CHRONIC DISEASE MANAGEMENT 2024
https://doi.org/10.33591/sfp.50.2.u5

Unit No. 5

ASSESSMENT AND MANAGEMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE

Dr Wai Chun Tao Desmond

ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) has become the most common chronic liver disease in the world. Overall improvement in public health, active screening of blood products, and universal vaccination against hepatitis B have led to a drop in incidence of hepatitis B and C worldwide. NAFLD is strongly associated with metabolic syndrome. With an increase in overweight status and obesity worldwide, it is not surprising that NAFLD is on the rise. Diagnosis of NAFLD requires confirmation of fatty infiltration in liver, as well as liver damage such as elevated liver enzymes and the presence of fibrosis. Currently, the best treatment for NAFLD is weight loss, and the proven method would be dieting with regular exercises. Vitamin E and pioglitazoles are promising medications for treating NAFLD, but each has their shortcomings. Until more studies are conducted, lifestyle modification remains the only reliable way to treat NAFLD. Family physicians also ought to look out for cardiovascular diseases, as well as be vigilant in cancer screening, as NAFLD is associated with higher risks of ischemic heart disease and cancer.

Keywords: Fatty Liver, metabolic syndrome, diabetes mellitus, cirrhosis

SFP2024; 50(2): 28-30

TERMINOLOGY

WHAT IS NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)?

There must be evidence of fat in liver of ≥5 percent, usually confirmed by imaging studies, with no secondary causes such as significant alcohol consumption, medications, or genetic disorders.

NAFLD comprises of a spectrum of diseases, depending on the degree of inflammation, and extent of liver fibrosis.

DR WAI CHUN TAO DESMOND
Gastroenterologist
Desmond Wai Liver and Gastroenterology Diseases Centre
Mount Elizabeth Novena Specialist Centre

NAFLD can be categorised histologically into:

1. Non-alcoholic fatty liver (NAFL), which refers to presence of fat in liver without significant inflammation or fibrosis. Risk of progression to cirrhosis or liver failure is minimum.
2. Non-alcoholic steatohepatitis (NASH), which refers to presence of fat with inflammation. NASH can progress to cirrhosis.
3. NASH cirrhosis, which refers to cirrhosis with current or previous histological of steatosis or steatohepatitis.

HOW PREVALENT IS NAFLD?

No population study has been done in Singapore. But judging from some cohort studies, NAFLD is common locally. One local study showed that NAFLD is present in 56 percent of patients undergoing cholecystectomy. Another local study showed that among attendees to a public health forum, 40 percent had ultrasonic evidence of NAFLD. Note that these studies are biased and could have overestimated the prevalence of NAFLD in Singapore.

Population studies in Asia like Hong Kong, China, and Bangladesh, showed NAFLD to be present in about 25-40 percent of the general population. Fortunately, less than 5 percent of NAFLD patients have significant fibrosis. Hence, we can postulate that NAFLD is prevalent in 25-40 percent of the Singapore population, with the majority (about 95 percent) without significant fibrosis.

NAFLD is particularly common in patients with metabolic syndrome. NAFLD is present in more than 95 percent of obese patients undergoing bariatric surgery. Two-thirds of diabetics and half of the patients with dyslipidemia have NAFLD.

WHAT IS THE NATURAL HISTORY OF NAFLD?

Generally speaking, patients with NAFL alone have a very low risk of progression to liver cirrhosis. However, patients with steatohepatitis, especially those with fibrosis, may progress to cirrhosis or even liver cancer. The progression is believed to take more than a decade, with weight gain being an important predictor of progression.

Interestingly, longitudinal follow-up studies have showed that cancer and cardiovascular diseases are the top two causes of death in patients with NAFLD. Liver complications such as hepatocellular carcinoma, liver cirrhosis, and liver failure are only ranked as the third most common cause of death for patients with NAFLD.

Possible explanations include overweight status and metabolic syndrome, which are risk factors for certain cancers, such as pancreatic, breast, and colon cancer. Additionally, patients with NAFLD would have concurrent metabolic syndrome, which in itself is a risk factor for cardiovascular disease.

HOW DO I CONFIRM THE DIAGNOSIS OF NAFLD?

First, there must be documentation of fat in liver, which is usually diagnosed via ultrasound scan. Most of my patients with NAFLD have their disease diagnosed via routine screening. Fatty liver is rarely diagnosed on CT or even laparoscopy when patients undergo abdominal or pelvic surgeries.

Second, there may be liver inflammation, thus their liver profile may show elevated GGT or ALT.

Third, alternative causes of liver injuries, such as viral hepatitis B or alcohol, should be excluded. The safe limit of alcohol has been of much debate. The consensus is that the safe limit of alcohol consumption for a man is 21 units a week, and 14 units for a woman. One unit of alcohol is approximately one can of beer, one glass of wine, or one shot of hard liquor.

Fourth, NAFLD is almost always associated with metabolic syndrome, thus clinicians ought to look out for overweight status, hypertension, dyslipidemia, diabetes, or pre-diabetes. On the other hand, in patients without any evidence of metabolic syndrome or significant alcohol consumption, a diagnosis of NAFLD is unlikely.

HOW CAN I STAGE SEVERITY OF NAFLD?

NAFLD progresses into the following stages: pure fat, steatohepatitis, fibrosis, then cirrhosis.

The ideal method to stage the disease is percutenaous liver biopsy, which could identify the degree of inflammation and stage of fibrosis. However, as biopsy is associated with a small risk of complications (about 1 percent) such as hemoperitoneum, patients rarely agree to it.

While transaminases such as ALT and GGT may reflect degree of liver inflammation, they can only act as a guide as they do not correlate accurately with inflammation in liver histology.

Several non-invasive methods of assessment for NAFLD are available commercially.

Hepatic steatosis can be accurately quantified by MR imaging. MR Elastography can also identify the amount of liver fibrosis, as well as identifying any focal liver lesions, but its limited availability and high cost make it difficult for general use in primary care.

Several panels utilise laboratory and clinical markers, such as platelets, albumin, BMI, age, ALT, etc to insert into a particular formula to estimate the risk of liver fibrosis. Some of these are available for use in Singapore.

Fibroscan®, which measures liver stiffness, is also available locally to estimate the amount of liver fibrosis. Fibroscan® is cheaper than MR Elastography. Note, however, that 10-25 percent of fibroscan studies may fail to obtain reliable readings due to patient factors. Besides, an appropriate probe size is needed for different patient sizes.

HOW SHOULD I MANAGE AT A PRIMARY CARE CLINIC?

Establishing the diagnosis, i.e., confirming presence of fat in liver, with exclusion of alternative liver diseases is the first line of management.

One also ought to look for other components of metabolic syndrome as they are almost always present in all patients with NAFLD.

The next step is to establish the severity of liver damage by non-invasive methods. Those with advanced fibrosis or cirrhosis should be referred for specialist care.

Lifestyle modification is the mainstay of treatment for NAFLD and should be done at the primary care level.

The most proven management of NAFLD is weight loss. Weight loss of 3-5 percent from baseline often leads to improvement in hepatic steatosis. Further weight loss of 7-10 percent would lead to improvement of inflammation and fibrosis histologically.

Exercising alone may not be sufficient in improving the stage of NAFLD, thus exercising should be combined with dieting. A hypocaloric diet, i.e., creation of a calorie deficit, plus moderate-intensity exercise, is likely to provide the best likelihood of sustaining weight loss.

My personal experience is that constant reminders and regular review of patients, providing insights, going through patient's dietary and social history, are important in helping patients adhere to hypocaloric diet and a regular exercise regime.

Metformin has been discarded as a treatment of choice as meta-analysis showed no benefits in improvement in liver histology.

Pioglitazone, vitamin E at 800 IU/day have been showed to improve liver histology in NASH patients. However, Pioglitazone use is associated with weight gain and increased bone loss, as well as a small risk of bladder cancer. Therefore pioglitazone should be used only for those with biopsy proven NASH and with informed consent.

Vitamin E at a dose of 400 IU/day has been associated with an increased risk of prostate cancer and all-cause mortality in some studies. Hence, its benefits and risks ought to be

discussed with patients before starting it. Vitamin E is not recommended for NAFLD patients with liver biopsy, with cirrhosis, or with diabetes.

Newer diabetic medications like GLP-1 agonists have showed promising results in managing weight loss but its use in NAFLD is currently not recommended yet.

Bariatric surgeries, which lead to significant weight loss, can lead to improvement in liver histology. But careful patient selection, as well as long-term post-op support, are important in ensuring maintenance in weight loss.

HOW TO DO DIETING?

There is no simple answer to this. I often joke with my patients that if there is a simple method to lose weight, there will no fat doctors!

But a few points can be written on losing weight.

Firstly, there must be a calorie deficit whereby a patient's calorie intake is less than his requirement. The type of diet, be it in low carbo diet, ketogenic diet, Mediterranean diet, Subway diet, etc is not important. Studies have showed that these diets can all help to reduce weight. The most important part of dieting is its sustainability, as many studies showed that only a quarter to a third of participants have the discipline to complete a one-year programme to lose weight.

Many of my patients lost weight with a ketogenic diet. But being Asians, it is difficult to not consume rice or bread so most cannot sustain a ketogenic diet.

Second, the patient must have enough insight into the problem to improve self-motivation. And emotional support from his or her family members is essential for success.

Third, foods that contain simple sugar, like desserts, soft drinks, or snacks should be minimised or rationed.

Fourth, a low-calorie diet leads to reduced metabolic rate and muscle loss. Therefore, any form of dieting should be accompanied with a moderate amount of exercise to avoid loss of lean mass and maintenance of metabolic rate.

Finally, we as physicians must be aware of the adverse effects of different types of diets. For instance, intermittent fasting, i.e., eating for only eight hours over a 24-hour period can help in losing weight significantly. But patients often feel lethargic, cold, and dizzy when they first embark on intermittent fasting. Patients who operate heavy machinery or drive a taxi, for instance, may not be suitable for intermittent fasting. In addition, skipping breakfast has been shown to be associated with gallstone formation, hence we must first warn patients about all these before recommending it to them.

REFERENCES

1. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018 Jan;67(1):328-357. doi: 10.1002/hep.29367. Epub 2017 Sep 29. PMID: 28714183.
2. European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. J Hepatol. 2016 Jun;64(6):1388-402. doi: 10.1016/j.jhep.2015.11.004. Epub 2016 Apr 7. PMID: 27062661.
3. Wong VW, Chan WK, Chitturi S, Chawla Y, Dan YY, Duseja A, et al. Asia-Pacific Working Party on Non-alcoholic Fatty Liver Disease guidelines 2017-Part 1: Definition, risk factors and assessment. J Gastroenterol Hepatol. 2018 Jan;33(1):70-85. doi: 10.1111/jgh.13857. PMID: 28670712.
4. Chitturi S, Wong VW, Chan WK, Wong GL, Wong SK, Sollano J, et al. The Asia-Pacific Working Party on Non-alcoholic Fatty Liver Disease guidelines 2017-Part 2: Management and special groups. J Gastroenterol Hepatol. 2018 Jan;33(1):86-98. doi: 10.1111/jgh.13856. PMID: 28692197.

LEARNING POINTS

- **NAFLD is now the most common cause of liver disease in Singapore, as well as the rest of the world. It will emerge as the leading cause of cirrhosis, liver cancer, and liver-related mortality in time to come.**
- **NAFLD is associated with metabolic syndrome and the family doctor ought to look out for and treat different components of metabolic syndrome.**
- **There is currently no magic way to lose weight. Much effort in taking low-calorie diets and doing daily exercises must be preached to all patients constantly.**