VOLUME 28 NUMBER 3 JULY 2022

pISSN 2287-2728
eISSN 2387-285X

CLINICAL and MOLECULAR HEPATOLOGY

The forum for latest knowledge of hepatobiliary diseases

Fatty liver and risk of dementia

NAFLD increases a risk of stroke

DPP-4 inhibitor-specific biomarkers in NAFLD

LPS promotes HCC by NETs formation via TLR4

CLIF-SOFA score and sepsis

KASL

pISSN 2287-2728
eISSN 2287-285X

CLINICAL and MOLECULAR HEPATOLOGY

https://doi.org/10.3350/cmh.2022.0097
Clinical and Molecular Hepatology 2022;28:481-482

Editorial

Association of nonalcoholic fatty liver disease with incident dementia later in life among elderly adults

Byoung Seok Ye

Department of Neurology, Yonsei University College of Medicine, Seoul, Korea

Keywords: Non-alcoholic fatty liver disease; Dementia; Alzheimer's disease; Metabolic syndrome; Epidemiology

See Article on Page 510

In the recent issue of *Clinical and Molecular Hepatology*, Jeong et al.[1] provided evidence that non-alcoholic fatty liver disease (NAFLD) is associated with the risk of developing dementia in the elderly, especially in the form of Alzheimer's disease (AD). Currently, it is not clear whether 1) hepatic pathophysiology related to NAFLD per se is important for the risk of dementia or 2) NAFLD only reflects the underlying metabolic syndrome that is further related to an increased risk of dementia. Previous studies have shown that metabolic syndrome is closely related to NAFLD.[2-6] Also, the authors defined the presence of NAFLD based on the fatty liver index (FLI) that is calculated using the serum triglyceride, body mass index (BMI), and waist circumference, all of which have a close relationship with the definition of metabolic syndrome. Therefore, with the idea that screening for NAFLD could be a good way to find underlying metabolic syndrome, future studies are warranted to assess the potential benefit of treatment for NAFLD in the population-level risk of dementia occurrence.

AD is a slowly progressive disorder with a long prodromal period. Although it is well proven that FLI accurately reflects the severity of NAFLD in a general population level,[7] the relationship between FLI and NAFLD has not been clearly elucidated in patients with dementia or at-risk population, such as mild cognitive impairment (MCI) showing 10–15% annual rate of progression to AD dementia.[8] Moreover, several risk factors for dementia, such as higher BMI or lower education, during normal aging could be paradoxically associated with slower clinical deterioration in MCI patients[9] or AD dementia patients.[10] The underlying progression of dementia pathology could induce weight loss for at-risk population, which could explain the paradoxical relationship between BMI and dementia. On the other hand, more efficient brain network obtained by higher education could delay the onset of dementia symptoms, given the same burden of AD pathology. However, once dementia symptom does begin, the rate of clinical decline in patients with higher education tend to be faster with higher burden of AD pathology. Further studies are warranted to confirm whether FLI or NAFLD is differently associated with cognitive dysfunction or dementia risk according to the level of cognitive status at study inclusion.

Corresponding author : **Byoung Seok Ye**
Department of Neurology, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Korea
Tel: +82-2-2228-1609, Fax: +82-2-393-0705, E-mail: romel79@yuhs.ac
https://orcid.org/0000-0003-0187-8440

Editor: Young Chang, Soonchunhyang University Hospital Seoul, Korea

Received : Apr. 9, 2022 / **Revised :** May 7, 2022 / **Accepted :** May 11, 2022

It is also noteworthy that sex had interaction effect with FLI on dementia risk (Supplementary Tables 6 and 7 in Jeong et al.[1]). Specifically, lower FLI was associated with lower risk of dementia in men, but not in women. In contrast, higher FLI was associated with dementia risk in women, but not in men. There could be several explanations for this interaction. First, lower FLI could be an important protective factor for men with low-to-intermediate BMI, while higher FLI could be an important risk factor for women with intermediate-to-high BMI. Second, although men and women have different mean BMI and waist circumference,[11,12] the calculation formula for FLI is not sex-specific. Different effect of FLI on dementia risk according to sex could be originated from the lack of consideration for factors that are different by sex in the FLI calculation formula. Further elucidation considering the sex-specific cut-offs for FLI and BMI may be needed to identify a true association between NAFLD and dementia risk.

Lewy body disease (LBD), including Parkinson's disease (PD) and dementia with Lewy bodies, is the second most common degenerative cause of dementia; however, it is clinically underdiagnosed in dementia patients.[13] In this study, LBD was not considered as a cause of dementia. A recent study showed that NAFLD is differently associated with the risk of PD by sex in that NAFLD is associated with lower risk of PD in men, while it is associated with higher risk in women.[14] As patients with mixed dementia from AD/LBD are common but usually diagnosed as AD dementia, future studies are needed to confirm whether NAFLD is differently associated with underlying causes of dementia.

Conflicts of Interest

The author has no conflicts to disclose.

REFERENCES

1. Jeong S, Oh YH, Choi S, Chang J, Kim SM, Son JS, et al. Association of nonalcoholic fatty liver disease with incident dementia later in life among elder adults. Clin Mol Hepatol 2022;28:510-521.
2. Lonardo A, Ballestri S, Marchesini G, Angulo P, Loria P. Nonalcoholic fatty liver disease: a precursor of the metabolic syndrome. Dig Liver Dis 2015;47:181-190.
3. Paschos P, Paletas K. Non alcoholic fatty liver disease and metabolic syndrome. Hippokratia 2009;13:9-19.
4. Godoy-Matos AF, Silva Júnior WS, Valerio CM. NAFLD as a continuum: from obesity to metabolic syndrome and diabetes. Diabetol Metab Syndr 2020;12:60.
5. Vanni E, Bugianesi E, Kotronen A, De Minicis S, Yki-Järvinen H, Svegliati-Baroni G. From the metabolic syndrome to NAFLD or vice versa? Dig Liver Dis 2010;42:320-330.
6. Adams LA, Waters OR, Knuiman MW, Elliott RR, Olynyk JK. NAFLD as a risk factor for the development of diabetes and the metabolic syndrome: an eleven-year follow-up study. Am J Gastroenterol 2009;104:861-867.
7. Papagianni M, Sofogianni A, Tziomalos K. Non-invasive methods for the diagnosis of nonalcoholic fatty liver disease. World J Hepatol 2015;7:638-648.
8. Petersen RC. Mild cognitive impairment. Continuum (Minneap Minn) 2016;22(2 Dementia):404-418.
9. Ye BS, Jang EY, Kim SY, Kim EJ, Park SA, Lee Y, et al. Unstable body mass index and progression to probable Alzheimer's disease dementia in patients with amnestic mild cognitive impairment. J Alzheimers Dis 2016;49:483-491.
10. Stern Y. Cognitive reserve in ageing and Alzheimer's disease. Lancet Neurol 2012;11:1006-1012.
11. Stevens J, Katz EG, Huxley RR. Associations between gender, age and waist circumference. Eur J Clin Nutr 2010;64:6-15.
12. Dagan SS, Segev S, Novikov I, Dankner R. Waist circumference vs body mass index in association with cardiorespiratory fitness in healthy men and women: a cross sectional analysis of 403 subjects. Nutr J 2013;12:12.
13. Walker Z, Possin KL, Boeve BF, Aarsland D. Lewy body dementias. Lancet 2015;386:1683-1697.
14. Jeong SM, Lee HR, Jang W, Kim D, Yoo JE, Jeon KH, et al. Sex differences in the association between nonalcoholic fatty liver disease and Parkinson's disease. Parkinsonism Relat Disord 2021;93:19-26.

Abbreviations:

AD, Alzheimer's disease; BMI, body mass index; FLI, fatty liver index; LBD, Lewy body disease; MCI, mild cognitive impairment; NAFLD, non-alcoholic fatty liver disease; PD, Parkinson's disease