF centre or clinic.

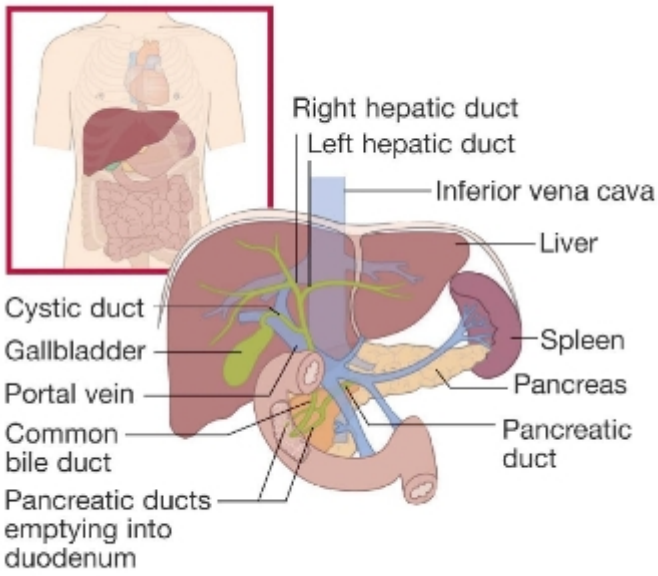
Originally written by Dr David Honeybourne, Consultant Physician, Birmingham Heartlands Hospital and Dr Marianne Samyn, Consultant in Paediatric Hepatology, Kings College Hospital, London. February 2011

Reviewed by Dr Marianne Samyn in January 2017

Contents

Structure and function of a healthy liver

The liver is located in the upper part of the abdomen, just under the right-hand side of the diaphragm muscle under the ribs.



The liver has many functions, including:

- processing digested food from the intestine
- controlling levels of fats, amino acids and glucose in the blood
- combating infections
- clearing the blood of particles and infections, including bacteria
- neutralising and destroying all drugs and toxins
- manufacturing bile
- storing iron, vitamins and other essential chemicals
- breaking down food and turning it into energy
- manufacturing, breaking down and regulating numerous hormones including sex hormones
- making enzymes and proteins which are responsible for most chemical reactions in the body, for example those involved in blood clotting and repair of damaged tissues.

How CF affects the liver

Liver disease in people with CF can be related to problems with the drainage of bile out of the liver via the bile ducts and gallbladder or also to scarring in the liver known as fibrosis and cirrhosis.

Bile ducts and gallbladder

Cystic fibrosis causes problems with the normal secretion and function of bile due to cells being unable to transfer chloride effectively. This means the bile can become sticky, causing irritation and inflammation in the ducts and potentially obstructing bile ducts by formation of gallstones.

Fibrosis and cirrhosis

Scarring, or fibrosis, can develop in the livers of people with cystic fibrosis. In severe cases, this can lead to cirrhosis which is a more severe form of scarring that is irreversible and can affect the normal functioning of the liver. Liver tissue becomes hard when it is scarred and this causes increased pressure in one of the blood vessels flowing into the liver (portal vein) leading to the development of enlarged blood vessels (varices) surrounding the digestive system as well as enlargement of the spleen. This is known as portal hypertension.

Scarring can also be caused by fatty changes in the liver, also known as steatosis. It is not known why this happens, but fat can irritate the liver and cause scarring.

Clinical signs and symptoms of CF-related liver disease

The majority of patients with CF-related liver disease will experience no or mild symptoms and signs related to their liver disease. As children are screened from a young age, a diagnosis of CF-related liver disease can be based on some changes on the liver ultrasound scan or mildly abnormal liver blood test results in the absence of any signs or symptoms. For patients with more advanced liver disease the following signs and symptoms can be noted:

Hepatomegaly

Means the liver is enlarged. It is not uncommon for patients with CF to have an enlarged liver. If this is in the context of advanced liver disease and cirrhosis, you may notice swelling in the upper-right side of the abdomen.

Splenomegaly

Means the spleen is enlarged, and develops when there is scarring in the liver. Associated symptoms include heaviness and swelling in the upper-left side of the abdomen, extending across the abdomen in severe cases.

Jaundice

Refers to the yellow discolouration of the skin and whites of the eyes that occurs when bile can’t clear from the liver and is instead excreted through the skin and urine. Associated symptoms can be itching, pale stools and dark coloured urine and difficulty in digesting food. In more advanced liver disease the jaundice reflects poor liver function. Jaundice is also common when a patient develops gallstones, which can obstruct the bile flow out of the liver. Alternatively jaundice can be noted after developing a drug reaction, including to some types of antibiotics, however this is rare.

Bleeding (bruising, nosebleeds and visible veins on the abdominal wall)

With scarring in the liver and portal hypertension present, blood flow is redirected away from the liver, to smaller blood vessels which are more fragile and more likely to cause bleeding. Also low platelet count in the context of splenomegaly and impaired production of clotting factors by the liver will make patients with portal hypertension and severe liver disease more prone to bleeding. Apart from more superficial bleeding with bruising and nose bleeds, patients with portal hypertension can develop varices mainly in their intestine which can bleed and present by either vomiting blood or passing blood through the back passage.

Poor growth and muscle wasting

As the liver is involved in processing nutrients, liver disease can cause poor growth and muscle wasting mainly relating to the malabsorption of fat and vitamins. This can make patients more susceptible to infections including chest infections and can also cause tiredness.

Ascites

In advanced liver disease the reserve function of the liver starts to fail, leading to low albumin (a protein) levels in the blood and accumulation of excessive fluid in the abdomen.

Diagnosis

Tests carried out in a CF clinic can look at the structure and appearance of the liver, or the function of the liver.

Ultrasound scan

The structure of the liver is usually assessed by an ultrasound (echo) liver scan, which involves moving a probe gently across the skin over the liver. This is entirely painless and only takes around ten minutes to complete. The size of the liver and spleen are assessed together to see if there is any enlargement of the bile ducts or evidence of gallstones. A new type of scan called a fibroscan measures the amount of fibrous tissue, including scar tissue, in the liver.

MRI scan

If stones are present in the bile ducts or gallbladder during an ultrasound scan, a more detailed MRI scan may be required to look at the bile duct system. It does not require any radiation but you must lie very still during the tests and young children sometimes need to be sedated for this to be possible.

Blood tests

The function of the liver can be assessed using blood tests such as blood bilirubin levels, liver enzymes, clotting tests and vitamin levels.

Liver biopsy

If there is doubt about the diagnosis of CF-related liver disease or to exclude other types of liver disease a biopsy may be required. This is very rare. The skin over the surface of the liver is numbed with an anaesthetic and a needle briefly inserted into the liver to obtain a small sample, which is sent off for microscopic analysis. In children this will be carried out under sedation or a general anaesthetic.

Nutrition and body-mass assessment

Malnutrition is a common problem in people with CF-related liver disease and maximising nutritional status is important. Many people with advanced liver disease require nutritional support, such as tube feeding. An overall assessment of nutrition is important and muscle mass may be measured as bodyweight may not give an accurate assessment of nutritional status. Skinfold measurement in the upper arms or handgrip strength can be used as indicators of muscle strength, and DEXA scans that assess bone density can give a guide to muscle mass. As liver disease can also aggravate fat malabsorption it is important to regularly review pancreatic enzyme (Creon) dosing to ensure optimal absorption.

Endoscopy

If the blood pressure in the portal vein is raised and the spleen is enlarged it is important to check for enlarged blood vessels (varices) in the gut. Depending on the individual, this may require an annual endoscopy, where an endoscope (a long, thin tube with a light and camera at one end) is used to look down the oesophagus and into the stomach to check for varices. If found, these can be treated to prevent blood from leaking out of them by looping and tying tiny bands around the blood vessels during the endoscopy. Alternatively, the vessels may be injected with a chemical that causes them to shrivel and reduces the risk of bleeding. In children, endoscopies are carried out under general anaesthetic.

Patients presenting with acute bleeding from varices, will require admission to hospital as an emergency for stabilisation and will require an urgent endoscopy to investigate the source of bleeding and treat accordingly.

Monitoring

Most children with cystic fibrosis will have their liver function checked through blood tests at their annual review, and sometimes a baseline ultrasound scan will also be used.

Many adult specialist CF centres now use a joint CF/liver clinic to monitor their patients. A liver physician (hepatologist) and CF physician will both see people with CF who are suspected of having significant liver problems.

Treatment

URSO

Ursodeoxycholic acid (also known as URSO or UDCA) has been used to treat people with significant CF-related liver disease for years. It occurs naturally in small amounts in bile and can alter the composition of bile, making it more soluble so that it can flow through the liver more easily. Some studies have shown that the drug causes an improvement in symptoms and liver blood tests. While long-term benefit is uncertain, clinicians agree that it is worth trying in patients with significant CF-related liver disease.

In the UK, URSO tablets come in three strengths: 150mg, 250mg and 300mg. For smaller children it is also available as a liquid preparation. The drug is usually well-tolerated and can be used by children and adults, but in rare cases may cause itching of the skin, rashes, nausea, vomiting or diarrhoea.

Vitamin K

Bleeding problems may be due to a reduction in adequate amounts of clotting factors being made by the liver and this may be helped in some cases by taking Vitamin K tablets daily.

In liver disease some vitamins are not appropriately absorbed from the food and therefore need to be supplemented. Most people with CF already take vitamin supplements. In CF-related liver disease Vitamin K is added.

Endoscopy/surgery

In case of bleeding from the intestine, patients with portal hypertension and advanced liver disease, regular endoscopy with banding and/or sclerotherapy may be considered. If bleeding from varices persists after these treatment, older children and adults can be considered for TIPSS, a radiological procedure where a connection between the portal vein and the larger veins that drain blood to the heart is made, reducing pressure in the portal vein.

The raised blood pressure in the portal vein may also be helped by a variety of drugs, including propanalol, which is a blood-pressure lowering medicine.

Liver transplants

If liver disease progresses to such an extent that complications such as liver failure develop, liver transplantation is considered. As CF-related liver problems are usually apparent by late childhood, some liver transplants may be required in children still under the care of a paediatric team.

The outlook after liver transplantation is good, although the optimum timing for transplantation can be difficult to decide. A multidisciplinary approach between the CF and liver unit teams is used to advise the patient. Liver transplantation restores the liver function, but also requires lifelong immunosuppressive medication to prevent the organ being rejected.

Conclusion

The outlook for most people with cystic fibrosis who experience liver problems is generally very good. Most will show little or no deterioration over time, and often a clinic review once a year with a scan and blood tests is all that's required. Complications can be managed with careful monitoring and treatment, although a small minority do deteriorate and require transplantation.

Additional reading

For more information about the liver, please visit the British Liver Trust webpage at www.britishlivertrust.org.uk.

The Child Liver Disease Foundation have developed a leaflet specifically for families affected by CF-related liver disease, please visit www.childliverdisease.org.

Please note that permission to reproduce the liver image and text on page 3 is not granted outside of this factsheet.

Further information

The Cystic Fibrosis Trust provides information about cystic fibrosis through our factsheets, leaflets and other publications.

Most of our publications are available through our helpline and can be downloaded from our website. Visit cysticfibrosis.org.uk/publications.

The Cystic Fibrosis Trust helpline can help you with a range of issues, no matter how big or small. Our trained staff can provide a listening ear, practical advice, welfare/benefits information or direct you to other sources of support. The helpline can be contacted on 0300 373 1000 or helpline@cysticfibrosis.org.uk and is open Monday to Friday, 9am – 5pm.

Calls to 0300 numbers cost no more than 5p per minute from a standard BT residential landline. Charges from other landlines and mobile networks may vary, but will be no more than a standard geographic call and are included in all inclusive minutes and discount schemes. If you are worried about the cost of the call please let us know and we'll call you back.

You can also find more information at our website cysticfibrosis.org.uk.

Cystic Fibrosis Trust
2nd Floor One Aldgate
London
EC3N 1RE
020 3795 1555

cysticfibrosis.org.uk

More factsheets available at:
cysticfibrosis.org.uk/publications

Cystic Fibrosis Trust

cysticfibrosis.org.uk