



Metabolic Dysfunction-Associated Steatotic Liver Disease

(Formerly Non-Alcoholic Fatty Liver Disease)

For some time, experts have been concerned with the language used in the name “non-alcoholic fatty liver disease”. The term was outdated, referring to what the disease isn’t associated with (alcohol) rather than what it is associated with (metabolic dysfunction, insulin resistance). In addition, they found the terms “alcoholic” and “fatty” to be stigmatising.

Recently, a panel of 236 liver disease experts, including researchers, healthcare experts, and patient advocates, from 56 countries participated in four online surveys and two meetings to determine a more appropriate name for this condition. They settled on metabolic dysfunction-associated steatotic liver disease (MASLD) and also changed the name of the associated condition non-alcoholic steatohepatitis (NASH) to metabolic dysfunction-associated steatohepatitis (MASH). The emphasis on metabolic dysfunction is important, as many people previously diagnosed with NAFLD had other underlying metabolic conditions. Because of this, they also proposed that those diagnosed with MASLD should have at least one of the following conditions in addition to liver disease: type 2 diabetes, overweight or obesity, or some other type of evidence of metabolic dysregulation.

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, sex, 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 can repair itself, it is susceptible to damage from many different sources, including viruses, toxins, inherited conditions, and even the body’s own immune system.

Metabolic Dysfunction-Associated Steatotic Liver Disease

MASLD is a condition in which fat accumulates in the cells of the liver (hepatocytes) in an individual who has metabolic disease (e.g., type 2 diabetes or obesity) and who does not drink an excessive amount of alcohol. 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 guide them on ways to address this disease before significant liver damage occurs. MASLD is a treatable condition that individuals can often address with lifestyle modifications.

Development of MASLD

MASLD 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:

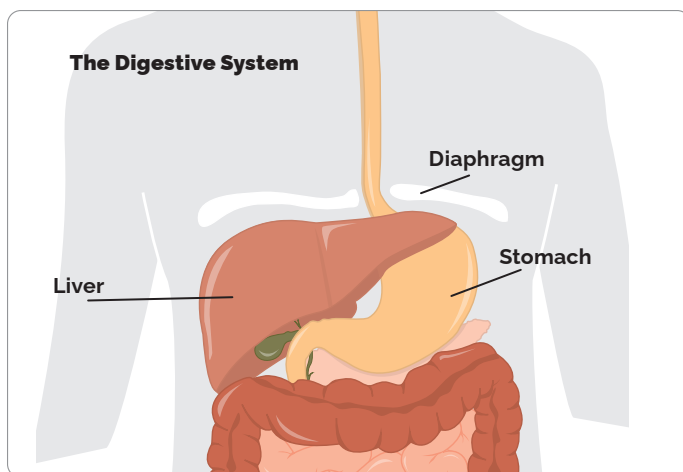
- obesity
- diabetes or pre-diabetes
- high cholesterol
- high blood pressure
- sedentary lifestyle
- the use of certain medications

The medical community does not yet know exactly why MASLD 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 (metabolic dysfunction-associated steatohepatitis, or MASH).

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 accepted guidelines as to who needs further investigation for this condition, other than those who have unexplained liver enzyme abnormalities.

Symptoms

Many individuals with MASLD 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 MASLD 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 metabolic dysfunction-associated steatotic 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 people are newly diagnosed with metabolic dysfunction-associated steatotic liver disease, it is important that they see 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 MASLD remains important in certain circumstances, especially 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, which 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 many 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 typically 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.

No matter which tool is 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 metabolic dysfunction-associated steatotic 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 MASLD, 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 a

person's risk of developing MASLD, 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 MASLD. 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, 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. Early research is demonstrating that some weight-loss drugs could help improve MASLD.

Dietary and Lifestyle Modifications

While research is ongoing to identify medications suitable for widespread use in the management of MASLD, 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 manage 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 get at least 150 minutes of moderate- to vigorous-intensity aerobic activity a week, in bouts of 10 minutes or more, to achieve health benefits. Some activities that meet these criteria include brisk walking, jogging, cycling, and dancing. This is also a reasonable goal for people living with metabolic dysfunction-associated steatotic 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 registered dietitian may also help you reach your goals.

Metabolic Dysfunction-Associated Steatohepatitis

While MASLD is mostly benign, left unaddressed it can develop into a much more harmful disease-state called metabolic dysfunction-associated steatohepatitis (MASH), which involves inflammation of the liver. MASH affects approximately 20% of those with MASLD. 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 MASH develop cirrhosis, which is a serious problem that can lead to many complications. It can even be deadly: a recent study found that 11% of patients with metabolic dysfunction-associated steatohepatitis are at risk of death from liver-related illness. Fortunately, medications are on the horizon to treat this condition.

Outlook

The future of metabolic dysfunction-associated steatotic 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, MASLD can lead to MASH, 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.

About the Gastrointestinal Society

The GI (Gastrointestinal) Society is a registered Canadian charity committed to improving the lives of people with gastrointestinal and liver conditions, supporting research, advocating for appropriate patient access to healthcare, and promoting gastrointestinal and liver health.

Want to learn more on this subject? The *Inside Tract*®, the GI Society's quarterly newsletter, provides the latest on digestive and liver research, disease and disorder treatments (e.g., medications, nutrition), and a whole lot more. If you have any kind of digestive problem, then you will want this timely, informative publication. **Subscribe today!**

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Gastrointestinal Society

231-3665 Kingsway
Vancouver, BC V5R 5W2

Phone: 604-873-4876

Toll-free: 1-866-600-4875

Fax: 1-855-875-4429

Email: info@badgut.org

Website: www.badgut.org

Charitable Registration Number: 817065352RR0001

