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Two Drinks per Day Does Not Take Your Fatty Liver Away

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In this issue of HEPATOLOGY, Fredrik Åberg and co-authors[1] put an end to the ongoing debate whether moderate alcohol drinking (less than 20 g of alcohol/day or 2 drinks per day) could be helpful for the health of subjects with nonalcoholic fatty liver disease (NAFLD) and, therefore, if patients with NAFLD may be allowed to drink not more than 2 drinks per day. NAFLD is booming worldwide, together with the increasing prevalence of type2 diabetes mellitus (T2DM), obesity, and metabolic syndrome.[2-4] NAFLD is now the most common liver disorder in Western countries and affects as many as 25%-30% of adults, and NAFLD might shortly become the most common liver disease worldwide.[2] Cardiovascular disease (CVD) and not liver disease is the leading cause of death among patients with NAFLD.[5,6] Moderate drinking (vs. abstinence) has been associated with a lower risk of CVD in the general population. This conclusion has been challenged in a more recent study where moderate consumption of alcohol did not reduce the risk of CVD in patients with NAFLD.[7] Therefore, this practical issue is not yet completely clarified. Which is the answer that the hepatologist and the General Practioner should give a patient with NAFLD asking: "Doctor, can I keep on drinking a couple of glasses of wine every day?" The current assumption is that low or moderate alcohol consumption should be forbidden in patients with chronic liver disease (CLD). Therefore, subjects with CLD, regardless of its etiology, are usually warned to avoid any kind of alcoholic beverage. An answer as to whether moderate drinking (1 to 2 drinks per day) is safe in patients with NAFLD can be found from what is described by Åberg et al.[1]

They followed up 6,771 (84%) of the 8,028 Finnish persons that had been enrolled in the Finnish Population Health 2000 Study. Through a two-stage stratified procedure, the Finnish Population Health Study was intended to be representative of the entire Finnish population. Hospitalization data were obtained from the National Hospital Discharge Register, cancer data from the Finnish Cancer Registry, and the cause of death from the Statistics Finland database. This is an ideal research setting for evaluating the burden of liver or any disease because it starts with a general population and links events occurring later in life using reliable sources about disease and death. Åberg et al. are to be congratulated for contributing to our knowledge about the burden of liver disease in the general population. After a mean (SD) follow-up time of 11 years, there were 84 liver-related outcomes, that is, 60 hospitalizations for liver disease, nine primary liver cancers, and 15 liver-related deaths corresponding to an incidence rate of 1.2%. When only hospitalizations for liver disease and liver-related deaths were considered (n = 75), 47 occurred in the 5,224 men drinking less than 30 g/day of ethanol or women drinking less than 20 g/day of ethanol, yielding an incidence rate of 0.9%. Among the 710 men drinking more than 30 g/day of ethanol or women drinking more than 20 g/day of ethanol, the corresponding number was 47, yielding an incidence rate of 3.9%. These numbers tell that although incident liver disease was more common among heavy drinkers, it was present also among non-heavy drinkers as defined by current guidelines. The

Abbreviations: BMI, body mass index; CLD, chronic liver disease; CVD, cardiovascular disease; LDL, low-density lipoprotein; NAFLD, nonalcoholic fatty liver disease; T2DM, type2 diabetes mellitus; WC, waist circumference.

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researchers evaluated potential predictors of incident liver disease using multivariable Cox regression coupled with backward step-wise selection of variables found to be statistically significant at univariable analysis. These approaches (univariable selection of predictors and step-wise regression) have many drawbacks that the researchers correctly reported in the Discussion. The use of ratios as predictors of incident liver disease, that is, the total cholesterol/low-density lipoprotein (LDL) cholesterol ratio and the waist circumference (WC)/body mass index (BMI) ratio, is also potentially prone to problems because ratios defy most of the assumptions made by common statistical methods.[8] Nonetheless, the use of these ratios deserve further evaluations in future studies preferably also by using other approaches avoiding the potential inadequacies of ratios.[8]

By exploring the interaction of alcohol and metabolic syndrome together, alcohol was a significant risk for the worsening of liver disease in the general population even when average alcohol intake was within the limits currently defining NAFLD. The strength of this population study is the prospective design, use of a unique National Register, and original holistic approach that does not distinguish from the beginning NAFLD from alcoholic fatty liver disease on the basis of an empirical, predefined, and sometimes unreliable classification.[9] The outcomes measured were strong ones: mortality or important liver event, such as hepatic decompensation, and hepatocellular carcinoma.

Another important finding was that BMI alone did not predict severe liver disease whereas WC/BMI, thus a central/visceral adiposity, was a strong driver of liver disease. It appears that for a good liver-risk assessment, the single metabolic parameters should not be considered alone, whereas lipid abnormality, visceral obesity, insulin resistance, T2DM, and alcohol consumption should be considered at the same time. In fact, this is the first report that cholesterol/LDL cholesterol have been shown to be associated with incident severe liver disease risk, and that among normal no-risk drinkers, alcohol has been found as an independent risk factors for more severe liver disease

In conclusion, this study suggests that the alcohol and metabolic risk factors for progression of liver disease should be considered always together, especially when the design of the study is a cohort population study. It seems that, in real life, we cannot suggest to our patient with NAFLD to go on drinking a small amount of alcohol, because also only 2 drinks per day do not protect the liver from damage, but, on the contrary, promote the progression to a more severe liver disease.

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REFERENCES

1) Åberg F, Helenius-Hietala J, Puukka P, Färkkilä M, Jula A. Interaction between alcohol consumption and metabolic syndrome in predicting severe liver disease in the general population. HEPATOLOGY 2018;67:2141-2149.
2) Younossi Z, Anstee QM, Marietti M, Hardy T, Henry L, Eslam M, et al. Global burden of NAFLD and NASH: trends, predictions, risk factorsand prevention. Nat Rev Gastroenterol Hepatol 2017 Sep 20. doi: 10.1038/nrgastro.2017.109. [Epub ahead of print]
3) Allen AM, Terry TM, Larson JJ, Coward A, Somers VK, Kamath PS. Nonalcoholic fatty liver disease incidence and impact on metabolic burden and death: a 20 year-community study. HEPATOLOGY 2017 Sep 23. doi: 10.1002/hep.29546. [Epub ahead of print]
4) Dai W, Ye L, Liu A, Wen SW, Deng J, Wu X, Lai Z. Prevalence of nonalcoholic fatty liver disease in patients with type 2 diabetes mellitus: a meta-analysis.. Medicine (Baltimore) 2017; 96:e8179.
5) Lonardo A, Nascimbeni F, Maurantonio M, Marrazzo A, Rinaldi L, Adinolfi LE. Nonalcoholic fatty liver disease: evolving paradigms. World J Gastroenterol 2017;23:6571-6592.
6) VanWagner LB, Ning H, Allen NB, Ajmera V, Lewis CE, Carr JJ, et al. Alcohol use and cardiovascular disease risk in patients with nonalcoholic fatty liver disease. Gastroenterology 2017;153: 1260-1272.e3.
7) Poli A, Marangoni F, Avogaro A, Barba G, Bellentani S, Bucci M, et al. Moderate alcohol use and health: a consensus document. Nutr Metab Cardiovasc Dis 2013;23:487-504.
8) Curran-Everett D. Explorations in statistics: the analysis of ratios and normalized data. Adv Physiol Educ 2013;37:213-219.
9) Bellentani S, Tiribelli C. Is it time to change NAFLD and NASH nomenclature? Lancet Gastroenterol Hepatol 2017;2:547-548.