Diagnosis and Treatment of Fatty Liver Associated with Diabetes, Obesity, and Dyslipidemia

About half of patients with diabetes also have fatty liver, and the condition may progress to severe liver disease without noticeable symptoms. In Japan, liver cirrhosis and liver cancer account for 9.3% of deaths among patients with diabetes, which is higher than the 6.6% attributable to cerebrovascular disease.

Patients with diabetes may therefore progress from fatty liver to metabolic steatohepatitis, and then to liver cirrhosis or liver cancer. For this reason, fatty liver and the degree of liver fibrosis should be checked regularly.

Do you know the difference between obesity and obesity disease? Obesity means a condition in which BMI (body mass index) is 25 or higher. If obesity is accompanied by dyslipidemia, such as high cholesterol or triglycerides, or by hypertension, it is considered obesity disease and requires treatment.

When BMI is high, it is important to determine which component of the body has increased. A high amount of muscle is not a problem. However, if body water is increased and edema is present, or if body fat is increased, appropriate measures are required. When fat is increased, the location of fat deposition should also be assessed, including visceral fat and fat deposition in the liver (Figure 1).

Figure 1. Accurate assessment of fat amount and deposition sites

1) Calculate BMI (Body Mass Index).

BMI = body weight (kg) / height (m) / height (m)

BMI >= 25 indicates obesity. BMI < 18.5 indicates underweight. Both increase disease risk.

Example: height 170 cm and weight 80 kg -> BMI = 80 / 1.7 / 1.7 = 27.7, classified as obesity.

2) Why is body weight high? Use BIA (InBody) to quantify total body water, fat mass, and muscle mass.

Example: Bodybuilder	High muscle; BMI >= 25, fat not high.
Example: Cirrhosis with edema	High body water; BMI >= 25, fat not high.
Example: Sarcopenia	Low muscle; fat high even if BMI < 25.

3) Is fat deposition visceral or subcutaneous?

FAT CT is used to determine visceral fat obesity (Figure 2).

4) Examine fat deposition in the liver using FibroScan (Figure 3).

A related term for obesity disease is metabolic syndrome. It is defined as visceral fat obesity accompanied by abnormalities in at least two of the following: blood pressure, blood glucose, and serum lipid levels. It also includes people with high visceral fat despite a BMI below 25, often called hidden obesity.

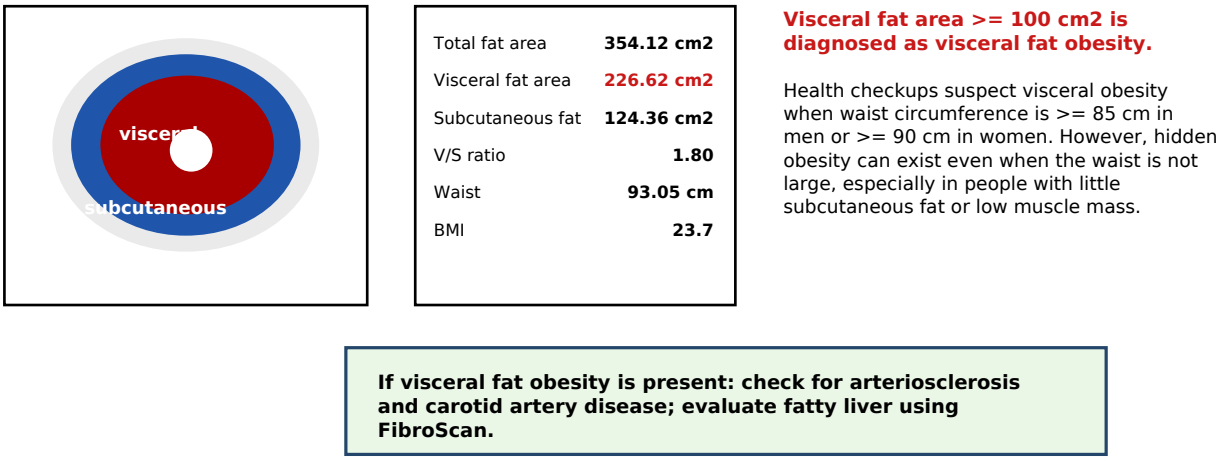
In metabolic syndrome, especially in patients with diabetes or dyslipidemia, the risk of myocardial infarction and cerebral infarction has long been considered high. To check for arteriosclerosis, we first recommend carotid ultrasonography. If arterial plaque or calcification is found, we recommend further detailed evaluation.

People with a large amount of visceral fat often have fat deposition not only in blood vessels, but also in organs, particularly in the liver. Fatty liver is therefore common, and the risk of liver cirrhosis and liver cancer is also higher.

For this reason, patients with obesity should first have total body fat mass quantified using InBody. Next, body fat distribution should be assessed by visceral fat CT. CT is performed at the level of the umbilicus, and the areas of subcutaneous fat and visceral fat are measured. If the visceral fat area is 100 cm2 or greater, the patient is diagnosed with visceral fat obesity.

Figure 2. Visceral fat CT examination: "Fat Scan"

An abdominal CT slice at the umbilical level is analyzed. Software colors and measures visceral and subcutaneous fat areas. Red indicates visceral fat and blue indicates subcutaneous fat.



Fat deposition in the liver is further quantified using FibroScan (Figure 3). At the same time, the degree of liver fibrosis should be assessed to estimate the risk of liver cirrhosis and liver cancer. At our hospital, these measurements allow us to understand the patient's condition accurately and determine the appropriate treatment strategy.

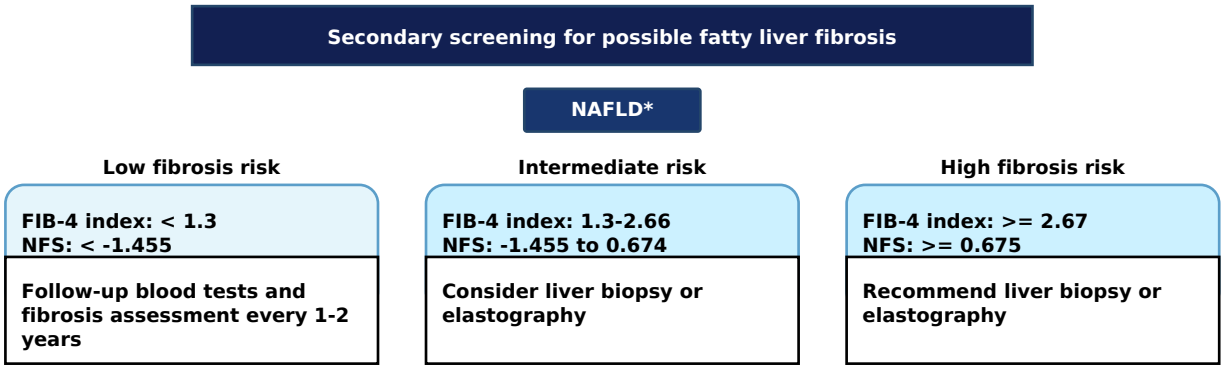
Figure 3. Quantification of liver fibrosis and fat deposition using FibroScan

1) A probe is placed on the right side of the abdomen. 2) The result displays CAP (fat amount) and liver stiffness.

Compared with liver biopsy, FibroScan can be performed easily by applying a probe without hospitalization. It is painless, places little burden on the patient, and can be repeated. It quantifies liver stiffness and fat deposition. These values help determine the stage of liver disease, estimate liver cancer risk, and evaluate treatment response when measured about every 3 months.

The risk of liver cancer in patients with fatty liver can be evaluated by the degree of liver fibrosis. Fibrosis refers to the accumulation of collagen in the liver, which makes the liver harder. The Japan Society of Hepatology provides follow-up methods based on each patient's level of risk (Figure 4).

Figure 4. Patients with diabetes or dyslipidemia should have liver fibrosis assessed



Perform hepatocellular carcinoma surveillance according to the degree of fibrosis.

Adapted from the NAFLD/NASH Clinical Practice Guidelines 2020. *Terminology has shifted from non-alcoholic to metabolic-associated nomenclature.

Common and convenient methods for assessing liver fibrosis include the FIB-4 index (Figure 5), ultrasound elastography, and FibroScan (Figure 3).

Figure 5. FIB-4 Index

The FIB-4 index is a scoring system based on blood test data (ALT, AST, and platelet count). It helps estimate liver fibrosis.

FIB-4 index = AST (IU/L) x age (years) / [10 x platelet count (10^4/uL) x square root of ALT (IU/L)]

Low: <= 1.3 - low risk; follow-up observation.
Intermediate: 1.3-2.67 - chronic hepatitis may be present; detailed evaluation is recommended.
High: >= 2.67 - cirrhosis or advanced chronic hepatitis is common; treatment is required.

FIB-4 index calculation site

Available on the Japanese Society of Hepatology website:

https://www.jsh.or.jp/medical/guidelines/medicalinfo/eapharma.html

Example input data

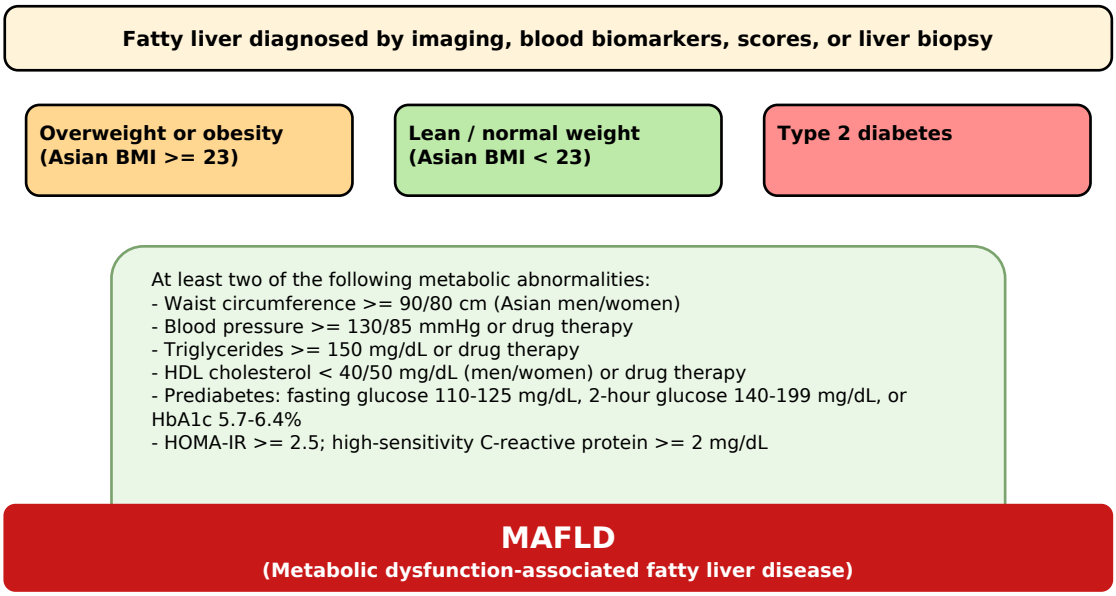
Age: 65 years
AST: 48 IU/L
ALT: 32 IU/L
Platelets: 9.8 x 10^4/uL

The FIB-4 result is 5.63.
This indicates a high possibility of cirrhosis and the need for detailed examination.

A new disease concept has been proposed: metabolic dysfunction-associated fatty liver disease, or MAFLD (Figure 6). Diagnostic criteria for MAFLD apply to patients with fatty liver who also meet one of the following conditions: 1) overweight or obesity, defined in Japanese patients as BMI >= 23 kg/m2; 2) lean or normal weight with at least two metabolic abnormalities, such as hypertension, visceral fat accumulation, impaired glucose tolerance, or dyslipidemia; or 3) type 2 diabetes.

Under this concept, fatty liver is not divided into alcoholic and non-alcoholic categories according to alcohol intake, and the presence or absence of viral liver disease such as hepatitis B or hepatitis C is not used to exclude the diagnosis. Because obesity in Japanese patients is defined strictly as BMI >= 23 kg/m2, patients with diabetes and fatty liver should be carefully monitored for progression to liver cirrhosis or liver cancer as MAFLD.

Figure 6. Diagnostic criteria for MAFLD



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In 2023, the disease names non-alcoholic fatty liver disease and non-alcoholic steatohepatitis (NAFLD and NASH) were changed to metabolic dysfunction-associated steatotic liver disease (MASLD) and metabolic dysfunction-associated steatohepatitis (MASH). The word non-alcoholic was replaced because it can suggest heavy drinking and is not ideal as a medical term. The new terminology emphasizes the relationship between fatty liver and metabolic dysfunction.

When obesity is accurately assessed and liver fibrosis is identified, diet and exercise therapy should be provided, and medication should be used when necessary. However, MASLD cannot be cured easily with medication alone. Patients need to review their daily lifestyle, including diet and exercise.

Using the CAP score obtained by FibroScan as an indicator of liver fat content, patients should be encouraged to understand their own condition and continue lifestyle modification persistently. At our hospital, a specialized outpatient clinic is available on Tuesday and Thursday afternoons.

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