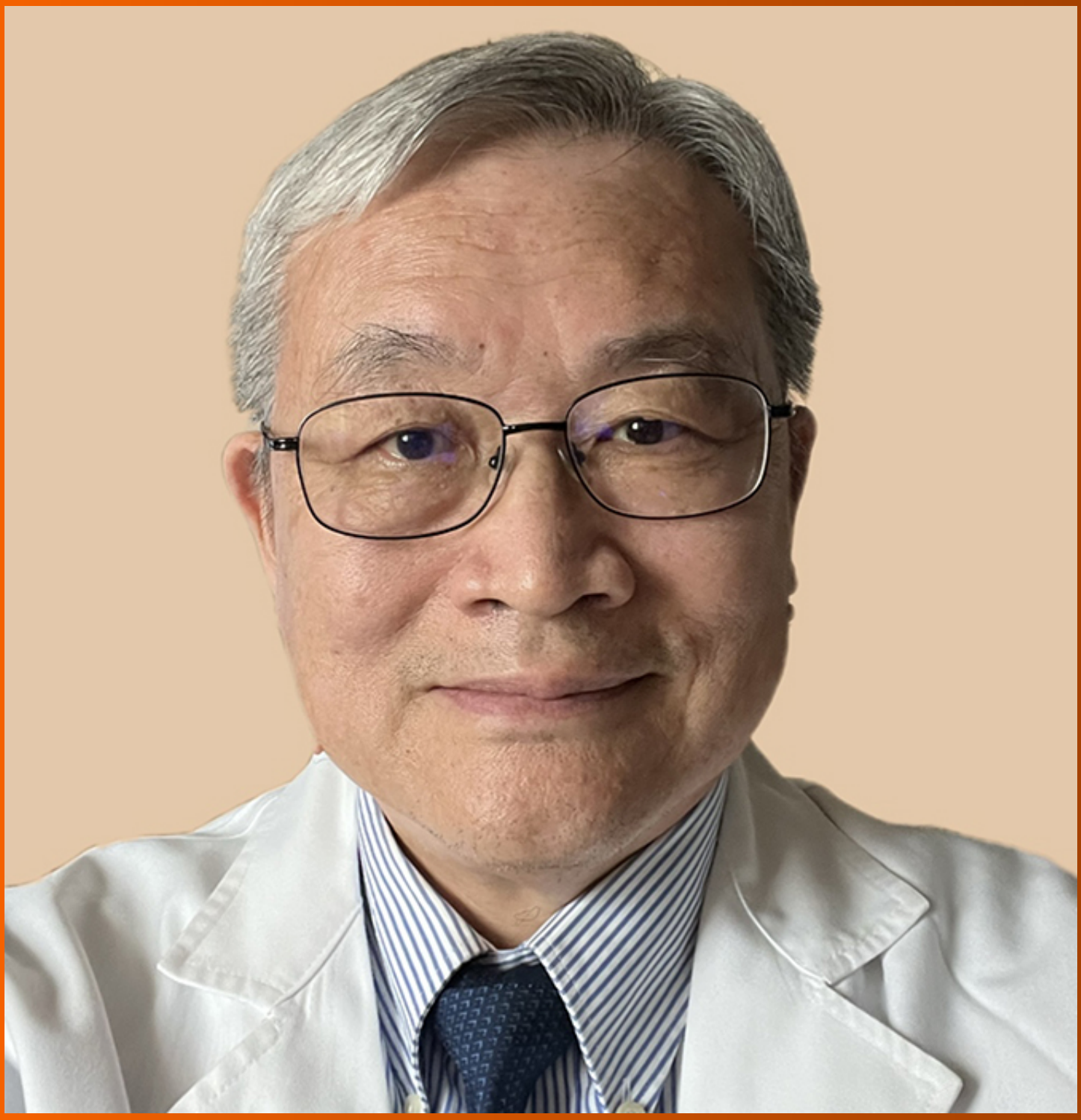
ISSN 1007-9327 (print)
ISSN 2219-2840 (online)

World Journal of *Gastroenterology*

World J Gastroenterol 2024 July 28; 30(28): 3361-3455



Published by Baishideng Publishing Group Inc

World Journal of Gastroenterology

Contents

Weekly Volume 30 Number 28 July 28, 2024

EDITORIAL

MINIREVIEWS

ORIGINAL ARTICLE

Retrospective Study

Observational Study

Basic Study

LETTER TO THE EDITOR

World Journal of Gastroenterology

Weekly Volume 30 Number 28 July 28, 2024

Contents

ABOUT COVER

Editorial Board Member of *World Journal of Gastroenterology*, Dar-In Tai, MD, PhD, Senior Attending Doctor, Professor, Department of Gastroenterology and Hepatology, Chang Gung Memorial Hospital, Taipei 105, Taiwan. tai48978@cgmh.org.tw

AIMS AND SCOPE

The primary aim of *World Journal of Gastroenterology* (*WJG*, *World J Gastroenterol*) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. *WJG* mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

INDEXING/ABSTRACTING

The *WJG* is now abstracted and indexed in Science Citation Index Expanded (SCIE), MEDLINE, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for *WJG* as 4.3; Quartile: Q1. The *WJG*'s CiteScore for 2023 is 7.8.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Yu-Xi Chen*; **Production Department Director:** *Xiang Li*; **Cover Editor:** *Jia-Ru Fan*.

NAME OF JOURNAL
World Journal of Gastroenterology

ISSN
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LAUNCH DATE
October 1, 1995

FREQUENCY
Weekly

PUBLICATION DATE
July 28, 2024

PUBLISHING PARTNER
Shanghai Pancreatic Cancer Institute and Pancreatic Cancer Institute, Fudan University
Biliary Tract Disease Institute, Fudan University

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

POLICY OF CO-AUTHORS
https://www.wjgnet.com/bpg/GerInfo/310

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

PUBLISHING PARTNER's OFFICIAL WEBSITE
https://www.shca.org.cn
https://www.zs-hospital.sh.cn

World Journal of Gastroenterology

Submit a Manuscript: https://www.f6publishing.com

World J Gastroenterol 2024 July 28; 30(28): 3447-3451

DOI: 10.3748/wjg.v30.i28.3447

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LETTER TO THE EDITOR

Exploring non-invasive diagnostics for metabolic dysfunction-associated fatty liver disease

Biao Qu, Zheng Li

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification
Scientific Quality: Grade B
Novelty: Grade B
Creativity or Innovation: Grade B
Scientific Significance: Grade B

P-Reviewer: Kotlyarov S

Received: April 24, 2024
Revised: July 1, 2024
Accepted: July 8, 2024
Published online: July 28, 2024
Processing time: 90 Days and 8.2 Hours

Biao Qu, Department of Clinical Pharmacology, The Second Hospital of Anhui Medical University, Hefei 230601, Anhui Province, China

Zheng Li, Jiangsu Engineering Research Center of Cardiovascular Drugs Targeting Endothelial Cells, College of Health Sciences, School of Life Sciences, Jiangsu Normal University, Xuzhou 221000, Jiangsu Province, China

Corresponding author: Zheng Li, PhD, Lecturer, Pharmacist, Jiangsu Engineering Research Center of Cardiovascular Drugs Targeting Endothelial Cells, College of Health Sciences, School of Life Sciences, Jiangsu Normal University, No. 101 Shanghai Road, Xuzhou 221000, Jiangsu Province, China. lizhengcpu@163.com

Abstract

The population with metabolic dysfunction-associated fatty liver disease (MAFLD) is increasingly common worldwide. Identification of people at risk of progression to advanced stages is necessary to timely offer interventions and appropriate care. Liver biopsy is currently considered the gold standard for the diagnosis and staging of MAFLD, but it has associated risks and limitations. This has spurred the exploration of non-invasive diagnostics for MAFLD, especially for steatohepatitis and fibrosis. These non-invasive approaches mostly include biomarkers and algorithms derived from anthropometric measurements, serum tests, imaging or stool metagenome profiling. However, they still need rigorous and widespread clinical validation for the diagnostic performance.

Key Words: Metabolic dysfunction-associated fatty liver disease; Non-invasive diagnostics; Circulating biomarkers; Imaging biomarkers; Stool microbial biomarkers

Core Tip: Metabolic dysfunction-associated fatty liver disease (MAFLD) is a burdensome public health problem. The diagnostic assessment of MAFLD is an important step for timely management. Extensive effort and encouraging progress have been made to establish non-invasive tests to diagnose steatohepatitis and fibrosis.

Citation: Qu B, Li Z. Exploring non-invasive diagnostics for metabolic dysfunction-associated fatty liver disease. *World J Gastroenterol* 2024; 30(28): 3447-3451
URL: https://www.wjgnet.com/1007-9327/full/v30/i28/3447.htm
DOI: https://dx.doi.org/10.3748/wjg.v30.i28.3447

TO THE EDITOR

We read with great interest the article by Trinks *et al*[1] on the omics-based biomarkers as diagnostic tools for metabolic dysfunction-associated fatty liver disease (MAFLD). Due to its global epidemic, MAFLD becomes a burdensome public health problem[2]. The development of steatohepatitis, especially liver fibrosis, is most strongly associated with poorer long-term outcomes and increased incidence of liver-related mortality[3-5]. It is in this context that identification of people at risk of progression to advanced stages is necessary to timely offer interventions and appropriate care. Currently, liver biopsy is still the reference standard for diagnosis and staging of MAFLD. However, it is an invasive approach with poor compliance and a small but appreciable risk of complications[6]. Besides, it is also expensive, prone to sampling bias, and has high intra- and interobserver variability[6-8]. These inherent limitations have driven the need for non-invasive approaches to replace liver biopsy in severity assessment and risk stratification of patients with MASLD. In this regard, extensive effort and encouraging progress have been made in this filed. There is now increased availability of non-invasive tests, and some become increasingly incorporated into routine clinical practice[9-12]. These non-invasive approaches mostly include biomarkers and algorithms derived from anthropometric measurements[9], serum tests[10], imaging[11], or stool metagenome profiling[12].

Anthropometric measurements

Anthropometric indicators have been used for prediction of MASLD, such as body mass index, abdomen, waist, and chest circumferences, and trunk fat. These indicators are easy to be determined with simple and affordable equipment, thus making them ideal for use in remote areas or in primary clinical practice[9]. Recently, artificial intelligence, such as machine learning and deep learning, has been applied to assist anthropometric diagnostics of MAFLD[13]. However, these indicators are still limited by suboptimal accuracy, especially in detecting fibrosis[13].

Serum biomarkers and related panels

Increased serum triglycerides, alanine aminotransferase (ALT), aspartate aminotransferase (AST), or ALT/AST ratio are not accurately predictive of MAFLD severity[14,15]. Related panels derived from these biochemical indicators are also subject to low accuracy and specificity, such as fatty liver index for hepatic steatosis, and Bayesian Argumentation *via* Delphi score (body mass index, AST/ALT ratio, and presence of diabetes) for hepatic fibrosis[16,17]. Despite these limitations, they are still commonly used for screening owing to general applicability. Recently, some novel serum biomarkers have been proposed as promising alternatives for diagnosis of non-alcoholic steatohepatitis (NASH) and fibrosis. Circulating concentrations of cytokeratin-18 (CK-18) fragments were proposed to be the most reliable predictor of steatohepatitis[18], and its combination with other indicators in a biomarker panel could further increase the diagnostic performance[19]. However, it has relatively low power to determine the severity of NASH fibrosis[20]. Serum Pro-C3 and metalloprotease-1 inhibitor, are emerging biomarkers for fibrosis with excellent diagnostic performance[21,22]. Subsequently, several biomarker panels are proposed, such as MACK-3 (HOMA-IR, AST, and CK-18 M30)[23] and ADAPT (age, platelet count, diabetes, and PRO-C3)[24], and their diagnostic performance is evaluated in comparative diagnostic accuracy studies[10,25]. In addition, the application of innovative omics technologies has screened out some novel serum biomarkers[26,27], but their accuracy, reproducibility, and reliability have not yet gone through analytical/biological and clinical cohort validation.

Imaging biomarkers

Conventional ultrasonography is the first-line imaging test for detecting hepatic steatosis[28], and newer quantitative ultrasound-based techniques demonstrate superior performance[29]. As a contrast, magnetic resonance imaging-proton density fat fraction is considered more accurate at quantifying liver fat than ultrasonography[30], and even liver biopsy [31]. Current imaging-based biomarkers have poor diagnostic performance for steatohepatitis, especially distinguishing steatohepatitis from fibrosis[32]. Ultrasound-based measurements of liver stiffness by vibration-controlled transient elastography (VCTE), commercially marketed as FibroScan, have demonstrated very good diagnostic accuracy for advanced fibrosis[33]. Likewise, magnetic resonance elastography (MRE) shows low failure rate in diagnosis of advanced fibrosis[34]. More importantly, MRE outperforms VCTE in diagnostic accuracy for earlier stages of fibrosis[30].

Gut-microbiome-derived biomarkers

Dysregulation of the gut microbiome is implicated in the progression of MAFLD as evidenced by several studies[35,36]. This association could be translated into diagnostic capacity for MAFLD. A latest study characterized gut microbiome compositions using metagenomic sequencing of stool samples from patients with biopsy-proven MAFLD, and established a gut microbiome-based metagenomic signature to differentiate between mild or moderate and advanced fibrosis[12]. These microbial biomarkers achieved robust diagnostic accuracy in small samples, and further studies are needed to validate their clinical utility.

In summary, progress has been made in the identification of novel non-invasive diagnostics for MAFLD, including biomarkers and algorithms integrating biomarkers. Although none of biomarkers achieved the sufficient performance to replace liver biopsy in diagnosis of steatohepatitis and fibrosis, some diagnostics are promising tools for identifying advanced fibrosis.

FOOTNOTES

Author contributions: Li Z designed the article; Qu B and Li Z drafted and revised the article.

Supported by The National Natural Science Foundation of China, No. 82104525.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

Country of origin: China

ORCID number: Zheng Li 0000-0002-2882-6600.

S-Editor: Luo ML
L-Editor: Wang TQ
P-Editor: Zhang L

REFERENCES

1 **Trinks J**, Mascardi MF, Gadano A, Marciano S. Omics-based biomarkers as useful tools in metabolic dysfunction-associated steatotic liver disease clinical practice: How far are we? *World J Gastroenterol* 2024; **30**: 1982-1989 [PMID: 38681130 DOI: 10.3748/wjg.v30.i14.1982]

2 **Estes C**, Razavi H, Loomba R, Younossi Z, Sanyal AJ. Modeling the epidemic of nonalcoholic fatty liver disease demonstrates an exponential increase in burden of disease. *Hepatology* 2018; **67**: 123-133 [PMID: 28802062 DOI: 10.1002/hep.29466]

3 **Angulo P**, Kleiner DE, Dam-Larsen S, Adams LA, Bjornsson ES, Charatcharoenwitthaya P, Mills PR, Keach JC, Lafferty HD, Stahler A, Haflidadottir S, Bendtsen F. Liver Fibrosis, but No Other Histologic Features, Is Associated With Long-term Outcomes of Patients With Nonalcoholic Fatty Liver Disease. *Gastroenterology* 2015; **149**: 389-397 [PMID: 25935633 DOI: 10.1053/j.gastro.2015.04.043]

4 **Dulai PS**, Singh S, Patel J, Soni M, Prokop LJ, Younossi Z, Sebastiani G, Ekstedt M, Hagstrom H, Nasr P, Stal P, Wong VW, Kechagias S, Hultcrantz R, Loomba R. Increased risk of mortality by fibrosis stage in nonalcoholic fatty liver disease: Systematic review and meta-analysis. *Hepatology* 2017; **65**: 1557-1565 [PMID: 28130788 DOI: 10.1002/hep.29085]

5 **Hagström H**, Nasr P, Ekstedt M, Hammar U, Stål P, Hultcrantz R, Kechagias S. Fibrosis stage but not NASH predicts mortality and time to development of severe liver disease in biopsy-proven NAFLD. *J Hepatol* 2017; **67**: 1265-1273 [PMID: 28803953 DOI: 10.1016/j.jhep.2017.07.027]

6 **Davison BA**, Harrison SA, Cotter G, Alkhouri N, Sanyal A, Edwards C, Colca JR, Iwashita J, Koch GG, Dittrich HC. Suboptimal reliability of liver biopsy evaluation has implications for randomized clinical trials. *J Hepatol* 2020; **73**: 1322-1332 [PMID: 32610115 DOI: 10.1016/j.jhep.2020.06.025]

7 **Ratziu V**, Charlotte F, Heurtier A, Gombert S, Giral P, Bruckert E, Grimaldi A, Capron F, Poynard T; LIDO Study Group. Sampling variability of liver biopsy in nonalcoholic fatty liver disease. *Gastroenterology* 2005; **128**: 1898-1906 [PMID: 15940625 DOI: 10.1053/j.gastro.2005.03.084]

8 **Merriman RB**, Ferrell LD, Patti MG, Weston SR, Pabst MS, Aouizerat BE, Bass NM. Correlation of paired liver biopsies in morbidly obese patients with suspected nonalcoholic fatty liver disease. *Hepatology* 2006; **44**: 874-880 [PMID: 17006934 DOI: 10.1002/hep.21346]

9 **Almeida NS**, Rocha R, Cotrim HP, Daltro C. Anthropometric indicators of visceral adiposity as predictors of non-alcoholic fatty liver disease: A review. *World J Hepatol* 2018; **10**: 695-701 [PMID: 30386462 DOI: 10.4254/wjh.v10.i10.695]

10 **Sanyal AJ**, Shankar SS, Yates KP, Bolognese J, Daly E, Dehn CA, Neuschwander-Tetri B, Kowdley K, Vuppalanchi R, Behling C, Tonascia J, Samir A, Sirlin C, Sherlock SP, Fowler K, Heymann H, Kamphaus TN, Loomba R, Calle RA. Diagnostic performance of circulating biomarkers for non-alcoholic steatohepatitis. *Nat Med* 2023; **29**: 2656-2664 [PMID: 37679433 DOI: 10.1038/s41591-023-02539-6]

11 **Ajmera V**, Loomba R. Imaging biomarkers of NAFLD, NASH, and fibrosis. *Mol Metab* 2021; **50**: 101167 [PMID: 33460786 DOI: 10.1016/j.molmet.2021.101167]

12 **Loomba R**, Seguritan V, Li W, Long T, Klitgord N, Bhatt A, Dulai PS, Caussy C, Bettencourt R, Highlander SK, Jones MB, Sirlin CB, Schnabl B, Brinkac L, Schork N, Chen CH, Brenner DA, Biggs W, Yooseph S, Venter JC, Nelson KE. Gut Microbiome-Based Metagenomic Signature for Non-invasive Detection of Advanced Fibrosis in Human Nonalcoholic Fatty Liver Disease. *Cell Metab* 2019; **30**: 607 [PMID: 31484056 DOI: 10.1016/j.cmet.2019.08.002]

13 **Razmpour F**, Daryabeygi-Khotbehsara R, Soleimani D, Asgharnezhad H, Shamsi A, Bajestani GS, Nematy M, Pour MR, Maddison R, Islam SMS. Application of machine learning in predicting non-alcoholic fatty liver disease using anthropometric and body composition indices. *Sci Rep* 2023; **13**: 4942 [PMID: 36973382 DOI: 10.1038/s41598-023-32129-y]

14 **Younossi ZM**, Loomba R, Anstee QM, Rinella ME, Bugianesi E, Marchesini G, Neuschwander-Tetri BA, Serfaty L, Negro F, Caldwell SH, Ratziu V, Corey KE, Friedman SL, Abdelmalek MF, Harrison SA, Sanyal AJ, Lavine JE, Mathurin P, Charlton MR, Goodman ZD, Chalasani

NP, Kowdley KV, George J, Lindor K. Diagnostic modalities for nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, and associated fibrosis. *Hepatology* 2018; **68**: 349-360 [PMID: 29222917 DOI: 10.1002/hep.29721]

15 **Verma S**, Jensen D, Hart J, Mohanty SR. Predictive value of ALT levels for non-alcoholic steatohepatitis (NASH) and advanced fibrosis in non-alcoholic fatty liver disease (NAFLD). *Liver Int* 2013; **33**: 1398-1405 [PMID: 23763360 DOI: 10.1111/liv.12226]

16 **Fedchuk L**, Nascimbeni F, Pais R, Charlotte F, Housset C, Ratziu V; LIDO Study Group. Performance and limitations of steatosis biomarkers in patients with nonalcoholic fatty liver disease. *Aliment Pharmacol Ther* 2014; **40**: 1209-1222 [PMID: 25267215 DOI: 10.1111/apt.12963]

17 **McPherson S**, Stewart SF, Henderson E, Burt AD, Day CP. Simple non-invasive fibrosis scoring systems can reliably exclude advanced fibrosis in patients with non-alcoholic fatty liver disease. *Gut* 2010; **59**: 1265-1269 [PMID: 20801772 DOI: 10.1136/gut.2010.216077]

18 **Kwok R**, Tse YK, Wong GL, Ha Y, Lee AU, Ngu MC, Chan HL, Wong VW. Systematic review with meta-analysis: non-invasive assessment of non-alcoholic fatty liver disease--the role of transient elastography and plasma cytokeratin-18 fragments. *Aliment Pharmacol Ther* 2014; **39**: 254-269 [PMID: 24308774 DOI: 10.1111/apt.12569]

19 **Shen J**, Chan HL, Wong GL, Choi PC, Chan AW, Chan HY, Chim AM, Yeung DK, Chan FK, Woo J, Yu J, Chu WC, Wong VW. Non-invasive diagnosis of non-alcoholic steatohepatitis by combined serum biomarkers. *J Hepatol* 2012; **56**: 1363-1370 [PMID: 22314419 DOI: 10.1016/j.jhep.2011.12.025]

20 **Cusi K**, Chang Z, Harrison S, Lomonaco R, Bril F, Orsak B, Ortiz-Lopez C, Hecht J, Feldstein AE, Webb A, Louden C, Goros M, Tio F. Limited value of plasma cytokeratin-18 as a biomarker for NASH and fibrosis in patients with non-alcoholic fatty liver disease. *J Hepatol* 2014; **60**: 167-174 [PMID: 23973932 DOI: 10.1016/j.jhep.2013.07.042]

21 **Leeming DJ**, Grove JI, Kaye P, Hoad C, Francis S, Nielsen MJ, Karsdal MA, Guha IN, Aithal GP. Estimation of serum "true collagen type III formation" (Pro-C3) levels as a marker of non-alcoholic steatohepatitis in a prospective cohort. *J Hepatol* 2017; **66**: S154 [DOI: 10.1016/S0168-8278(17)30582-2]

22 **Abdelaziz R**, Elbasel M, Esmat S, Essam K, Abdelaaty S. Tissue Inhibitors of Metalloproteinase-1 and 2 and Obesity Related Non-Alcoholic Fatty Liver Disease: Is There a Relationship. *Digestion* 2015; **92**: 130-137 [PMID: 26329758 DOI: 10.1159/000439083]

23 **Boursier J**, Anty R, Vonghia L, Moal V, Vanwolleghem T, Canivet CM, Michalak S, Bonnafous S, Michielsen P, Oberti F, Iannelli A, Van Gaal L, Patouraux S, Blanchet O, Verrijken A, Gual P, Rousselet MC, Driessen A, Hunault G, Bertrais S, Tran A, Calès P, Francque S. Screening for therapeutic trials and treatment indication in clinical practice: MACK-3, a new blood test for the diagnosis of fibrotic NASH. *Aliment Pharmacol Ther* 2018; **47**: 1387-1396 [PMID: 29577364 DOI: 10.1111/apt.14621]

24 **Daniels SJ**, Leeming DJ, Eslam M, Hashem AM, Nielsen MJ, Krag A, Karsdal MA, Grove JI, Neil Guha I, Kawaguchi T, Torimura T, McLeod D, Akiba J, Kaye P, de Boer B, Aithal GP, Adams LA, George J. ADAPT: An Algorithm Incorporating PRO-C3 Accurately Identifies Patients With NAFLD and Advanced Fibrosis. *Hepatology* 2019; **69**: 1075-1086 [PMID: 30014517 DOI: 10.1002/hep.30163]

25 **Vali Y**, Lee J, Boursier J, Petta S, Wonders K, Tiniakos D, Bedossa P, Geier A, Francque S, Allison M, Papatheodoridis G, Cortez-Pinto H, Pais R, Dufour JF, Leeming DJ, Harrison SA, Chen Y, Cobbold JF, Pavlides M, Holleboom AG, Yki-Jarvinen H, Crespo J, Karsdal M, Ostroff R, Zafarmand MH, Torstenson R, Duffin K, Yunis C, Brass C, Ekstedt M, Aithal GP, Schattenberg JM, Bugianesi E, Romero-Gomez M, Ratziu V, Anstee QM, Bossuyt PM; Liver Investigation: Testing Marker Utility in Steatohepatitis (LITMUS) consortium investigators. Biomarkers for staging fibrosis and non-alcoholic steatohepatitis in non-alcoholic fatty liver disease (the LITMUS project): a comparative diagnostic accuracy study. *Lancet Gastroenterol Hepatol* 2023; **8**: 714-725 [PMID: 36958367 DOI: 10.1016/S2468-1253(23)00017-1]

26 **Mayo R**, Crespo J, Martínez-Arranz I, Banales JM, Arias M, Mincholé I, Aller de la Fuente R, Jimenez-Agüero R, Alonso C, de Luis DA, Vitek L, Stritesky J, Caballería J, Romero-Gómez M, Martín-Duce A, Mugüerza Huguet JM, Busteros-Moraza JI, Idowu MO, Castro A, Martínez-Chantar ML, Ortiz P, Bruha R, Lu SC, Bedossa P, Noureddin M, Sanyal AJ, Mato JM. Metabolomic-based noninvasive serum test to diagnose nonalcoholic steatohepatitis: Results from discovery and validation cohorts. *Hepatol Commun* 2018; **2**: 807-820 [PMID: 30027139 DOI: 10.1002/hep4.1188]

27 **Sanyal AJ**, Williams SA, Lavine JE, Neuschwander-Tetri BA, Alexander L, Ostroff R, Biegel H, Kowdley KV, Chalasani N, Dasarathy S, Diehl AM, Loomba R, Hameed B, Behling C, Kleiner DE, Karpen SJ, Williams J, Jia Y, Yates KP, Tonascia J. Defining the serum proteomic signature of hepatic steatosis, inflammation, ballooning and fibrosis in non-alcoholic fatty liver disease. *J Hepatol* 2023; **78**: 693-703 [PMID: 36528237 DOI: 10.1016/j.jhep.2022.11.029]

28 **Strauss S**, Gavish E, Gottlieb P, Katsnelson L. Interobserver and intraobserver variability in the sonographic assessment of fatty liver. *AJR Am J Roentgenol* 2007; **189**: W320-W323 [PMID: 18029843 DOI: 10.2214/AJR.07.2123]

29 **Han A**, Zhang YN, Boehringer AS, Montes V, Andre MP, Erdman JW Jr, Loomba R, Valasek MA, Sirlin CB, O'Brien WD Jr. Assessment of Hepatic Steatosis in Nonalcoholic Fatty Liver Disease by Using Quantitative US. *Radiology* 2020; **295**: 106-113 [PMID: 32013792 DOI: 10.1148/radiol.2020191152]

30 **Park CC**, Nguyen P, Hernandez C, Bettencourt R, Ramirez K, Fortney L, Hooker J, Sy E, Savides MT, Alquiraish MH, Valasek MA, Rizo E, Richards L, Brenner D, Sirlin CB, Loomba R. Magnetic Resonance Elastography vs Transient Elastography in Detection of Fibrosis and Noninvasive Measurement of Steatosis in Patients With Biopsy-Proven Nonalcoholic Fatty Liver Disease. *Gastroenterology* 2017; **152**: 598-607 [PMID: 27911262 DOI: 10.1053/j.gastro.2016.10.026]

31 **Noureddin M**, Lam J, Peterson MR, Middleton M, Hamilton G, Le TA, Bettencourt R, Changchien C, Brenner DA, Sirlin C, Loomba R. Utility of magnetic resonance imaging versus histology for quantifying changes in liver fat in nonalcoholic fatty liver disease trials. *Hepatology* 2013; **58**: 1930-1940 [PMID: 23696515 DOI: 10.1002/hep.26455]

32 **Jayaswal ANA**, Levick C, Selvaraj EA, Dennis A, Booth JC, Collier J, Cobbold J, Tunnicliffe EM, Kelly M, Barnes E, Neubauer S, Banerjee R, Pavlides M. Prognostic value of multiparametric magnetic resonance imaging, transient elastography and blood-based fibrosis markers in patients with chronic liver disease. *Liver Int* 2020; **40**: 3071-3082 [PMID: 32730664 DOI: 10.1111/liv.14625]

33 **Siddiqui MS**, Vuppalanchi R, Van Natta ML, Hallinan E, Kowdley KV, Abdelmalek M, Neuschwander-Tetri BA, Loomba R, Dasarathy S, Brandman D, Doo E, Tonascia JA, Kleiner DE, Chalasani N, Sanyal AJ; NASH Clinical Research Network. Vibration-Controlled Transient Elastography to Assess Fibrosis and Steatosis in Patients With Nonalcoholic Fatty Liver Disease. *Clin Gastroenterol Hepatol* 2019; **17**: 156-163 [PMID: 29705261 DOI: 10.1016/j.cgh.2018.04.043]

34 **Wagner M**, Corcuera-Solano I, Lo G, Esses S, Liao J, Besa C, Chen N, Abraham G, Fung M, Babb JS, Ehman RL, Taouli B. Technical Failure of MR Elastography Examinations of the Liver: Experience from a Large Single-Center Study. *Radiology* 2017; **284**: 401-412 [PMID: 28045604 DOI: 10.1148/radiol.2016160863]

35 **Hoyles L**, Fernández-Real JM, Federici M, Serino M, Abbott J, Charpentier J, Heymes C, Luque JL, Anthony E, Barton RH, Chilloux J, Myridakis A, Martinez-Gili L, Moreno-Navarrete JM, Benhamed F, Azalbert V, Blasco-Baque V, Puig J, Xifra G, Ricart W, Tomlinson C, Woodbridge M, Cardellini M, Davato F, Cardolini I, Porzio O, Gentileschi P, Lopez F, Foufelle F, Butcher SA, Holmes E, Nicholson JK,

Postic C, Burcelin R, Dumas ME. Molecular phenomics and metagenomics of hepatic steatosis in non-diabetic obese women. *Nat Med* 2018; **24**: 1070-1080 [PMID: 29942096 DOI: 10.1038/s41591-018-0061-3]

36 **Sharpton SR**, Ajmera V, Loomba R. Emerging Role of the Gut Microbiome in Nonalcoholic Fatty Liver Disease: From Composition to Function. *Clin Gastroenterol Hepatol* 2019; **17**: 296-306 [PMID: 30196156 DOI: 10.1016/j.cgh.2018.08.065]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com