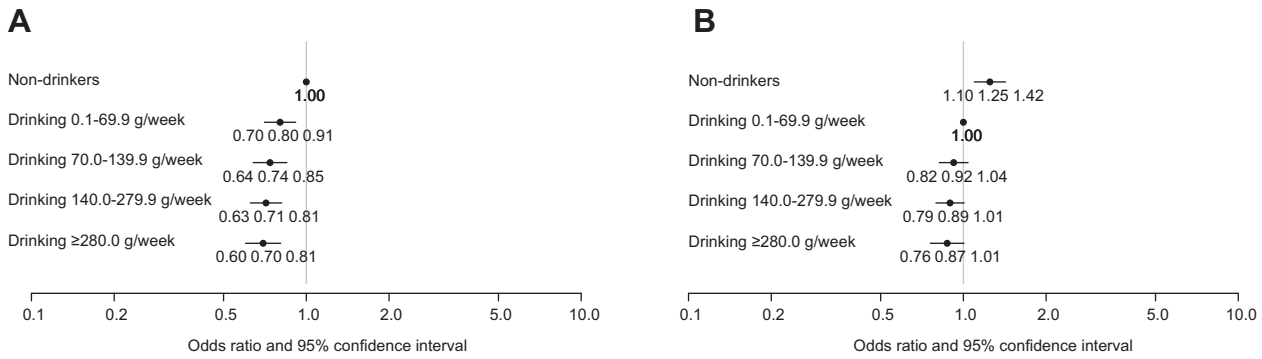

Fig. 1. Odds ratio for fatty liver in each category of the average weekly alcohol consumption in men. (A) The odds ratio for fatty liver was analyzed with non-drinkers as reference and adjusted for smoking status and regular exercise; or (B) analyzed with drinking 0.1–69.9 g/week as reference and adjusted for age, smoking status, and regular exercise.

threshold may differ in each person, at present, we cannot specify what distinguishes individuals who develop fatty liver as a result of alcohol consumption from those who do not.

Conflict of interest

The authors declare that they have no conflicts to disclose regarding funding or other conflicts of interest with respect to this manuscript.

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Akio Moriya
Department of Medicine, Mitoyo General Hospital, Kanonji, Japan

Yoshiaki Iwasaki*
Health Service Center, Okayama University, Okayama, Japan
Department of Gastroenterology and Hepatology, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Okayama, Japan
*Corresponding author.
E-mail address: yiwasaki@cc.okayama-u.ac.jp

Souhei Ohguchi
Junpukai Health Maintenance Center, Okayama, Japan

Kazuhide Yamamoto
Department of Gastroenterology and Hepatology, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Okayama, Japan

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Non-alcoholic fatty liver disease: Severity of fibrosis and its relationships with clinical and biological variables

To the Editor:

The paper of Petta *et al.* [1] throws new light on an important issue. Indeed, no data were previously available on the impact of the severity of liver damage on cardiac function and structural remodeling for patients affected by NAFLD. Moreover, this study partially clarifies the relationship between visceral adiposity and severe liver fibrosis in these patients. However, some comments might be useful for a deeper interpretation of these findings. In fact, some of our previous work shows that various circulating molecules (i.e., adiponectin, TGF β1, e-selectin, and endothelin) play a significant role in left ventricular remodeling [2,3], progression of renal function impairment [4,5], and in the manifestation of left ventricular dysfunction [6–8] in central obese subjects.

A recent study by Akyildiz *et al.* [9] found that higher serum levels of the hormone FGF 21 were associated with larger epicardial fat thickness in obese women. All the above-mentioned molecules are related to both inflammation and fibrosis at various levels. Thus, these manuscripts could have been discussed in the paper. Nonetheless, these data will be useful for future

research that want to investigate the complex pathway among severity of liver damage, visceral obesity, insulin resistance and cardiac functional and structural abnormalities.

Finally, we have to highlight a crucial inaccuracy in the logistic multivariate analysis. The authors included in the logistic multivariate model (see Table 2 in original manuscript) two related variables as visceral obesity (computed from waist circumference measured in each patient) and epicardial fat thickness. It is widely known that epicardial fat thickness clearly reflects visceral adiposity. In particular, Iacobellis *et al.* [10] demonstrated that waist circumference is one of the best predictors of epicardial adipose tissue. So the inclusion of the two variables in the same logistic predictor model defines the phenomenon of collinearity. This event takes place when two or more independent variables are almost nearly perfectly correlated. When they are used in the same model as predictors, an important statistical assumption of the multivariate analysis is violated. Consequently, collinearity results in uninterpretable and biased parameter estimates and inflated standard errors. The authors ought to have used the term of abdominal obesity instead of visceral since pericardial fat is just a measure of the visceral fat. Moreover, abdominal obesity and epicardial fat thickness variables should never be inputted as predictors into the model together. On the contrary, only one of the two variables should be inputted at a time together with other predictors. Conclusions should be based on suggestions from adjusted Odds Ratios and their confidence intervals. This computational mistake could have partially changed the conclusions and should have been properly considered in both the results and discussion sections. We hope that these suggestions will be useful for the readers to formulate the right opinion about these findings that remain crucial and stimulate further research in this field of liver diseases.

Conflict of interest

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Salvatore Corrao*
2nd Internal Medicine Department, National Relevance Hospital Trust, ARNAS Civico, Di Cristina e Benfratelli, Palermo, Italy
Centre of Research for Effectiveness and Appropriateness in Medicine (CREAM), Biomedical Department of Internal Medicine and Subspecialties [DiBiMIS], University of Palermo, Italy
*Corresponding author.
E-mail address: salvatore.corrao@unipa.it

Carmelina Rinollo
2nd Internal Medicine Department, National Relevance Hospital Trust, ARNAS Civico, Di Cristina e Benfratelli, Palermo, Italy

Rosario Scaglione
Centre of Research for Effectiveness and Appropriateness in Medicine (CREAM), Biomedical Department of Internal Medicine and Subspecialties [DiBiMIS], University of Palermo, Italy