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Nonalcoholic fatty liver disease: What nurses need to know

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TEFI / SHUTTERSTOCK

Abstract: Nonalcoholic fatty liver disease (NAFLD) is defined as storage of excess fat in the liver not caused by heavy alcohol consumption. Nonalcoholic steatohepatitis is the severe form of NAFLD. This article discusses causes, diagnosis, and nursing interventions for patients with either disorder.

Keywords: cirrhosis, diabetes mellitus, fatty liver disease, hepatic fibrosis, insulin resistance, magnetic resonance elastography, NAFLD, NAFLD Activity Score, NASH, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, transient elastography

AFFECTING UP TO 100 million people in the US and up to 35% of the population worldwide, nonalcoholic fatty liver disease (NAFLD) is defined as storage of excess fat in the liver not caused by heavy alcohol consumption. Nonalcoholic steatohepatitis (NASH) is the more severe form of NAFLD. Unlike NAFLD, NASH is characterized by significant hepatic inflammation.[2] An estimated 10% to 20% of people with NAFLD develop NASH (see *How fatty liver develops*).[1,4]

Worldwide, the number of people age 65 or older is projected to increase from 524 million in 2010 to nearly 1.5 billion in 2050. Because advancing age is a major risk factor for NAFLD, its incidence is expected to increase as the population ages. NAFLD and NASH are now leading indications for liver transplantation in the US.[5-8] This article discusses causes, diagnosis, and nursing interventions for patients with NAFLD and NASH.

Metabolic syndrome and other risk factors

NAFLD is a complex disease dictated by both genetic and acquired factors, including metabolic syndrome (also called insulin resistance syndrome). NAFLD is considered the hepatic manifestation of metabolic syndrome.[3,8-10] Under criteria established by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III), metabolic syndrome is defined as the presence of any three of the following five factors.[10]

- abdominal obesity, defined as a waist circumference of 102 cm (40 in) or more in men and 88 cm (35 in) or more in women.
- serum triglycerides 150 mg/dL (1.7 mmol/L) or more, or drug treatment for elevated triglycerides.
- serum high-density lipoprotein (HDL) cholesterol less than 40 mg/dL (1 mmol/L) in men and less than 50 mg/dL (1.3 mmol/L) in women, or drug treatment for low HDL cholesterol.
- BP 130/85 mm Hg or more, or drug treatment for elevated BP.
- fasting plasma glucose (FPG) 100 mg/dL (5.6 mmol/L) or more, or drug treatment for elevated blood glucose.

Currently, up to 25% of the US population is affected by metabolic syndrome and approximately 90% of patients with NAFLD have more than one feature of metabolic syndrome.[8,11] Metabolic syndrome is associated with cardiovascular disease and type 2 diabetes.

Here is a closer look at major risk factors associated with NAFLD and NASH.

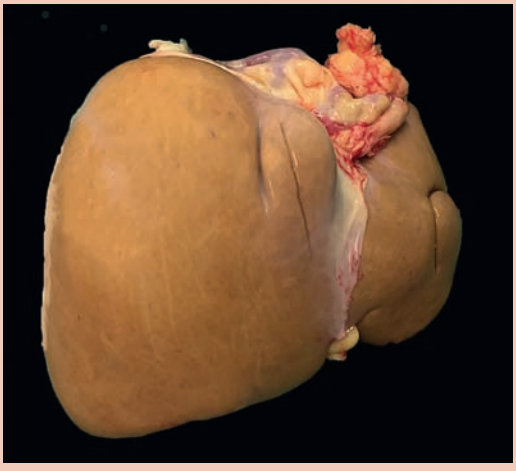
- **Older age.** Aging is a significant risk factor for several chronic liver diseases and disorders, including NAFLD and NASH.[7,12] Recent studies show increased rates of NAFLD among older adults compared with younger patients.[12,13]

Because of age-related cellular, tissue, and functional changes in the aging liver, older patients have significantly worse disease than younger patients. With advancing age, the liver loses functional capacity, becoming more susceptible to damage from alcohol, drugs, and toxins, and less able to regenerate or tolerate transplantation.[8,11,12] Additional stressors affecting the aging liver include systemic metabolic diseases and disorders, such as systemic inflammation, insulin resistance, hypertension, type 2 diabetes mellitus, and obesity.[11,12]

The loss of hepatocytes associated with the aging process leads to reductions in serum levels of albumin and increases in alkaline phosphatase and aminotransferase levels. The metabolism of cholesterol in the liver also decreases with the aging process, increasing blood cholesterol levels over time.[7]

- **Obesity.** Approximately 30% of obese patients and up to 90% of morbidly obese patients have a fatty liver.[5,6] However, not all patients with NAFLD are overweight or obese. From 8% to 10% of NAFLD patients have a body mass index of less than 25 and are considered lean, supporting the role of genetics in development of the disease.[4]
- **Diabetes mellitus.** An estimated 1 in 10 middle-aged American adults has diabetes mellitus.[11] In a large prospective study, patients with diabetes were shown to have a significantly higher incidence of NAFLD and hepatocellular carcinoma (HCC) than individuals without diabetes.[11] Along with cardiovascular disease, malignancies are common causes of death in patients with NAFLD and NASH.[13]
- **Insulin resistance (IR).** Characterized by a widespread diminished cellular response to insulin, IR is both a key component of metabolic syndrome and a risk factor for NAFLD.[5] Normally, insulin is released in response to food consumption and increased blood glucose levels, promoting cellular uptake of glucose in skeletal muscle, adipose tissue, and the liver. With IR, cells cannot readily absorb glucose from the bloodstream, leading

How fatty liver develops[30]



Fatty liver is caused by an accumulation of triglycerides in liver cells. Normally, liver cells contain some fat, which is either oxidized and used for energy or converted to triglycerides. This fat is derived from free fatty acids released from adipose tissue. Abnormal accumulation occurs when the delivery of free fatty acids to the liver is increased, as in starvation and diabetes mellitus, or when the intrahepatic metabolism of lipids is disturbed, as in alcoholism.

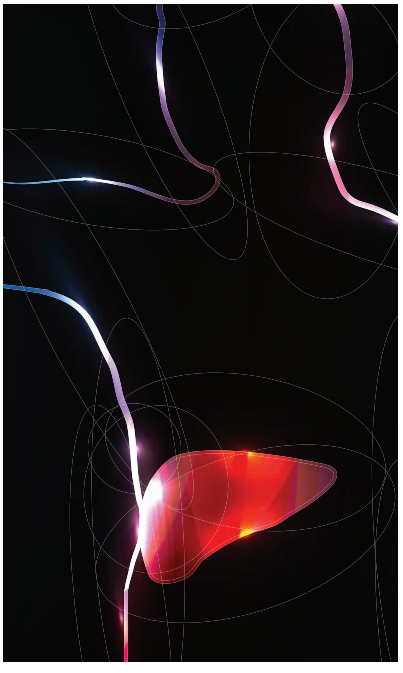
The liver shown here was harvested from a patient with risk factors for nonalcoholic fatty liver disease. It has the characteristic swollen and yellow appearance of fatty liver disease. The biopsy showed moderate large-droplet steatosis but no steatohepatitis or fibrosis.

Photo courtesy of Dr. Amit Mathur, Transplantation Surgery, Mayo Clinic Arizona.

to hyperglycemia. Hyperglycemia stimulates further insulin production, resulting in hyperinsulinemia.[6] The combined effect of hyperinsulinemia and IR leads to increased free fatty acid in the liver and increased production of triglycerides, which can cause or worsen hepatic steatosis.[5,14]

The presence of IR is an independent predictor of advanced liver fibrosis in patients with NAFLD.[7] Due to the strong association between reduced insulin sensitivity and increased incidence of cardiovascular disease with NAFLD, diabetes screening for patients with NAFLD is suggested.[8]

- **Obstructive sleep apnea (OSA).** Hypoxia secondary to OSA has been linked to IR and lipogenesis, causing a systemic proinflammatory state. Recent research has linked the presence and severity of hypoxia secondary to OSA to the severity of liver fibrosis associated with NASH.[14]
- **Polycystic ovary syndrome (POS).** This disorder is also associated with IR. Because 55% of women with POS present with NAFLD, women with POS should be evaluated for NAFLD.[8]
- **Gender.** The incidence of NAFLD is known to be higher in males and postmenopausal females than other groups.[7]
- **Drugs.** NAFLD can be triggered by many medications, such as amiodarone, aspirin, estrogens, glucocorticoids, methotrexate, tamoxifen, and tetracycline.[7]
- **Genetic factors.** Recent evidence supports a strong genetic connection between development of NAFLD and progression to NASH.[13,15,16] Ethnicity is also considered to be a risk factor, with Hispanic individuals being more susceptible than people in non-Hispanic groups.[4]
- **Diet.** Poor dietary choices are important factors in the development and progression of NAFLD.[12,14,17] A diet that is high in red and processed meats, refined sugars and grains, saturated fats, high-fat dairy products, and sugary beverages are associated with a greater likelihood for development of metabolic disorders such as type 2 diabetes, obesity, and IR—all of which can progress to NAFLD and NASH.[7,14]



The most common initial signs and symptoms of NAFLD are nonspecific, such as fatigue, and do not correlate to disease severity.

In addition, excessive calorie intake can result in accumulation of excessive triglycerides and free fatty acids in the liver, leading to hepatic steatosis.[7] This effect is known to occur rapidly, within days to weeks.[6,7] One study of patients referred to an urban hospital-based lipid clinic showed a NAFLD prevalence of 50%.[5] Excessive calorie intake of unhealthy diet options combined with a sedentary lifestyle are known factors contributing to fatty liver, making healthy dietary choices essential to prevent or slow progression of NAFLD.[4]

- **Other factors.** Additional known risks for development of NAFLD include inflammatory bowel disease, inborn errors of metabolism, and occupational exposure to toxins such as organic solvents.[7]

Notes about NASH

Up to 20% of patients with NAFLD progress to NASH, which is associated with hepatic tissue damage, inflammation, cirrhosis, hepatocellular necrosis, and liver failure.[4,7,18]

Cirrhosis is a late stage of hepatic fibrosis and is generally considered to be irreversible in advanced stages.[19] NASH is associated with rapid progression of liver fibrosis and the potential to develop HCC and eventual liver failure.[4,5,7,11] Cirrhosis is present in 70% to 90% of patients with HCC. According to the World Health Organization, HCC is the fifth most common cancer worldwide and was the second most common cause of cancer-related death in 2015.[11]

Morbidity from NASH is on the rise. Cirrhosis caused by NASH increased 170% for individuals on the US liver transplant waitlist between 2004 and 2013. NASH-associated cirrhosis is now the second leading indication for liver transplantation in the US.[15]

Assessment and diagnosis

The most common initial signs and symptoms of NAFLD are nonspecific, such as fatigue and malaise, and do not correlate to the severity of disease. Some patients report pain in the right upper abdomen early in disease. Hepatosplenomegaly is present in up to 50% of patients; however, as the disease progresses, the liver shrinks in size and the spleen enlarges. Pruritus, hyperbilirubinemia, and jaundice may also occur.[7]

Diagnostic lab and imaging findings suggesting NAFLD include elevated liver enzymes and hepatic steatosis visible on transabdominal liver ultrasound.[14,18] Transabdominal

liver ultrasound, which is noninvasive and widely available, is the preferred initial radiologic study to assess for fatty infiltration of the liver.[11]

Other noninvasive methods used to assess liver function and structure include a liver fibrosis panel. The presence of circulating biomarkers can identify the extent of liver damage.[5,7] Common serologic biomarkers associated with liver dysfunction include elevated aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase, and cytokeratin-18.[4-6]

Although elevated liver enzymes can be present, NAFLD cannot be diagnosed by blood tests alone.[20] Besides excluding excessive alcohol consumption and other possible causes of chronic liver disease, the clinician must establish the presence of hepatic steatosis by imaging or biopsy (see *Ruling out alcoholic steatohepatitis*).[2]

Transient elastography (TE), a noninvasive method to assess the extent of liver stiffness, can provide an estimate of liver fibrosis.[4] TE measures liver stiffness with a device that utilizes an ultrasound-like probe to send shear waves to the liver and back to the probe. It has been shown to have a high degree of accuracy in predicting advanced fibrosis.[14] TE is highly sensitive for distinguishing between absent, mild, and severe fibrosis and is useful to track disease progression over time.[7,21]

Magnetic resonance elastography (MRE) is a modification of MRI that enables analysis of the entire liver; in contrast, TE focuses on a smaller part of the liver. However, MRE is not widely available. Although slightly less accurate in estimating the extent of liver disease than MRE, TE is portable and widely available at the point of care.[5]

Calculating the FIB-4 index[3,23,32]

$$\text{FIB-4} = \frac{\text{Age (}years\text{)} \times \text{AST (}U/L\text{)}}{\text{Platelet count (}10^9/L\text{)} \times \sqrt{\text{ALT (}U/L\text{)}}} =$$

Using this formula, clinicians can use an online calculator to calculate a patient's FIB-4 index, an indicator of fibrosis severity.

Gauging disease severity

For patients diagnosed with NAFLD, the nonalcoholic fatty liver activity score (NAS) can be used to guide treatment decisions. Based on biopsy results, the NAS is the sum of scores for steatosis (0 to 3), lobular inflammation (0 to 3), and hepatocellular ballooning (0 to 2).[2]

Fibrosis, which is not included in the NAS, can be staged separately as follows:[22]

- F0: no scarring (no fibrosis)
- F1: minimal scarring
- F2: significant fibrosis
- F3: fibrosis spreading and forming bridges with other fibrotic liver areas (severe fibrosis)
- F4: cirrhosis (advanced scarring).

Another widely used fibrosis scoring system is a calculation using the fibrosis-4 (FIB-4) index, which was originally developed to stage liver disease in patients with chronic hepatitis C virus infection. The FIB-4 index is based on patient age, platelet count, and AST and ALT levels. FIB-4 calculations are simple and results are available immediately (see *Calculating the FIB-4 index*).[4,23]

FIB-4 results can be used to guide the decision to perform an invasive liver biopsy. For example, a low FIB-4 index may indicate that medical management without an invasive liver biopsy is appropriate.[4] The current American Association for the Study of Liver Disease (AASLD) guidelines recommend the use of NAS, FIB-4, TE, and MRE, if available, to identify patients at high risk for liver fibrosis.[4,24]

When is liver biopsy indicated?

For most patients, clinical assessment, noninvasive studies, scoring tools, and imaging techniques are enough to diagnose NAFLD. However, a liver biopsy is considered the gold standard for assessing the extent of hepatocellular damage seen in NAFLD and to accurately identify progression to NASH.[2,5,12] Liver biopsy may be indicated to confirm the diagnosis, assess the severity of liver damage, and identify the stage of liver fibrosis.[5,25]

Liver biopsy should be considered in patients with NAFLD who are at increased risk for advanced fibrosis or NASH, but the healthcare provider must weigh the risks and benefits.[24] A liver biopsy is expensive and carries some risk for morbidity and mortality. Additionally, because the liver biopsy specimen represents a very small sample of the total liver tissue volume,

Ruling out alcoholic steatohepatitis[7,31]

In order to diagnose NAFLD, the clinician must rule out alcohol as the cause of fatty liver. Alcoholic steatohepatitis may be ruled out when the patient consumes less than 20 g of alcohol a day. In the US, one alcoholic drink contains about 14 g of pure alcohol. This is the amount found in 12 oz of regular beer, 5 oz of wine, or 1.5 oz of distilled spirits. The patient's clinical history, dietary history, medication use, occupational exposure to organic solvents, and family history of liver disease should also be investigated.

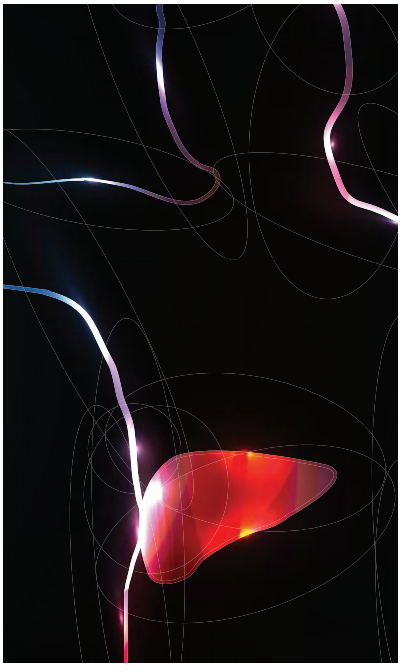
accurate interpretation requires expertise.[24,25]

Initial management

A fundamental component of NAFLD and NASH management is lifestyle modification. Importantly, this includes avoiding alcohol, a known hepatotoxin, to prevent further liver damage.[18]

The European Association for the Study of the Liver states that a 7% weight reduction may be adequate for resolving hepatic steatosis and liver inflammation. The AASLD recommends that a decrease of 10% body weight may resolve mild to moderate fibrosis, reduce hepatic inflammation, and recover some loss of liver function.[4,7,16] A large randomized controlled trial involving 154 patients with NAFLD demonstrated that lifestyle modifications including a 7% to 10% weight reduction and aerobic exercise over a 1-year period resulted in remissions of 64% in the lifestyle modification group, compared with only 20% in the control group. Remissions were reported as improvements in liver enzyme levels, reduced liver fat, and decreased liver fibrosis.[26]

Dietary and calorie restriction are key interventions in preventing and managing NAFLD. A reduction of 450 to 1,000 kilocalories per day has proven to be both safe and effective for this population.[7] Nutritional recommendations for patients with NAFLD include carbohydrate intake of 40% to 50% of total dietary intake, with an increase in the amount of complex carbohydrates that are rich in dietary fiber.[7,14,17] Tight control of diabetes and/or IR, treatment of dyslipidemia, and discontinuing offending causative agents are also important management strategies.[8] It is also recommended that fat intake be less than 30% of the daily calorie intake, with an increase of mono- and polyunsaturated fats over saturated fats.[7,14,17]



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To promote weight loss, if indicated, and encourage lifestyle and dietary modifications, nurses should explain the implications of metabolic syndrome to their patients. Referral to a dietitian may be beneficial. Results from one study revealed that reading a brochure resulted in 6% of participants achieving a 5% weight loss but meeting every other week with a dietitian for 3 months produced a 4% to 11% weight loss.[8]

For severely obese patients, bariatric surgery is effective to reduce body weight and improve glycemic control, quality of life, and long-term survival. Bariatric surgery may also lead to improvement in some obesity-related comorbidities, such as OSA. Although bariatric surgery offers benefits for appropriate candidates, no randomized controlled trials have been conducted to examine the benefits of bariatric surgery for patients with NAFLD and the appropriateness of bariatric surgery for patients with NAFLD is not yet established.[7,17] However, the AASLD states that bariatric surgery improves or eliminates comorbid disease in most patients and improves long-term outcomes from cardiovascular disease and malignancy, the two most common causes of death in patients with NAFLD, so bariatric surgery can be considered in eligible obese individuals with NAFLD or NASH.[24]

Exercise is known to reduce IR and promote a healthy weight. Aerobic or resistance exercise of moderate intensity, three to four times a week for 20 to 40 minutes per session, is effective for fat mobilization from the liver. However, it is recommended that increased physical activity be accompanied by a healthier diet to achieve the desired goals.[4,8,17]

Pharmacotherapy

The AASLD recommends that pharmacologic treatments be generally limited to patients with biopsy-proven NASH and fibrosis.[11,20] For appropriate patients, prescribed medications may include the following.

- Pioglitazone, an oral hypoglycemic agent, has been shown to improve fibrosis, inflammation, and steatosis in patients with and without type 2 diabetes who have NASH confirmed by liver biopsy.[7,17,24,27]
- The use of statins is somewhat controversial due to the potential for statin-induced hepatotoxicity. However, three trials—the Incremental Decrease in End Points Through Aggressive Lipid Lowering (IDEAL) trial, Greek Atorvastatin and Coronary Heart Disease Evaluation (GREACE) trial, and Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial—all demonstrated the improvement of liver enzymes in patients with NAFLD. These trials

endorsed the safe use of statins even in patients with compensated cirrhosis.[7,24]

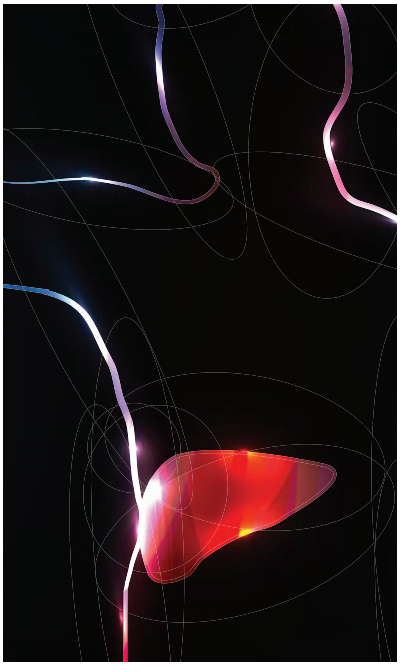
The statin ezetimibe was examined in a 24-month trial with 45 patients newly diagnosed with NAFLD via liver biopsy. The results of this trial demonstrated that ezetimibe significantly improved visceral fat areas, fasting insulin, concentration of triglycerides, total cholesterol, levels of small low-density lipoproteins and very small low-density lipoproteins, as well as significantly lowering levels of serum ALT and C-reactive protein, an inflammatory marker.[7] A recent meta-analysis showed that ezetimibe improved NAS in individuals with NAFLD but did not improve hepatic steatosis.[28]

The AASLD states that statins do not place patients with NAFLD or NASH at higher risk for serious liver injury; therefore, statins may be prescribed to treat dyslipidemia in patients with NAFLD and NASH. However, it is recommended that statins be avoided in patients with decompensated cirrhosis.[17,24]

- Vitamin E is an antioxidant and free-radical scavenger that protects the structural components of cell membranes. The AASLD states that vitamin E may be considered for adults without diabetes who have biopsy-proven NASH.[5,24]
- Vaccinations against hepatitis A and hepatitis B are recommended, as are pneumococcal and influenza vaccines and other standard immunizations recommended for the general population.[11,27]

Patient teaching

Nurses are in a strategic position to educate patients, caregivers, and families about NAFLD and NASH. Collaborating with healthcare team members in other disciplines, nurses can work with patients and families to develop a practical plan of care that will help patients lose and maintain weight, make informed dietary



Collaborating with other healthcare team members, nurses can work with patients and families to develop a practical plan of care.

choices, and manage comorbidities such as diabetes. Teaching points include the following.

- Stress the importance of avoiding alcohol and medications or substances that exacerbate liver disease.
- Inform patients that a diet rich in fruits, vegetables, and whole grains has been proven beneficial as part of the treatment plan for NAFLD and NASH.
- Advise patients to develop and maintain a safe and effective exercise and activity plan. Unless contraindicated, a goal of 30 minutes per day several times a week has been shown to have many benefits for patients with NAFLD and NASH, including weight reduction and management, cholesterol control, and increased exercise tolerance.[14,29]
- Tell patients who are overweight that weight loss can help reduce hepatosteatosis and can be achieved either by a hypocaloric diet alone or in conjunction with increased physical activity. A combination of a hypocaloric diet (daily reduction by 450 to 1,000 kcal) and moderate-intensity exercise is likely to provide the best likelihood of sustaining weight loss over time and reducing hepatosteatosis.[8,24]
- Educate patients, caregivers, and families about managing diabetes with diet choices, medications, exercise, and regular blood glucose monitoring.
- Advise patients to keep a written record or journal including signs and symptoms, even those that may seem unrelated to their condition, and to write down any questions they want to ask the provider at the next appointment.
- Recommend maintaining a current list of all prescription and nonprescription medications, vitamins, and supplements, including over-the-counter (OTC) products. Tell patients to follow prescriber or manufacturer instructions on all medications and OTC drugs and to check with the healthcare provider before using any new drugs or herbal remedies, as not all products are safe.[8,24]
- Bring all relevant and requested medical records to healthcare appointments, including a current medication list.
- Suggest that a family member, caregiver, or friend accompany patients to appointments to ensure that all discussions and information reviewed are understood and remembered.[24]

The American Liver Foundation website, https://liverfoundation.org, is a useful resource for healthcare professionals, patients, and families who want to learn about liver health and disease. ■

REFERENCES

1. National Institute of Diabetes and Digestive and Kidney Disease. Definition & Facts of NAFLD & NASH. 2016. www.niddk.nih.gov/health-information/liver-disease/nafld-nash/definition-facts.

2. Sheth SG, Chopra S. Epidemiology, clinical features, and diagnosis of nonalcoholic fatty liver disease in adults. UpToDate. 2018. www.uptodate.com.

3. Sharma B, Savio J. Nonalcoholic steatohepatitis. StatPearls [Internet]. 2019. www.ncbi.nlm.nih.gov/books/NBK470243.

4. Sayiner M, Lam B, Golabi P, Younossi ZM. Advances and challenges in the management of advanced fibrosis in nonalcoholic steatohepatitis. *Therap Adv Gastroenterol*. 2018;11:17.

5. Sao R, Aronow WS. Association of non-alcoholic fatty liver disease with cardiovascular disease and subclinical atherosclerosis. *Arch Med Sci*. 2018; 14(6):1233-1244.

6. Sharp KPH, Schultz M, Coppell KJ. Is non-alcoholic fatty liver disease a reflection of what we eat or simply how much we eat? *JGH Open*. 2018;2(2): 59-74.

7. Lucas C, Lucas G, Lucas N, Krzowska-Firych J, Tomasiewicz K. A systematic review of the present and future of non-alcoholic fatty liver disease. *Clin Exp Hepatol*. 2018;4(3):165-174.

8. Advance Healthcare Network. Non-alcoholic fatty liver disease: an overview of key concepts for nurses. www.advanceweb.com. [e-pub November 17, 2014]

9. National Heart, Lung, and Blood Institute. Metabolic syndrome. www.nhlbi.nih.gov/health-topics/metabolic-syndrome.

10. Meigs JB. Metabolic syndrome (insulin resistance syndrome or syndrome X). UpToDate. 2019. www.uptodate.com.

11. Mak LY, Cruz-Ramón V, Chinchilla-López P, et al. Global epidemiology, prevention, and management of hepatocellular carcinoma. *Am Soc Clin Oncol Educ Book*. 2018;38:262-279.

12. Stahl EC, Haschak MJ, Popovic B, Brown BN. Macrophages in the aging liver and age-related liver disease. *Front Immunol*. 2018;9:2795.

13. Albhaisi S, Issa D, Alkhouri N. Non-alcoholic fatty liver disease: a pandemic disease with multisystem burden. *Hepatobiliary Surg Nutr*. 2018; 7(5):389-391.

14. Wisocky J, Paul S. The rising incidence of nonalcoholic fatty liver disease. *Nurse Pract*. 2017; 42(7):14-20.

15. Danford CJ, Yao ZM, Jiang ZG. Non-alcoholic fatty liver disease: a narrative review of genetics. *J Biomed Res*. 2018;32(5):389-400.

16. Kudaravalli P, Savio J. Nonalcoholic fatty liver. StatPearls [Internet]. 2019. www.ncbi.nlm.nih.gov/books/NBK541033.

17. Chalasani N, Younossi Z, Lavine JE, 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;67(1):328-357.

18. Polewiczowska B, Aldulaimi D. Recent advances in non-alcoholic fatty liver disease. *Gastroenterol Hepatol Bed Bench*. 2018;11(4):363-365.

19. Goldberg E, Chopra S. Cirrhosis in adults: etiologies, clinical manifestations, and diagnosis. UpToDate. 2018. www.uptodate.com.

20. Yao H, Qiao YJ, Zhao YL, et al. Herbal medicines and nonalcoholic fatty liver disease. *World J Gastroenterol*. 2016;22(30):6890-6905.

21. El-Gohary M, Moore M, Roderick P, et al. Local care and treatment of liver disease (LOCATE)—a cluster-randomized feasibility study to discover, assess and manage early liver disease in primary care. *PLoS One*. 2018;13(12):e0208798.

22. Pavlov CS, Casazza G, Nikolova D, et al. Transient elastography for measurement of liver fibrosis and cirrhosis in people with alcoholic liver disease. Cochrane. 2015. www.cochrane.org.

23. Fibrosis-4 (FIB-4) calculator. Hepatitis C Online. www.hepatitisc.uw.edu/page/clinical-calculators/fib-4.

24. Danford CJ, Connelly MA, Shalaurova I, et al. A pathophysiologic approach combining genetics and insulin resistance to predict the severity of nonalcoholic fatty liver disease. *Hepatol Commun*. 2018;2(12):1467-1478.

25. Isabela Andronescu C, Roxana Purcarea M, Aurel Babes P. The role of noninvasive tests and liver biopsy in the diagnosis of nonalcoholic fatty liver disease. *J Med Life*. 2018;11(3):243-246.

26. Zelber-Sagi S, Godos J, Salomone F. Lifestyle changes for the treatment of nonalcoholic fatty liver disease: a review of observational studies and intervention trials. *Therap Adv Gastroenterol*. 2016;9(3):392-407.

27. Chopra S, Lai M. Management of nonalcoholic fatty liver disease in adults. UpToDate. 2019. www.uptodate.com.

28. Lee HY, Jun DW, Kim HJ, et al. Ezetimibe decreased nonalcoholic fatty liver disease activity score but not hepatic steatosis. *Korean J Intern Med*. 2019;34(2):296-304.

29. Hearn C, Ellington BJ, Jones R. The role of the nurse practitioner in the management of nonalcoholic fatty liver disease. *Gastroenterol Nurs*. 2018;41(5):424-426.

30. Porth CS. *Essentials of Pathophysiology: Concepts of Altered Health States*. 4th ed. Philadelphia, PA: Wolters Kluwer; 2014.

31. Patel R, Gossman W. Alcoholic liver disease. StatPearls [Internet]. 2019. www.ncbi.nlm.nih.gov/books/NBK546632.

32. Sterling RK, Lissen E, Clumeck N, et. al. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV co-infection. *Hepatology*. 2006;43(6):1317-1325.

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The author and planners have disclosed no potential conflicts of interest, financial or otherwise.

DOI-10.1097/01.NURSE.0000654028.01550.56