ISSN: 2692-5206
AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

A SYSTEMATIC REVIEW OF FOLLOW-UP DISEASE PROGRESSION IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER

Khamidova M.I.

Department of Gospital therapy and EndocrinologyAssistant

Andijan State Medical Institute.

Abstract: Hepatosteatosis is defined as an excessive accumulation of triglycerides in hepatocytes. There are 2 main conditions associated with hepatic steatosis: non-alcoholic fatty liver disease (NAFLD) and alcoholic fatty liver disease (AFFLD). In addition, various causes are listed in the pathogenesis of hepatic steatosis, such as metabolic, nutritional, drug (chemotherapy and steroids), and hepatitis C virus (HCV) infection. [1] The natural course of hepatic steatosis varies depending on the etiology and concomitant conditions such as inflammation and fibrosis, which can progress to cirrhosis and liver failure. Therefore, it is important to diagnose and quantify liver steatosis. Liver biopsy is currently the gold standard for evaluating a patient with suspected liver steatosis.[1] However, there are potential drawbacks to liver biopsy, such as sampling error, variability in interpretation, cost, and associated morbidity. Therefore, imaging techniques are commonly used for this purpose. In this article, we will review the etiology, imaging patterns, and quantification of hepatic steatosis using traditional and advanced imaging techniques.

Key words: Hepatosteatosis, metabolic syndrome, NAFLD, metabolically healthy obesity, ultrasonography

NAFLD is the most common form of hepatic steatosis and affects 30%-40% of men and 15%-20% of women in the general population. This disease is considered a hepatic manifestation of metabolic syndrome and has a strong association with insulin resistance, atherosclerosis, obesity, dyslipidemia, and hypertension[3]. Risk factors for NAFLD include insulin resistance and metabolic syndrome i.e., three or more of the following: obesity, diabetes mellitus, hypertension, low high-density lipoprotein levels, and high triglyceride levels. Among these, obesity is the most common risk factor. However, people with normal body weight (body mass index [BMI; kg/m2] Compared to healthy people, patients with lean NAFLD had higher metabolic syndrome occurrence, diastolic blood pressure, hemoglobin A1c, and insulin resistance. Additionally, biochemical and hematologic markers, such as serum ALT, AST, Gamma glutamyl peptidase (γ-GT), and total bilirubin levels, were higher in patients with lean NAFLD than in healthy participants [1].Although the prevalence of metabolic syndrome in lean NAFLD was lower than in obese NAFLD, the impact of lean NAFLD was a stronger risk factor for higher rates of all-cause mortality, cirrhosis, and HCC than obese NAFLD.reported that patients with lean NAFLD showed advanced fibrosis stage, higher incidence of metabolic comorbidities, and higher all-cause mortality than obese NAFLD. Additionally ,that patients with lean NAFLD had a higher risk for cirrhosis, HCC than obese NAFLD. These results suggest the important role of metabolic disorders in this population. The etiology of lean NAFLD is assumed to be based on central obesity and visceral fat Therefore, the BMI-driven approach for NAFLD may need to be reappraised. BMI does not entirely explain the association between visceral fat and NAFLD.

ISSN: 2692-5206
AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

Moreover, the relationship between lean NAFLD and metabolic syndrome is still not fully understood, and more long-term studies are required[2].

Obese patients present with significant variations in metabolic abnormalities, such as hyperglycemia, hypertension, and dyslipidemia. Recently, these patients have been classified into different subphenotypes depending on their metabolic health status. Metabolically healthy obesity (MHO) is a concept derived from clinical observations that some obese people do not present with common metabolic abnormalites; the implications of this for the development of NAFLD across its subphenotypes remain vague. In a study that included 4,432 MHO people, 2,145 patients (48.4%) were presented NAFLD simultaneously. On the contrary, in 225 patients with NAFLD, 14 (6.2%) were metabolically healthy. MHO was considered as a risk factor of NAFLD development. [3]As mentioned earlier, the definition of NAFLD must exclude other causes that can result in inflammation and fatty changes. The significant amount of alcohol intake that differentiates NAFLD from alcoholic fatty liver disease ranges from 10 to 40 g (pure alcohol) a day, and this range varies between studies. The EASL guideline defined the amount of significant alcohol consumption as ≥210 g in men and ≥140 g in women weekly.3 These criteria were also applied in the Korean Association for the Study of Liver NAFLD guidelines.4 In the AASLD guidelines, the standard alcohol drink was defined as 14 g of pure alcohol, and significant alcohol consumption was defined as more than 21 standard drinks in men and 14 in women per week.[2] Recently, it has been suggested that the term NAFLD does not reflect the heterogeneous pathogenesis or various courses of fatty liver disease. Furthermore, the overestimation of the exclusion of alcohol has induced debate about the threshold of ‘significant’ alcohol consumption which is required for the diagnosis of NAFLD. In 2019, a consensus by 32 experts suggested an alternative terminology, metabolic (dysfunction)-associated fatty liver disease (MAFLD), to more accurately reflect the pathogenesis of this disease.[7] The diagnosis of MAFLD is based on the evidence of fat accumulation in the liver in the presence of one of the following three criteria: overweight/obesity, type 2 diabetes mellitus, and evidence of metabolic dysregulation.[4]

Abdominal imaging studies are often ordered instead of liver biopsy to confirm the clinical suspicion of NAFLD. This approach is rationalized because it avoids the risks associated with an invasive procedure. However, the risk of significant bleeding or death from “blind” percutaneous liver biopsy in patients with incidentally detected liver enzyme elevations is exceedingly rare, most likely far less than the figures derived from liver biopsy populations that included patients with conditions that increase biopsy-related morbidity and mortality, such as coagulopathy or liver tumor. In addition, the potential drawbacks of limiting diagnostic procedures to noninvasive tests must be considered. Ultrasonography is commonly used to screen for fatty liver disease. A recent study that correlated radiologic and histologic diagnoses in 24 healthy volunteers and 28 patients with elevated liver enzyme values demonstrated that ultrasound detection of fatty infiltration had a sensitivity of 67%, a specificity of 77%, a positive predictive value of 77%, and a negative predictive value of 67%. Thus, relying on ultrasound to diagnose fatty liver disease gives an incorrect diagnosis in 25% to 33% of patients. One study found computed tomography (CT) to be inferior to ultrasound in diagnosing fatty liver, mostly because associated hepatic iron overload produced a masking effect that decreased the sensitivity of CT scan. However, in another study, when test objects containing variable amounts of fat were scanned to generate a CT scan density calibration curve before patients with fatty livers were evaluated, an excellent

ISSN: 2692-5206
AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

correlation was seen between the hepatic fat content and liver-to-spleen density ratio. Thus calibrated CT scans might be useful in monitoring hepatic fat content. Proton nuclear magnetic resonance (NMR) spectroscopy has also been validated as a reliable test for quantifying liver fat. Hepatic triglyceride content assessed by proton NMR spectroscopy and by liver biopsy correlate almost perfectly. Thus, the latter approach seems to be the best noninvasive way for diagnosing and quantifying liver fat. However, the expense of various imaging modalities is not trivial, and none of these can distinguish simple steatosis from NASH or "uncomplicated" NASH from NASH with fibrosis. Hepatocellular steatosis is the hallmark of NAFL, and presence of more than 5% is required for diagnosis.[8] It is classified into two types: macrovesicular and microvesicular steatosis. Steatosis in NAFLD is usually macrovesicular; however, microvesicular steatosis may also be present in approximately 10% of patients with NAFLD.[5] Many previous studies have suggested that NAFL is a benign disease. Through the several studies performing paired or repeat liver biopsy, NAFL showed significantly superior overall prognosis, including progression to cirrhosis rather than NASH.[7] However, the concept that NAFL is a benign disease was challenged with the accumulation of evidence; it is now regarded as a progressive disease. Recent data suggest that nearly 25% of the patients with NAFL may develop fibrosis. The European Association for the Study of the Liver (EASL) Clinical Practice Guidelines recommend that patients with NAFL without metabolic risk factors should be monitored at 2–3-year intervals considering the low risk of progression.[5] The clinical factors associated with progression to NASH include hypertension, diabetes or insulin resistance, and low aspartate aminotransferase/alanine aminotransferase (AST/ ALT) ratio at the time of liver biopsy.[9] Rapid progression was also often observed with concomitant hepatic injury related to alcohol, toxin exposure, nutrients, drugs, chronic hepatitis C, or autoimmune liver disease. Hence, individuals who have inherited the "bad" tendency to have sustained inflammatory responses might be better off minimizing the consumption of alcohol or foods that stimulate cellular oxidant production and trigger inflammation or taking medications to improve their antioxidant/anti-inflammatory defenses, whereas others with "good" inflammation-control genes can be reassured that they can safely enjoy these pleasures.

References:

1. Loomba R, Sanyal AJ. The global NAFLD epidemic. Nat Rev Gastroenterol Hepatol. 2013;10:686–90.
2. Friedman SL, Neuschwander-Tetri BA, Rinella M, Sanyal AJ. Mechanisms of NAFLD development and therapeutic strategies. Nat Med. 2018;24:908–22
3. Idilman IS, Ozdeniz I, Karcaaltincaba M. Hepatic Steatosis: etiology, patterns, and quantification. Semin Ultrasound CT MR. 2016;37:501–10.
4. Molteni M, Gemma S, Rossetti C. The role of toll-like receptor 4 in infectious and noninfectious inflammation. Mediat Inflamm. 2016;2016:6978936.
5. Csak T, Velayudham A, Hritz I, Petrasek J, Levin I, Lippai D, et al. Deficiency in myeloid differentiation factor-2 and toll-like receptor 4 expression attenuates nonalcoholic steatohepatitis and fibrosis in mice. Am J Physiol Gastrointest Liver Physiol. 2011;300:G433–41.
6. Hasan ST, Zingg JM, Kwan P, Noble T, Smith D, Meydani M. Curcumin modulation of high fat diet-induced atherosclerosis and steatohepatosis in LDL receptor deficient mice. Atherosclerosis. 2014;232:40–51.

ISSN: 2692-5206
AMERICAN ACADEMIC PUBLISHER
INTERNATIONAL JOURNAL OF MEDICAL SCIENCES

7. Lee SB, Park GM, Lee JY, Lee BU, Park JH, Kim BG, et al. Association between non-alcoholic fatty liver disease and subclinical coronary atherosclerosis: an observational cohort study. J Hepatol 2018;68:1018-1024.
8. Jang HR, Kang D, Sinn DH, Gu S, Cho SJ, Lee JE, et al. Nonalcoholic fatty liver disease accelerates kidney function decline in patients with chronic kidney disease: a cohort study. Sci Rep 2018;8:4718. Erratum in: Sci Rep 2021;11(1):11139.
9. Lee JY, Kim KM, Lee SG, Yu E, Lim YS, Lee HC, et al. Prevalence and risk factors of non-alcoholic fatty liver disease in potential living liver donors in Korea: a review of 589 consecutive liver biopsies in a single center. J Hepatol 2007;47:239-244.