



Non-Alcoholic Fatty Liver Disease

The Liver

The liver is the largest solid internal organ. It is located underneath the ribcage in the right upper part of the abdomen. Although liver size depends on a person's age, body size, shape, gender, and disease state, in most adults, it is about the size of a football. The liver has many important functions. It acts as a filter for the blood. It metabolizes nutrients and other substances such as medications. It stores energy. It synthesizes proteins that are essential for our body to function, including those that help the blood to clot when we bleed. Although the liver is a very resilient organ that has the ability to repair itself, it is susceptible to damage from many different sources, including viruses, toxins, inherited conditions, and even our body's own immune system.

Non-Alcoholic Fatty Liver Disease

Non-alcoholic fatty liver disease (NAFLD) is a condition in which fat accumulates in the cells of the liver (hepatocytes). It affects more than 20-30% of adults in North America and is becoming increasingly common. Many people with this condition have no symptoms and medical professionals diagnose them as a part of an investigation into the cause of other abnormal lab tests or after they have had imaging of their abdomen for unrelated reasons. Over many years, excessive fat in the liver may result in significant damage. To help those with the condition, healthcare professionals must identify those at risk and counsel them on ways to address this disease before significant liver damage occurs. NAFLD is a treatable condition that individuals can often address with lifestyle modifications.

Development of Fatty Liver

NAFLD is not a transmissible condition (i.e., it does not spread from person to person). Rather, it is a condition that

occurs most often in individuals who have one or more of the following risk factors for developing the disease:

- obesity
- diabetes or pre-diabetes
- high cholesterol
- high blood pressure
- sedentary lifestyle
- the use of certain medications

The medical community does not yet know exactly why NAFLD affects some people with the above conditions and not others. It is also not completely understood why, for some people, fat will accumulate in the liver but not cause significant damage (benign steatosis), whereas in others, it results in significant damage (non-alcoholic steatohepatitis).

As the prevalence is very high in Canada, if you have one or more risk factors for the disease, it may be reasonable to discuss with your healthcare provider whether you are a candidate for further testing. However, at this time, there are no firm accepted guidelines as to who needs further investigation for this condition, other than those who have unexplained liver enzyme abnormalities.

Symptoms

Many individuals with NAFLD do not have any symptoms but, for those who do, symptoms are generally nonspecific, such as mild fatigue or discomfort in the abdomen. Over many years, the presence of fat might trigger inflammation in the liver, which may lead to formation of scar tissue. If very advanced, the amount of scar tissue in the liver may reach a level termed cirrhosis, which refers to a specific pattern and degree of scar tissue in the liver. For patients with cirrhosis, ongoing damage to the liver can eventually result in signs and symptoms, such as worsening fatigue, fluid accumulation in the abdomen (ascites),

bleeding from veins in the esophagus or stomach (varices), and confusion (encephalopathy). The goal in identifying NAFLD is to ensure appropriate monitoring, to offer guidance on how to treat the condition, and to decrease the chances of complications.

Diagnosis

Liver biopsy, which involves the use of a needle to take a sample of liver tissue so that it may be examined under the microscope, is the gold standard for diagnosing non-alcoholic fatty liver disease. While it is currently the only way to confirm the diagnosis, in practice, a combination of blood tests and imaging is usually sufficient for a physician to establish the diagnosis in many patients.

Investigations

When a person is newly diagnosed with non-alcoholic fatty liver disease, it is important that he or she sees a healthcare provider with specialized knowledge in that area. This may be a nurse, family doctor, or specialist (hepatologist or gastroenterologist), who will conduct initial investigations to ensure that the diagnosis is certain and to rule out other liver diseases that may co-exist. Most of this information can be obtained through physical examination, blood tests, and imaging of the abdomen.

The role of a liver biopsy in the diagnosis of NAFLD remains important in certain circumstances, in particular when the diagnosis is in question. In addition, a biopsy can also determine how much, if any, scar tissue is present in the liver. Staging is the process of determining the amount of scar tissue (fibrosis) in the liver and, in the past, a liver biopsy was the only tool used. A normal liver with no scar tissue present is stage 0. A combination of increasing amounts of scar tissue in the liver and a change in its pattern increases the classification to a higher stage. Stage 1 is minimal scar tissue and stage 4 is cirrhosis. Although a biopsy is a safe procedure, it is an invasive one, and accordingly carries some risks, including bleeding and post-procedure pain. One of the drawbacks of this procedure, other than its invasive nature, is the fact that it samples only a very small portion of a large organ, which means it is susceptible to sampling error.

Non-invasive Tools to Measure Fibrosis

A liver biopsy remains the gold standard for the staging of liver disease and it is still a good option for many patients. However, healthcare providers are increasingly using other effective tools to determine the degree of fibrosis in the liver. Of the emerging alternative staging methods, the following are the most commonly used in Canada.

FibroScan® is a non-invasive tool used to assess the degree of fibrosis in the liver. It is a technique used to measure liver stiffness, which is closely related to the degree of fibrosis in the liver. The scan involves the painless placement of a probe on the surface of the skin, and takes only a few minutes to complete. The area sampled is approximately 100 times greater than the area seen with a typical liver biopsy. This procedure results in a reliable reading for most people. FibroScan® is available at a number of centres across Canada.

FibroTest and APRI (AST-to-Platelet Ratio Index) are non-invasive tools that rely on calculations based on blood tests to measure the degree of fibrosis in the liver. FibroTest is likely not covered by medical plans and therefore will have associated out-of-pocket expenses. APRI is derived from a calculation using a simple equation based on common blood tests.

Regardless of the tool used to estimate fibrosis, expert interpretation is essential in ensuring the information gained is useful in making treatment decisions. In addition, a liver biopsy may still provide valuable information regarding disease activity that non-invasive tools cannot. Your healthcare provider will be able to determine which tests are best suited to your situation.

Management

Not everyone who has non-alcoholic fatty liver disease is at risk of developing progressive liver disease. However, because the management of this condition focuses on a healthy lifestyle, the chances of developing cardiovascular disease may also decrease.

Alcohol

Significant alcohol consumption is a known risk factor for accumulating fat in the liver. Most consider significant alcohol consumption to be more than 2 drinks a day. In someone with established NAFLD, limiting intake to no more than 1-2 drinks per day (one drink is 5 oz/148 mL of wine, 1.5 oz/44 mL of spirits, or 12 oz/355 mL of beer) and not consuming alcohol every day is a reasonable goal. In fact, complete abstinence from alcohol may be preferable.

Other Medical Conditions

As mentioned, other medical conditions, such as high cholesterol, diabetes, and high blood pressure, increase an individual's risk of developing NAFLD, and may worsen its severity if already present. Thus, optimal control of these risk factors is central to managing this disease. In general, the medications typically used to treat these risk factors are also safe in people with liver disease, and patients should discuss this further with their healthcare providers.

Medications

Researchers have studied many medications, vitamins, and supplements for their potential beneficial effects in the management of NAFLD. Unfortunately, to date, none of them have found evidence to justify their universal and widespread use for individuals with this condition. Some practitioners continue to use vitamin E and pioglitazone (Actos®; a medication used to treat diabetes), in certain situations, but there are limitations with respect to both efficacy and safety that patients should discuss in detail with their healthcare providers before pursuing treatment with these agents.

Dietary and Lifestyle Modifications

While research is ongoing to identify medications suitable for widespread use in the management of NAFLD, multiple well-designed trials have demonstrated lifestyle changes (exercise and dietary) that result in weight loss to be an effective way to manage this disease.

Individuals who are able to achieve a weight loss of between 3-10% of their total body weight by increasing activity levels and improving diet also achieve improvement in liver enzymes, reduced amounts of fat in their liver, and reduced inflammation in the liver.

The current *Canadian Physical Activity Guidelines* advise that all adults 18-64 years old should accumulate at least 150 minutes of moderate- to vigorous-intensity aerobic activity a week, in bouts of 10 minutes or more, to achieve health benefits. This is also a reasonable goal for people with non-alcoholic fatty liver disease who are not already exercising at this level. Beneficial dietary changes include limiting intake of high fat and high sugar foods, limiting portion size, and eating regular balanced meals by following *Canada's Food Guide*. Your healthcare provider can give you further advice on optimizing your exercise regimen and diet. Following the advice of a personal trainer and/or dietitian may also help you reach your goals.

Non-Alcoholic Steatohepatitis

While NAFLD is mostly benign, left unaddressed it can develop into a much more harmful disease-state called non-alcoholic steatohepatitis (NASH), which involves inflammation of the liver. NASH affects approximately 20% of those with NAFLD. It occurs when scar tissue (fibrosis) is visible in the liver. Fibrosis can develop into advanced scarring (cirrhosis) or liver cancer. About 20% of those diagnosed with NASH develop cirrhosis, which is a serious problem that can lead to many complications. In 2008 and 2009, 12% of British patients waiting for a liver transplant had cirrhosis caused by NASH. It can even be deadly: a recent study found that 11% of patients

with non-alcoholic steatohepatitis are at risk of death from liver-related illness. Fortunately, medications are on the near horizon to treat this condition.

Outlook

The future of non-alcoholic fatty liver disease lies in the education of healthcare providers and the public so that practitioners can identify and care for those with this condition. If left untreated, non-alcoholic fatty liver disease can lead to NASH, a more serious condition. We hope that research into new therapeutic options and an ongoing interest in learning more about this condition will, over the coming years, result in the following:

- an improved understanding of the pathophysiology of this condition,
- safe and effective medications for widespread use, and
- improved tools to diagnose and monitor this condition.

