

Letter to the Editor

Analysis of the correlation between non-alcoholic fatty liver disease and bone metabolism indicators in healthy middle-aged men

Dear Editor,

We read with great interest the article by Deng et al¹ on the relationship between bone metabolic indicators and non-alcoholic fatty liver disease (NAFLD) in healthy middle-aged men.

The authors found that body mass index (BMI), diastolic blood pressure, heart rate, blood glucose levels [fasting plasma glucose, postprandial blood glucose and hemoglobin A1c (HbA1c)] and insulin resistance were significantly higher in the NAFLD group than in the non-NAFLD control group. Moreover, the logistic regression analysis showed a positive association between the BMI, homeostasis model assessment (HOMA)-, HOMA-IR, HbA1c and procollagen type I propeptide (P1NP) with the occurrence of NAFLD. The authors speculated that the level of P1NP could be directly involved in lipid metabolism.

The association between NAFLD and P1NP was confirmed in a randomized controlled trial conducted in 46 patients with omega loop gastric bypass². In this study, in order to evaluate the stage of fibrosis and the related factors, a liver biopsy and laboratory tests were performed. The results showed an increase in the stage of fibrosis primarily associated with higher levels of HOMA2-insulin resistance (IR), P1NP, lower osteocalcin, albumin-corrected calcium, parathyroid hormone,

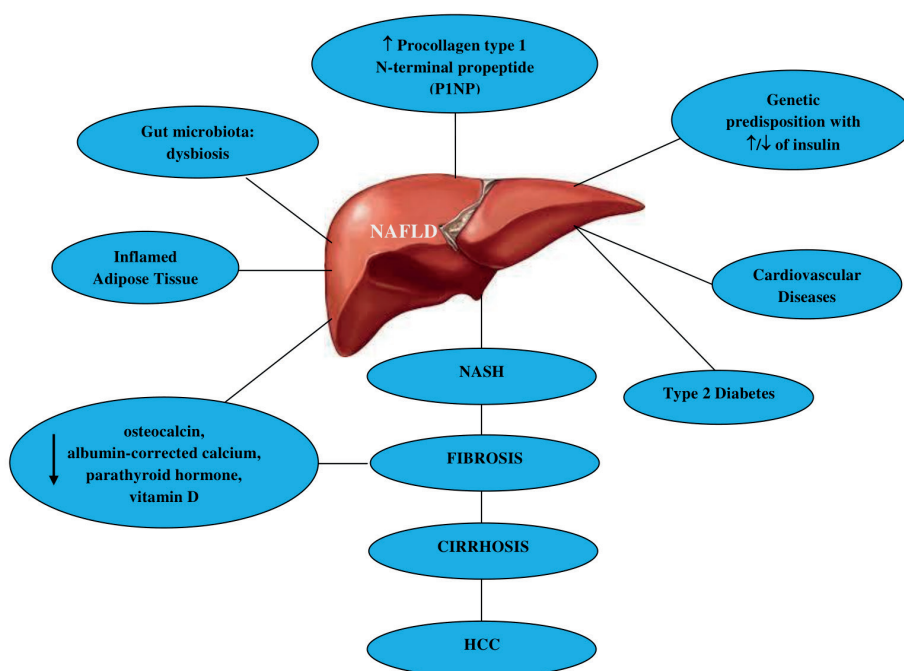


Figure 1. Factors associated with NAFLD and liver fibrosis.

vitamin D, male sex, and older age. Other independent risk factors for advanced fibrosis were metabolic syndrome ($p=0.052$) and diabetes ($p=0.035$).

In a randomized, placebo controlled study, Soifer et al³ investigated on a possible effect of metformin on P1NP in patients with NAFLD. At the end of the study, P1NP was significantly lower among patients who received daily metformin, than in the placebo group ($p<0.007$). Hence, the authors concluded that the effect on P1NP was independent from glucose lowering effect and due to the exposure to metformin.

Recently, Maagensen et al⁴ conducted an interesting cross-sectional cohort study in patients with either normal or impaired glucose metabolism undergoing the oral glucose tolerance test (OGTT) and an isoglycemic intravenous glucose infusion (IIGI). They found a pronounced suppression of P1NP during IIGI compared with OGTT, whilst an alteration of OGTT induced collagen type 1 C-telopeptide (CTX) suppression, in patients with NAFLD+ type 2 diabetes (T2D), though preserving in patients with either NAFLD or T2D. These results suggested that a coexistence of T2D and NAFLD may affect gut-bone axis.

To date, NAFLD is the most frequent liver disease, affecting about the 30% of population⁵; the possible evolution in non-alcoholic steato-hepatitis (NASH) increase the risk of advanced fibrosis/cirrhosis and liver cancer⁶. In this hot topic field, several factors should be evaluated, in particular the genetic profile, pro-inflammatory cytokines and diet^{5,7-9}.

In the post viral era, cirrhosis NAFLD/NASH related, might represent the main reason of liver transplantation¹⁰. Thus, the evaluation of risk factors and associated indicators might be fundamental in both prevention and management.

Conflict of interest

The authors declare no conflicts of interest.

References

- 1) DENG H, DAI Y, LU H, LI SS, GAO L, ZHU DL. Analysis of the correlation between non-alcoholic fatty liver disease and bone metabolism indicators in healthy middle-aged men. *Eur Rev Med Pharmacol Sci* 2018; 22: 1457-1462.
- 2) LUGER M, KRUSCHITZ R, KIENBACHER C, TRAUSSNIGG S, LANGER FB, PRAGER G, SCHINDLER K, KALLAY E, HOPPICHLER F, TRAUER M, KREBS M, MARCULESCU R, LUDVIK B. Prevalence of liver fibrosis and its association with non-invasive fibrosis and metabolic markers in morbidly obese patients with vitamin D deficiency. *Obes Surg* 2016; 26: 2425-2432.
- 3) SOIFER E, GAVISH D, SHARGORODSKY M. Does metformin treatment influence bone formation in patients with nonalcoholic fatty liver disease? *Horm Metab Res* 2015; 47: 556-559.
- 4) MAAGENSEN H, JUNKER AE, JORGENSEN NR, GLUUD LL, KNOP FK, VILSBOLL T. Bone turnover markers in patients with non-alcoholic fatty liver disease and/or type 2 diabetes during oral glucose and isoglycemic iv glucose. *J Clin Endocrinol Metab* 2018, doi: 10.1210/jc.2018-00176.
- 5) LONARDO A, NASCIBENI F, MAURANTONIO M, MARRAZZO A, RINALDI L, ADINOLFI E. Non-alcoholic fatty liver disease: evolving paradigms. *World J Gastroenterol* 2017; 23: 6571-6592.
- 6) RINALDI L, NASCIBENI F, GIORDANO M, MASETTI C, GUERRERA B, AMELIA A, FASCIONE MC, BALLESTRI S, ROMAGNOLI D, ZAMPINO R, NEVOLA R, BALDELLI E, IULIANO N, ROSATO V, LONARDO A, ADINOLFI LE. Clinical features and natural history of cryptogenic cirrhosis compared to hepatitis C virus-related cirrhosis. *World J Gastroenterol* 2017; 23: 1458-1468
- 7) DI FRANCA R, RINALDI L, CILLO M, VARRIALE E, FACCHINI G, D'ANIELLO C, MAROTTA G, BERRETTA M. Antioxidant diet and genotyping as tools for the prevention of liver disease. *Eur Rev Med Pharmacol Sci* 2016; 20: 5155-5163.
- 8) DI FRANCA R, RINALDI L, TROISI A, DI BENEDETTO F, BERRETTA M. Effect of anti-oxidant agents in patients with hepatocellular diseases. *Eur Rev Med Pharmacol Sci* 2015; 19: 3993-3995.
- 9) MILIONE S, DI CATERINO M, MONACO L, RINALDI L. Mediation of inflammation, obesity and fatty liver disease by advanced glycation endproducts. *Eur Rev Med Pharmacol Sci* 2018; 22: 578-579.
- 10) VALENTE G, RINALDI L, SGAMBATO M, PIAI G. Conversion from twice-daily to once-daily tacrolimus in stable liver transplant patients: effectiveness in a real-world setting. *Transplant Proc* 2013; 45: 1273-1275.

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