Gut and Liver
https://doi.org/10.5009/gnl220545
pISSN 1976-2283 eISSN 2005-1212

Review Article

Nonalcoholic Fatty Liver Disease as a Systemic Disease and the Need for Multidisciplinary Care

Masato Yoneda, Takashi Kobayashi, Michihiro Iwaki, Asako Nogami, Satoru Saito, and Atsushi Nakajima

Department of Gastroenterology and Hepatology, Yokohama City University Hospital, Yokohama, Japan

Article Info

Received December 30, 2022
Revised March 14, 2023
Accepted March 28, 2023
Published online August 10, 2023

Corresponding Author

Masato Yoneda
ORCID https://orcid.org/0000-0001-7815-549X
E-mail yoneda@yokohama-cu.ac.jp

Nonalcoholic fatty liver disease (NAFLD) is currently the most common chronic liver disease, and there has been a rapid increase in cases worldwide. NAFLD is rapidly becoming the leading cause of hepatocellular carcinoma and is also associated with an increased risk of cardiovascular disease or exacerbation of other organ diseases, thus posing a significant health problem from both a medical and a socioeconomic perspective. NAFLD is a systemic disease and requires the involvement of numerous medical professionals. Multidisciplinary collaboration, in which different professionals within different specialties come together and work together toward a common goal, supports better patient care by integrating perspectives of multiple experts and facilitating the exchange of opinions. Due to the large number of potential patients, gastroenterologists and hepatologists cannot manage the patients alone, and collaboration between specialists in various fields, including family doctors, dentists, nutritionists, and pharmacists is required for treatment of NAFLD. This review will discuss NAFLD from the perspective of various specialties and introduce multidisciplinary collaboration. **(Gut Liver 2023;17:843-852)**

Key Words: Non-alcoholic fatty liver disease; Cardiovascular diseases; Fatty liver; Patient care team

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is estimated to have a prevalence of 25.2% worldwide[1] and 29.6% in Asia,[2] of which nonalcoholic steatohepatitis (NASH) constitutes 10% to 20%, and the prevalence of NAFLD is projected to increase significantly by 2030.[3] Although NAFLD has a better prognosis than other liver diseases, especially viral hepatitis, it is associated with a risk of developing atherosclerotic disease, chronic kidney disease (CKD), and extrahepatic cancer. Angulo *et al.*[4] in 2015 and Hagström *et al.*[5] in 2017 first indicated that the main cause of death in NAFLD is not liver-related. Angulo *et al.*[4] reported that, in a histological study of 619 patients with NAFLD/NASH, followed for an average of 12.6 years, of which 33.2% of patients died, cardiovascular disease (CVD) was the most common cause of death (38.3%), exceeding liver-related deaths, such as cirrhosis or hepatocellular carcinoma. Similarly, Hagström *et al.*[5] reported a histological study following 646 patients with NAFLD/NASH for a mean of 20 years, in which 33.1% of patients died, with the most common cause of death being cardiovascular events (36.9%), followed by extrahepatic malignancies (25.7%), and liver-related death being only the fourth most common (7.9%). In a recent matched cohort study of 10,568 biopsy-verified NAFLD cases from Sweden, followed for a median of 14.2 years, the leading cause of death was extrahepatic cancer, followed by cardiovascular events, and liver-related events, with fibrosis progression in NAFLD associated with increased mortality (Fig. 1).[6]

NAFLD has attracted attention as a systemic disease due to its pathogenic mechanism, poor outcomes, and crosstalk with other organs.[7] If NAFLD/NASH and the associated complications are not proactively screened, they may progress unnoticed. However, due to the large number of potential patients, gastroenterologists and hepatologists cannot manage the patients alone, and collaboration between specialists in various fields, including family doctors, dentists, nutritionists, and pharmacists is required for treatment of NAFLD. This review will discuss NAFLD

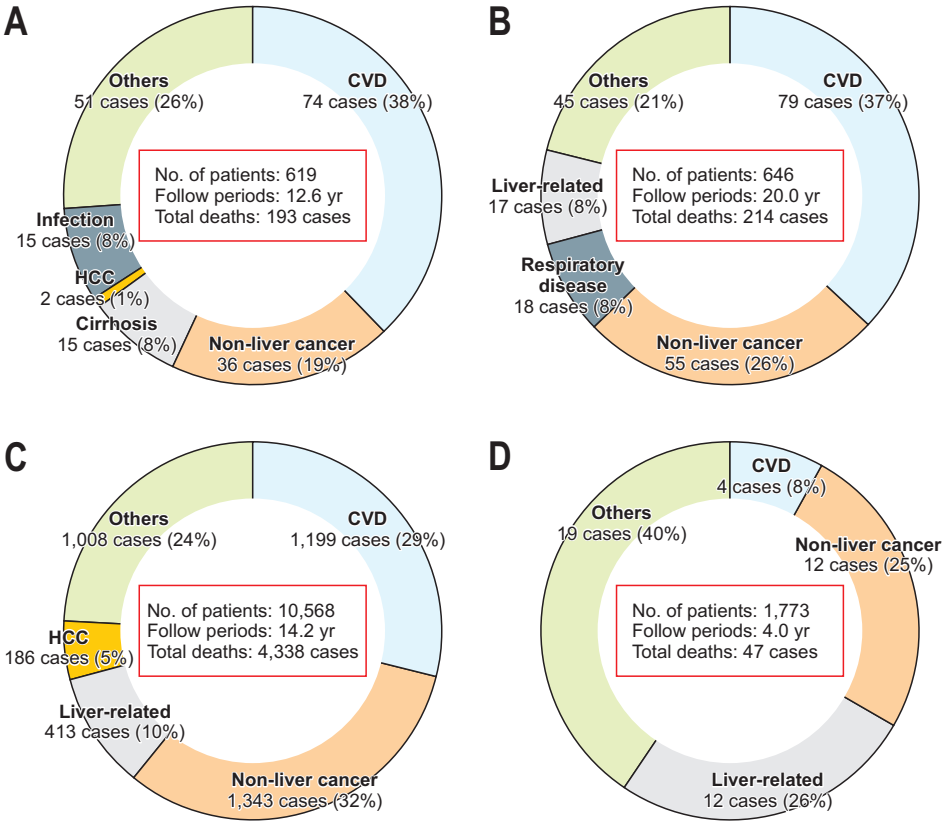

Fig. 1. Causes of death in NAFLD in a large cohort study. (A) From 1975 to 2005, 619 patients were diagnosed with NAFLD by liver biopsy, and 193 died or underwent liver transplantation during follow-up (median, 12.6 years).[4] (B) From 1971 to 2009, 646 patients were diagnosed with NAFLD by liver biopsy, and 214 died or underwent liver transplantation during follow-up (mean, 20.0 years).[5] (C) From 1966 to 2017, 10,568 patients were diagnosed with NAFLD by liver biopsy, and 4,338 died during follow-up (mean, 14.2 years).[6] (D) A prospective study. A total of 1,773 patients were diagnosed with NAFLD by liver biopsy, and 47 died during follow-up (mean, 4.0 years).[8] NAFLD, nonalcoholic fatty liver disease; CVD, cardiovascular disease; HCC, hepatocellular carcinoma.

from the perspective of various specialties and introduce multidisciplinary collaboration.

COLLABORATION WITH DIABETOLOGISTS

Obesity and type 2 diabetes mellitus are the diseases most frequently associated with the development and pathological progression of NAFLD/NASH (Fig. 2).[9] A 4-year multicenter prospective study of 773 patients with NAFLD showed a higher incidence of type 2 diabetes in patients with fibrosis stage F4 compared with those with fibrosis stages F0-F2 (7.53 events per 100 person-years vs 4.45 events per 100 person-years).[8] Diabetologists therefore strive to accurately diagnose NASH, especially in patients with advanced fibrosis. In 2019, the American Diabetes Association recommended that diabetic patients with fatty liver or abnormal liver function should be evaluated for NASH and fibrosis.[10] The 2023 American Diabetes Association consensus statement incorporates additional details regarding diagnosis and risk stratification of NASH in primary care and diabetes clinics, such as using the fibrosis-4 (FIB-4) index[11] to assess liver fibrosis risk, as well as explaining the rationale for fibrosis risk stratification in diabetic patients, and providing recommendations for when patients should be referred to a gastroenterologist

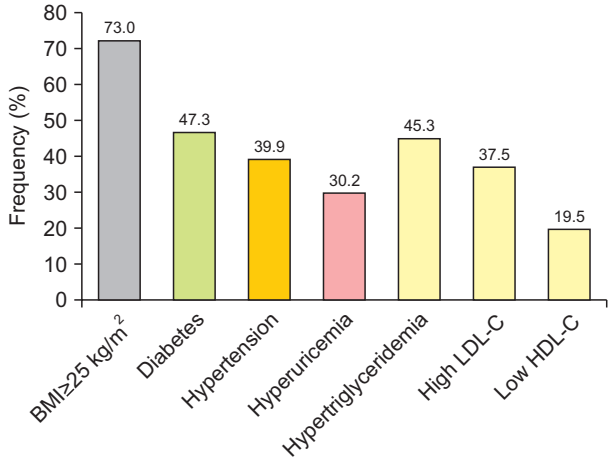

Fig. 2. NAFLD/NASH and associated lifestyle-related diseases. A multicenter cross-sectional study in Japan. Frequency of metabolic syndrome-related comorbidities in 1,365 patients with NAFLD.[9] NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; BMI, body mass index; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

or hepatologist.[12] In Europe, guidelines were jointly issued in 2016 by the European Association for the Study of the Liver (EASL), the European Association for the Study of Diabetes (EASD) and the European Association for the Study of Obesity (EASO).[13] The EASL-EASD-EASO clinical practice guideline also recommends the use of the FIB-

4 index and the NAFLD fibrosis score for NAFLD patients with type 2 diabetes and referral to a gastroenterologist in cases of advanced fibrosis.[13]

The two-step diagnostic algorithm uses a scoring system with a high negative predictive value and no facility restrictions to identify cases at risk for fibrosis progression, followed by elastography with high specificity at a specialized facility. A two-step assessment with serum-based FIB-4, followed by vibration-controlled transient elastography, can stratify the risk of liver-related complications in NAFLD.[14]

In a real-world study using data from more than 18 million people from four European countries, diabetes was reported as the strongest predictor of cirrhosis and liver cancer in patients with NAFLD or NASH, increasing the risk of developing these diseases approximately 2-fold.[15] In the U.S., there are 18.2 million patients with type 2 diabetes and NAFLD, of which 6.4 million (35%) are estimated to have NASH. Furthermore, it is estimated that concurrent type 2 diabetes and NAFLD will require 65,000 liver transplants and lead to 1.37 million cardiovascular-related deaths and 812,000 liver-related deaths, incurring $55.8 billion in medical costs over the next 20 years, thus indicating the clinical importance of measures for preventing type 2 diabetic NAFLD.[16] Pioglitazone, sodium-glucose co-transporter 2 (SGLT-2) inhibitors, and glucagon-like peptide 1 receptor agonists have been reported to improve both diabetes and NAFLD (Fig. 3).[17-21]

As many patients with type 2 diabetes also have NAFLD, it is important to know how to identify patients that require collaboration between diabetologists, gastroenterologists and hepatologists. For patients with NAFLD complicated by type 2 diabetes, diabetologists often recommend lifestyle changes and prescribe drug therapy. Furthermore, as type 2 diabetes is a risk factor for cirrhosis and hepatocellular carcinoma, diabetologists should regularly check for fibrosis development using the FIB-4 index, and gastroenterologists or hepatologists should evaluate liver fibrosis status using elastography and liver biopsy, as well as investigate potential esophageal varices and hepatocellular carcinoma in NAFLD with advanced fibrosis.

COLLABORATION WITH CARDIOLOGISTS

NAFLD is routinely encountered in cardiology. Targher *et al.*[22] conducted a 5-year prospective observational study of 2,103 patients with type 2 diabetes with no history of CVD, and reported that 248 patients experienced nonfatal myocardial infarction, coronary artery reconstruction, ischemic stroke, or cardiovascular death. Concurrent NAFLD was significantly associated with increased cardiovascular risk with an odds ratio of 1.84, even after adjusting for age, sex, smoking history, diabetes history, hemoglobin A1c, low-density lipoprotein cholesterol, liver enzymes, and medications.[22] A Japanese nationwide retrospective study, which followed 142,000 patients with NAFLD and 1.4 million patients without NAFLD for an average of 4 years, reported that the CVD incidence was 2.9 times higher in the NAFLD group than in the non-NAFLD

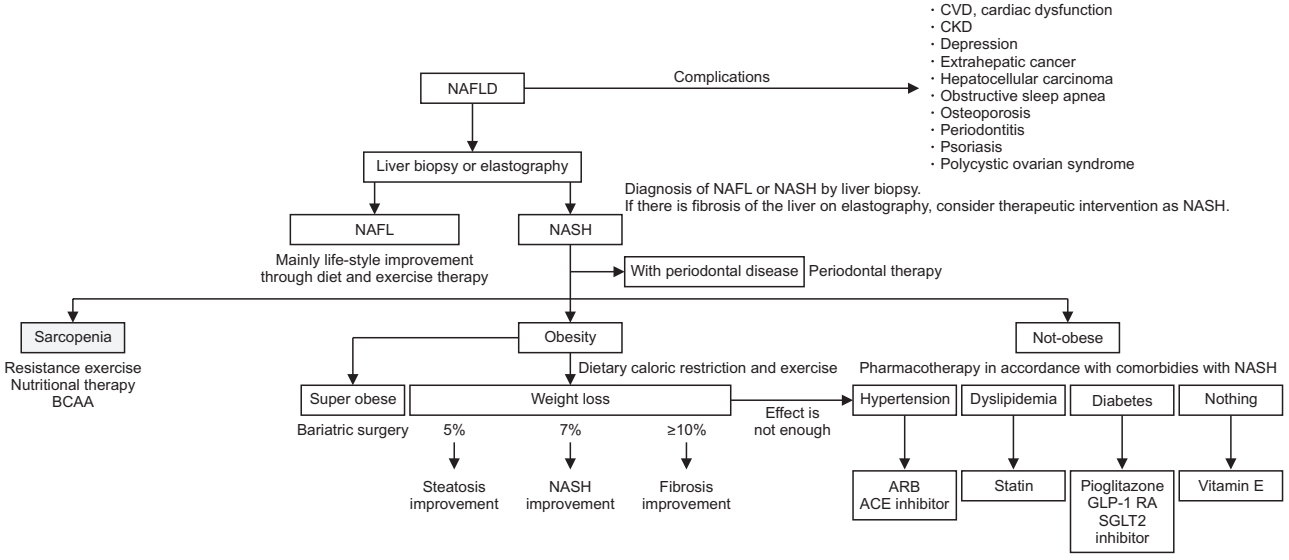

Fig. 3. NAFLD/NASH treatment flowchart.
NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; CVD, cardiovascular disease; CKD, chronic kidney disease; NAFL, nonalcoholic fatty liver; ARB, angiotensin II receptor blocker; ACE, angiotensin converting enzyme; BCAA, branched-chain-amino-acid; GLP-1, glucagon-like peptide 1; SGLT-2, sodium-glucose co-transporter 2.

group (2.82/1,000 person-years vs 0.97/1,000 person-years).[23]

Several studies have indicated that hepatic fibrosis contributes to atherogenesis.[24] Patients with fibrotic NASH may develop CVD and exhibit accelerated atherosclerosis, possibly as a result of increased hepatic production of prothrombogenic factors, such as vascular endothelial growth factor, hypoxia-inducible factor, intracellular adhesion molecule-1, vascular adhesion molecule-1, and fetuin-A.[24]

In addition to atherosclerosis, NAFLD can also affect cardiac function. Lee *et al.*[25] evaluated cardiac function using echocardiography and myocardial glucose uptake using 18FDG-PET in 118 patients with NAFLD and 190 patients without NAFLD. The results indicated that NAFLD patients have an increased left ventricular myocardial weight coefficient, left ventricular end-diastolic diameter, and left atrial volume index compared with non-NAFLD patients, indicating progressive myocardial remodeling. Liver stiffness measured by ultrasound elastography was significantly correlated with left ventricular diastolic dysfunction and impaired myocardial glucose uptake.[25] Canada *et al.*[26] performed cardiopulmonary exercise testing and stress echocardiography in 15 patients with NAFLD and 21 patients with NASH and discovered that maximal oxygen uptake was lower in patients with NASH than in patients with NAFLD, suggesting impaired exercise tolerance. Additionally, maximal oxygen uptake decreased with the progression of fibrosis. Similarly, echocardiographic E to E prime ratio (E/e') increased progressively with increasing liver fibrosis during exercise. As described above, the stage of liver fibrosis correlates with atherosclerotic pathology and left ventricular remodeling, suggesting a relationship with left ventricular dilatation capacity and exercise tolerance and therefore with heart failure.[26]

The association between NAFLD/NASH and CVD is not limited to ischemic heart disease, but also extends to heart failure, mainly diastolic failure, which is rapidly increasing among older patients. Primary and secondary prevention of heart failure and atherosclerotic disease, therefore, requires collaboration between gastroenterologists, hepatologists, and cardiologists. The Japanese Society of Gastroenterology and the Japan Society of Hepatology published the "NAFLD/NASH Guidelines 2020," which includes a flowchart for identifying CVDs (Fig. 4).[20,21]

COLLABORATION WITH NEPHROLOGISTS

A strong association between NAFLD and CKD has been suggested, regardless of the presence of potential confounders, such as obesity, hypertension, and type 2 diabetes (Fig. 5).[27] Patients with NAFLD, exhibit a much higher prevalence of CKD (20% to 50%) than patients without NAFLD.[27,28] Furthermore, several longitudinal studies reported that NAFLD and fibrosis development in NAFLD are risk factors for new-onset CKD.[29-31] Targher *et al.*[29] studied 1,760 patients with type 2 diabetes with normal renal function for a mean of 6.5 years and found that NAFLD was associated with new-onset CKD independently of other confounding factors, such as age, sex, body mass index (BMI), and dyslipidemia (hazard ratio=1.69). Sinn *et al.*[30] assessed liver fibrosis using the NAFLD fibrosis

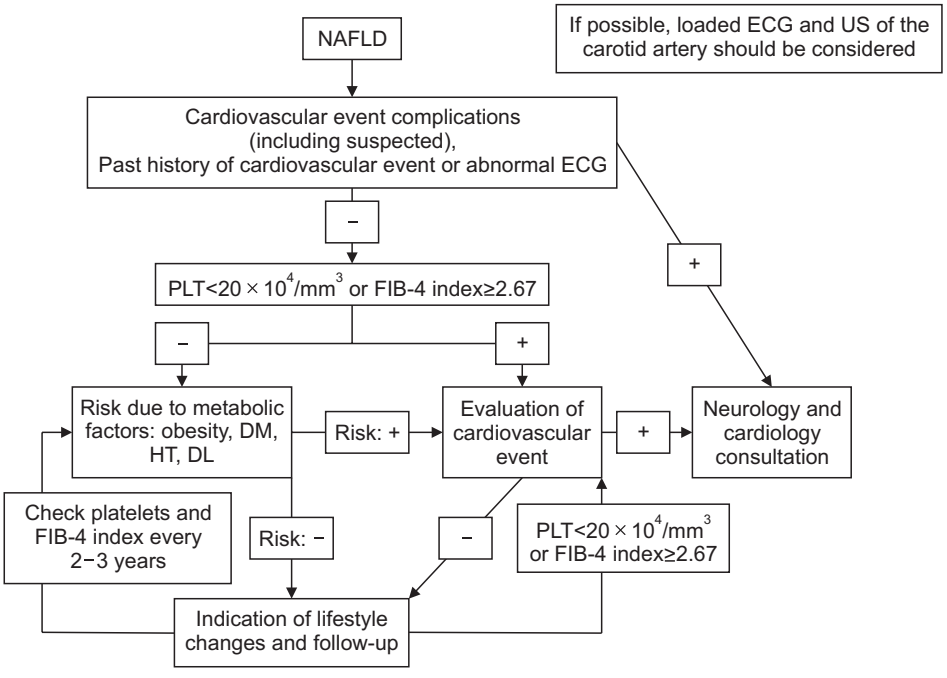

Fig. 4. Flowchart for cardiovascular event screening in patients with NAFLD (evidence-based clinical practice guidelines for NAFDL/NASH 2020 from the Japanese Society of Gastroenterology and the Japan Society of Hepatology).
NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; ECG, electrocardiogram; US, ultrasonography; PLT, platelet; FIB-4, fibrosis-4; DM, diabetes mellitus; HT, hypertension; DL, dyslipidemia.

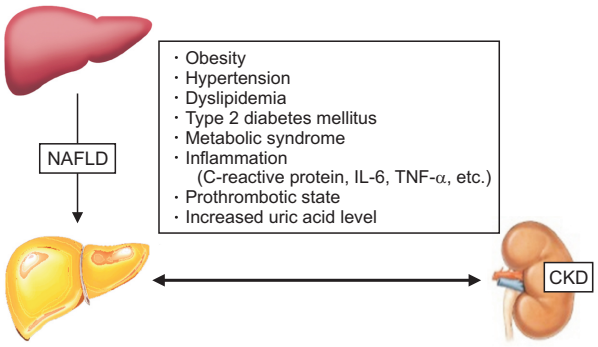

Fig. 5. Risk factors for patients with NAFLD and CKD.
NAFLD, nonalcoholic fatty liver disease; CKD, chronic kidney disease; IL-6, interleukin-6; TNF-α, tumor necrosis factor α.

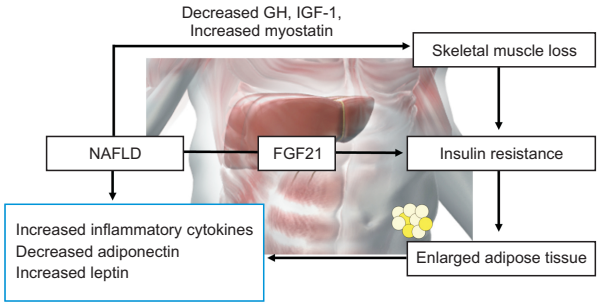

Fig. 6. Association between NAFLD and sarcopenia.
GH, growth hormone; IGF, insulin-like growth factor; NAFLD, nonalcoholic fatty liver disease; FGF21, fibroblast growth factor 21.

score and reported that CKD risk increases with increasing severity of NAFLD. A study by Jung *et al.*[31] showed that CKD risk was 5.40 times higher (95% confidence interval, 2.46 to 11.84; p<0.001) in the group with higher liver stiffness than in the group without fibrosis.

NAFLD and CKD are associated with poor outcomes and high costs, and have become major public health problems owing to their increasing prevalence. Due to the prevalence of CKD complications, glomerular filtration rate, and proteinuria (urinary microalbumin) should be checked regularly during NAFLD management to detect early renal failure. Recently, the renoprotective effect of SGLT2 inhibitors has been demonstrated in patients with CKD, both with and without concurrent type 2 diabetes.[32] Early intervention is important in CKD management, and in cases of CKD complicated with NAFLD, collaboration between nephrologists and gastroenterologists or hepatologists is necessary.

COLLABORATION WITH PSYCHIATRISTS

In 2015, Tomeno *et al.*[33] compared 32 patients with depression and biopsy-proven NAFLD with 226 patients with biopsy-proven NAFLD without depression and found that patients with NAFLD that suffer from depression have higher alanine transaminase (ALT) levels, more advanced liver-tissue disease, and were more resistant to conventional NAFLD treatment. An analysis of the 2007 to 2016 National Health and Nutrition Examination Survey database in the United States evaluated the prevalence of fatty liver, depression, and functional impairment due to depression in 484 adults (mean age, 47 years) and reported a higher prevalence of depression in patients with fatty liver, and patients with depression were 1.6 to 2.2 times more likely to have a fatty live.[34] A systematic review of 10 articles involving 2,041,752 patients with NAFLD reported that depression was significantly associated with NAFLD, and comorbidity was associated with increased annual mortality.[35] The prevalence of depression in patients with NAFLD was 18.2%, and risk factors for the development of depression in patients with NAFLD patients included diabetes, BMI, female sex, smoking, and history of pulmonary disease.[35]

NAFLD has also been associated with schizophrenia, and a study including 253 patients with schizophrenia/schizoaffective disorder patients reported that 108 (42.7%) patients had NAFLD and 13 patients (12.0%) exhibited fibrotic progression. NAFLD was more common in younger patients and females, and the association with BMI, total antipsychotic dose and risk of metabolic syndrome, and total antipsychotic dose and risk of hyperprolactinemia were significantly associated with NAFLD (p<0.001, p=0.049, p=0.041, respectively).[36] As both NAFLD and depression have a high incidence worldwide and are expected to increase in the future, multidisciplinary collaboration is required to access and diagnose NAFLD in patients with psychiatric disorders, and provide treatment and support for the presence of psychiatric comorbidities in NAFLD following diagnosis.

Depressed patients often have disordered eating habits, such as eating breakfast infrequently and snacking frequently. They also exercise less frequently and are therefore at increased risk for lifestyle-related diseases such as obesity, dyslipidemia, and NAFLD. In addition to treatment with antidepressants, physical and mental rest, psychotherapy, weight control, treatment and prevention of metabolic syndrome, diet, and exercise therapy are considered important in the treatment of depression,[37] and cooperation between psychiatrists, gastroenterologists, and dietitians is required for effective dietary and exercise therapy of patients with comorbid NAFLD and depression.

COLLABORATION WITH PHYSIATRISTS

The prevalence of NAFLD/NASH is increased in patients with sarcopenia, and the presence of sarcopenia increases the risk of developing NASH and liver fibrosis.[38,39] The pathogenesis of sarcopenia in NAFLD/NASH includes insulin resistance, decreased insulin growth factor-1, decreased myogenesis, and increased catabolism due to systemic inflammation and hepatokines. Inflammatory cytokines, such as tumor necrosis factor α. and interleukin-6, and hepatokines, such as fetuin-A and fibroblast growth factor 21, produced by visceral fat increase insulin resistance and protein catabolism, further reducing muscle mass (Fig. 6). Management of sarcopenia is crucial as it reduces life expectancy. Exercise therapy is effective in decreasing adipose tissue mass by burning visceral and subcutaneous fat as an energy source through increased energy expenditure, and in decreasing hepatic triglyceride synthesis through increased fatty acid uptake and improved insulin sensitivity in muscle. Although resistance exercise has been reported to improve fatty liver to the same extent as aerobic exercise but with less energy expenditure, no consensus has been reached regarding specific recommendations in terms of intensity and frequency exercise. The EASL-EASD-EASO clinical practice guidelines for NAFLD management recommends 150 to 200 minutes of moderate intensity aerobic activity distributed over three to five sessions per week, and states that "Resistance training is also effective and promotes musculoskeletal fitness, with effects on metabolic risk factors."[11,40] The effect of exercise therapy is correlated with baseline BMI, and hepatic steatosis and liver injury is more likely to be attenuated in patients with a higher BMI.[40-43] A meta-analysis of studies evaluating exercise intervention in NAFLD reported significant improvement in hepatic steatosis with continued exercise therapy even in the absence of weight loss.[40]

In addition to liver-related death, cardiovascular events are associated with the prognosis of NAFLD/NASH. In addition to reducing hepatic steatosis, regular exercise improves comorbidities associated with NAFLD, such as insulin resistance and CVD.[44]

Because sarcopenia is likely to impair activities of daily living and exercise tolerance, it is expedient to accurately assess the patient's condition and provide individualized exercise guidance. In obese patients with NAFLD/NASH, the presence and severity of comorbidities, such as ischemic heart disease and bone and joint disease, as well as potential worsening of these comorbidities by exercise, should be evaluated. Exercise therapy should be structured to be long-lasting, taking into consideration personal preferences, comorbidities, and weight-loss goals. Multifaceted intervention coordinated by a team of collaborating physicians, exercise therapists, dietitians, and nurses can facilitate sustained lifestyle improvement in patients with NAFLD/NASH.[45]

COLLABORATION WITH DENTISTS

As recent oral bacteriological and epidemiological studies have reported numerous detrimental effects of oral bacteria on the entire body, the concept of "Periodontal Medicine," in which periodontal disease is interactively involved in systemic diseases, has been proposed.[46] The association between periodontal disease and abnormal liver function was first reported by Furuta *et al.*[47] in 2010. Yoneda *et al.*[48] in 2012 first reported the association between *Porphyromonas gingivalis*, typical bacteria that cause periodontal disease, and NAFLD, detecting *P. gingivalis* in 21.7%, 35.4%, and 50.2% of health individual, patients with NAFL, NASH, respectively. Systematic review of 12 studies including 53,384 patients suggested that periodontitis may be a risk factor for NAFLD development and progression.[49] The National Health and Nutrition Examination Survey epidemiological study, which included 5,421 patients with oral conditions and fatty liver, found an association between NAFLD development and progression and fewer than 20 remaining teeth, moderate to severe periodontitis, and untreated dental caries.[50] In a cross-sectional study, Iwasaki *et al.*[51] reported an association between a Probing Pocket Depth ≥4 mm and higher NAFLD incidence.

P. gingivalis fimbriae (FimA) are filamentous cell surface components thought to play an important role in the invasion and colonization of periodontal tissues. Types II, Ib, and IV, which are highly pathogenic strains of FimA, were found in 50%, 30%, and 14.3% of patients with NAFLD, respectively.[48] Furthermore, there was a significant correlation between the progression of hepatic fibrosis and *P. gingivalis* antibody titers possessing FimA type IV in patients with NAFLD.[52]

Periodontal intervention may improve NAFLD pathogenesis, as demonstrated by a report of improved liver function, such as ALT and aspartate aminotransferase, 3 months after non-surgical periodontal treatment in 10 patients with NAFLD.[48] Kamata *et al.*[53] reported that scaling and root planing treatment in patients with NAFLD and periodontal disease improved ALT and decreased *P. gingivalis* IgG antibody titers. Periodontal therapy may therefore be useful as supportive therapy in the management of NAFLD, and a large, multicenter study is required to validate the efficacy of periodontal therapy in patients with NAFLD (Fig. 3).

In clinical practice, it is recommended that patients with NAFLD undergo the same oral examination as patients with diabetes, and if periodontal disease is present, aggressive periodontal treatment should be recommended. Physicians and dentists should actively collaborate to ensure thorough oral hygiene management, particularly in patients with NAFLD.

COLLABORATION WITH NUTRITIONISTS

The primary approach in the treatment of NAFLD/NASH is to address obesity and ameliorate insulin resistance through lifestyle modifications, such as diet and exercise.[54] NAFLD/NASH pathogenesis can be attenuated by weight loss, with a >7% weight loss allowing reduced hepatic steatosis, hepatic inflammation, and ballooning hepatocytes, and >10% weight loss allowing improved liver fibrosis (Fig. 3).[55] Nutritional therapy commonly recommends consumption of 50% to 60% carbohydrates and 20% to 25% fat, and restricted energy intake to induce weight loss. The EASL-EASD-EASO clinical practice guidelines suggest a 500–1,000 kcal/day reduction in energy intake to allow 0.5–1.0 kg/week weight loss.[13,56] Random control trials comparing the energy restriction effects of low-carbohydrate and low-fat diets found reductions in body weight, visceral fat, and liver steatosis with both dietary patterns.[57,58] However, the prevalence of NAFLD in non-obese individuals has been reported to range from 7% to 20%, with a tendentially higher prevalence in Asia. Even though non-obese patients with NAFLD have milder pathogenesis, including steatosis, ballooning hepatocytes, and fibrosis, lifestyle modifications are effective, and diet and exercise therapy interventions are required.

Excessive lipid intake increases the influx of free fatty acids into the liver and oxidative stress, which contributes to NAFLD/NASH development and progression. Particularly in diabetic and obese patients, insulin resistance prevents glycogenesis in the liver and fatty acid breakdown in visceral adipose tissue, which results in increased fatty acid influx from the portal vein to the liver. Furthermore, insulin promotes the synthesis of triglycerides stored in hepatocytes and inhibits their utilization, thus increasing intrahepatic fat content and affecting NAFLD development and progression. Hypertriglyceridemia is the most frequent lifestyle-related disease associated with NAFLD.[8] Also, 7-ketocholesterol, an oxidized form of cholesterol produced by freezing and cooking of foods and present in processed foods, has been associated with the development of CVD and hepatic steatosis.[59,60] Conversely, n-3 unsaturated fatty acids increase insulin sensitivity and decrease intrahepatic fat mass. The EASL-EASD-EASO clinical practice guidelines therefore recommend the Mediterranean diet, which is rich in tri-saturated fatty acids and low in carbohydrates, for patients with NAFLD.[55] Additionally, the Mediterranean diet may decrease intrahepatic fat even after weight loss.[61] If lipid intake exceeds 25% of the total energy intake, increasing the polyunsaturated fatty acid content is recommended,[62] and target intakes should be based on the management status, comorbidities, and dietary habits of the patient.

Excessive fructose intake is associated with increased blood triglycerides, weight gain, increased risk of NAFLD, and progression of liver fibrosis; however, the target fructose intake in NAFLD is unknown. However, fructose intake from beverages and foods containing fructose dextrose, high fructose liquid sugar, and isomerized sugar has recently increased.

To help patients with NAFLD improve their diet and maintain it over time, patients need to be educated about the various complications of NAFLD, such as the increased risk of hepatocellular carcinoma, diabetes, CVD, and CKD. It is important for patients to be informed that risk reduction is possible, and lifestyle modification is effective in the treatment of NAFLD. A multidisciplinary team including family members, physicians, nurses, nutritionists, and pharmacists can support patients in modulating their lifestyle, evaluating their improvement, and maintaining their motivation.

COLLABORATION WITH PHARMACISTS

Pharmacists play an important role in managing the appropriate use of medications to prevent the disadvantages caused by polypharmacy.[63] In the treatment of patients with NAFLD, drugs with potential efficacy include diabetes medications, such as pioglitazone, glucagon-like peptide 1 analogs, and SGLT2 inhibitors, and dyslipidemia medications, such as statins (Fig. 3).[64] In the treatment of patients with NAFLD and lifestyle-related diseases, it is crucial to have this background knowledge.[65] Additionally, pharmacists should have knowledge of side effects that may cause poor NAFLD control.[66]

Although pharmacotherapy is an option for NAFLD treatment, the fundamental management involves diet and exercise. Patients should be informed that drug therapy will only be effective in conjunction with appropriate lifestyle changes. Pharmacists also play a role in promoting appropriate drug use, providing the patient with information on existing medications and feedback from the patient to the entire healthcare team.

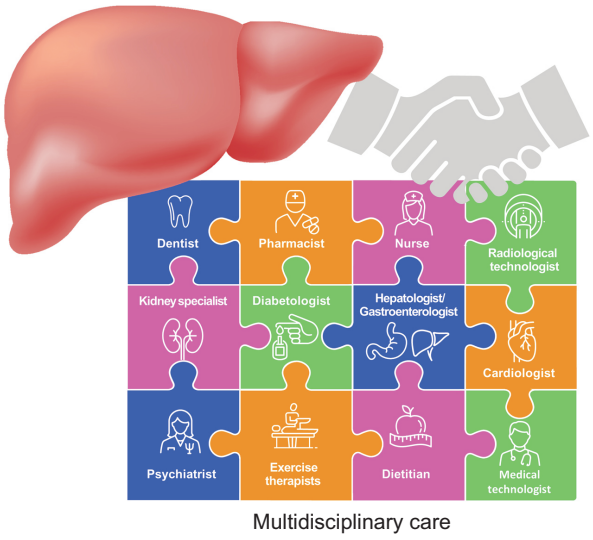

Fig. 7. Multidisciplinary collaboration needed for nonalcoholic fatty liver disease treatment.

CONCLUSION

NAFLD is rapidly becoming the leading cause of hepatocellular carcinoma and is also associated with an increased risk of CVD, thus posing a significant health problem from both a medical and a socioeconomic perspective. NAFLD is a systemic disease and requires the involvement of numerous medical professionals (Fig. 7). Multidisciplinary collaboration, in which different professions with different specialties come together and work together toward a common goal, supports better patient care by integrating perspectives of multiple experts and facilitating exchange of opinions. Furthermore, the global aging population, disasters, and infectious disease outbreaks may lead to a worldwide shortage of healthcare professionals, which may be alleviated by introducing collaboration and cooperative medicine. As human resources will always be required to maintain the quality of medical care, it is expedient to encourage collaborative medicine education of current and future healthcare teams.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGEMENTS

The administrative assistance of Naho Kobayashi, Ayako Ujiie, and Yoshiko Yamazaki is also gratefully acknowledged.

ORCID

Masato Yoneda https://orcid.org/0000-0001-7815-549X
Takashi Kobayashi https://orcid.org/0000-0002-7240-4851
Michihiro Iwaki https://orcid.org/0000-0002-7650-0699
Asako Nogami https://orcid.org/0000-0002-6923-365X
Satoru Saito https://orcid.org/0000-0002-5666-5218
Atsushi Nakajima https://orcid.org/0000-0002-6263-1436

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