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Epicardial fat in patients with non-alcoholic fatty liver disease

To the Editor:

We recently reported that epicardial fat thickness is significantly associated with the severity of liver fibrosis in patients with non-alcoholic fatty liver disease (NAFLD), and that in this clinical setting, morphological and functional cardiac alterations by echocardiography are inversely related with the severity of liver damage [1]. Of note, these associations were maintained after correction for both cardiometabolic and hepatic confounders including visceral adiposity.

In their letter [10], Corrao and colleagues suggest that some cytokines/adipocytokines as well as adiponectin, transforming growth factor β1, e-selectin, endothelin, and fibroblast growth factor 21 could explain the link we observed between the severity of liver disease and the presence of cardiac alterations. In this line in our paper we already suggested that "the inflammatory state that characterize NAFLD/NASH might be able to act systemically, affecting the homeostasis of different organs, including the heart, as already demonstrated for systemic atherosclerosis [2] and kidney damage [3]". Therefore we are planning to study the relationship between cytokines/adipocytokines levels, liver damage and cardiac alterations in NAFLD, as well as the role of genetic variants associated with NAFLD and its severity on the presence of cardiac alterations. We recently reported that gene variants in the *PNPLA3* and *TMS6F2* genes, can modulate the risk of atherosclerosis as well as the occurrence of cardiovascular events in patients with NAFLD or at high NAFLD risk [4,5].

Corrao and colleagues also question the approach we used for the multivariate model, assessing variables independently associated with severe liver fibrosis. Specifically, they raised concerns about the inclusion in the model of both visceral obesity and epicardial fat, because considered as a phenomenon of collinearity. We thank the authors to correctly explain this phenomenon and the implication that it can produce on data interpretation. However, we respectfully think that our analysis is not biased by collinearity. Epicardial fat [6], as well as other ectopic fat depots like liver or dorsocervical fat [7], are obviously strongly related to visceral obesity. However, they do not depend on visceral obesity only, because they can have an independent role in affecting liver and systemic damage. In this line, cross-sectional and prospective studies showed that both liver and visceral fat are independent risk factors for presence and occurrence of cardiovascular events [8,9]. So, we included both visceral and epicardial fat in the model for fibrosis to demonstrate that the effect of epicardial fat is independent of that of visceral fat.

Finally, in response to Ulucan and colleagues [11] we agree with the authors that the interference of epicardial fat with the autonomic nervous system could be one of the mechanisms linking this ectopic fat to liver damage. Accordingly, further clinical and experimental studies are needed in this topic.

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Conflict of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

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