Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Reply to: 'NAFLD or comorbidities, that is the question'

To the Editor:

We thank Ponziani *et al.* for their interest in our manuscript and for their thoughtful comments.[1] They raised the concern that the 37.6% prevalence of non-alcoholic fatty liver disease (NAFLD) in our cohorts was rather high compared to the 26.9% reported in Northeastern China and suggested that we may have over-diagnosed NAFLD. If NAFLD was over-diagnosed, the prevalence should be similar in the stable and progressive groups, as opposed to the marked difference, 25.8% *vs.* 87.2 %, respectively, observed in our study. Secondly, the 2 hospitals in our study are in Anhui (Eastern China) and Beijing (Northern China), not in Northeastern China (Liaoning, Jilin, Heilongjiang provinces), therefore using the 27.6% prevalence might not be relevant.[2]

We agree that hepatic steatosis index (HIS) is affected by inflammatory activities. To reduce over-diagnoses, we used the lowest alanine aminotransferase (ALT)/aspartate aminotransferase (AST) value from the medical records of the patients in the preceding 12 months before the COVID-19 diagnosis. If the patient had no ALT/AST records in the preceding 12 months, the lowest value during the current admission and follow-up was used to calculate HSI. Also, the mean AST and ALT values were not significantly different between the stable and progressive groups. If inflammation led to elevation of transaminases and subsequently over diagnosis of HIS as suggested, again it should affect both the stable and progressive groups equally.

In our cohort, 6/202 (3%) of patients fulfilled the criteria of excessive alcohol intake (≥30 g/d for man and ≥20 g/d for women), with 5/163(3.1%) and 1/39 (2.6%) in the stable and progressive groups, respectively ($p = 1.000$), as shown in Table 1.[3] Only 2/76 (2.6%) patients with excessive alcohol intake had NAFLD, and 4/126 (3.2%) with excessive alcohol intake did not have NAFLD ($p = 1.000$). Nonetheless, we acknowledge the limitation of non-invasive assessment of NAFLD.[4] However, with the priority concern being the safety of the medical staff and the patients with COVID-19, further non-invasive or invasive assessments (such as liver biopsy) were not undertaken. In the near future, we hope that efforts to create a "big data" collection, such as the "APCOLIS" study (APASL Covid Liver Injury Spectrum) (https://www.surveymonkey.com/r/covid-liver) will enhance our understanding of the role of NAFLD/MAFLD in COVID-19.[5] Though HIV infection was defined as a comorbidity, none of the patients in our cohort had positive HIV serology or documented HIV infection in the past. Fig. 1 showed that after multivariate analysis, male sex (odds ratio [OR] 3.1; 95% CI 1.1–9.4), age >60 years (OR 4.8; 95% CI 1.5–16.2), higher BMI (OR 1.3; 95% CI 1.0–1.8), underlying comorbidity (OR 6.3; 95% CI 2.3–18.8) and NAFLD (OR 6.4; 95% CI 1.5–31.2) were associated with progression of illness.

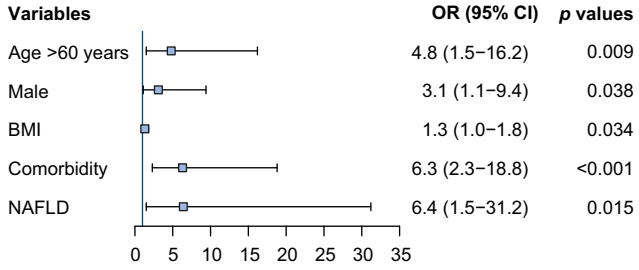

Fig. 1. Risk factors related to development of progressive COVID-19 by multivariate analysis. The solid box represents OR of multivariate Logistic regression, the thin black solid segment represents 95% CIs. The vertical line represents invalid line. BMI, body mass index; NAFLD, non-alcoholic fatty liver disease; OR, odds ratio.

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Conflict of interest

We declare no competing interests.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

DJ and DZ wrote the manuscript; GL provided guidance and proof-read the manuscript; all authors revised and approved the final version.

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Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhep.2020.05.006.

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Author names in bold designate shared co-first authorship

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MARC1 variant rs2642438 increases hepatic phosphatidylcholines and decreases severity of non-alcoholic fatty liver disease in humans

To the Editor:

We read with great interest the review by Trépo and Valenti on recent developments in genetics of NAFLD,[1] which highlighted the need for further confirmation of the association between the rs2642438 (p.A165T) variant in the mitochondrial amidoxime reducing component 1 (*MARC1*) gene and liver disease risk. This missense variant was recently shown to associate with protection from all-cause cirrhosis.[2] *MARC1*

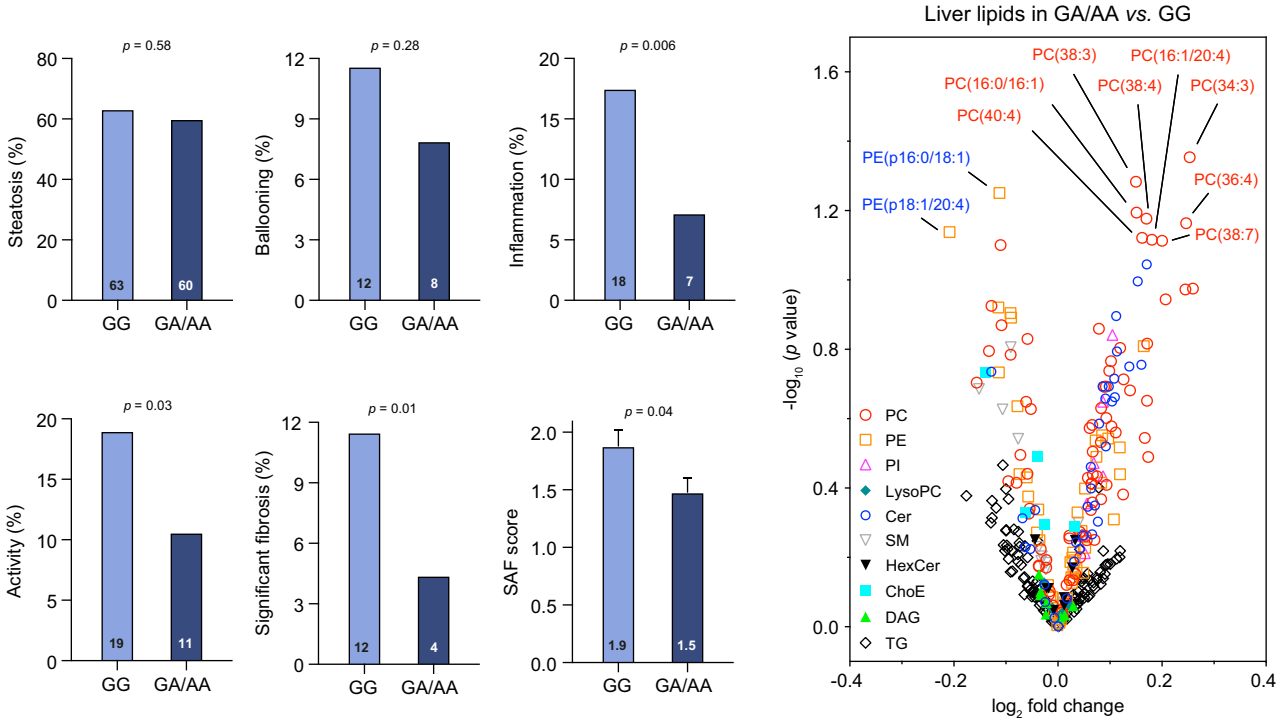

Fig. 1. *MARC1* rs2642438 associates with decreased severity of NAFLD and increased hepatic phosphatidylcholines. Bar plots show the proportion (%) of subjects with steatosis, ballooning, lobular inflammation, activity and significant fibrosis (F2-4), and total SAF score (mean ± SEM) in carriers ('GA/AA') and non-carriers ('GG') of the variant allele. Volcano plot shows differences in liver lipid composition in carriers ('GA/AA') compared to non-carriers ('GG'). Significances were determined by using Pearson's χ^2 test for categorical variables and unpaired Student's t test for continuous variables. Cer, ceramide; ChoE, cholesteryl ester; DAG, diacylglycerol; HexCer, hexosylceramide; LysoPC, lysophosphatidylcholine; NAFLD, non-alcoholic fatty liver disease; PC, phosphatidylcholine; PE, phosphatidylethanolamine; PI, phosphatidylinositol; SM, sphingomyelin; TG, triglyceride.

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