*Hospital, College of Medicine, Xi'an Jiaotong University, Xi'an, China*
*Department of Infectious Disease, The Second Affiliated Hospital, College of Medicine, Xi'an Jiaotong University, Xi'an, China*

Shu Zhang
*Department of Hepatology and Surgery, The Second Affiliated Hospital, College of Medicine, Xi'an Jiaotong University, Xi'an, China*
*Department of Experimental Therapeutics, The University of Texas, M.D. Anderson Cancer Center, Houston, TX 77030, USA*

Hong Deng
*Department of Infectious Disease, The Second Affiliated Hospital, College of Medicine, Xi'an Jiaotong University, Xi'an, China*

Zongfang Li*
*Department of Hepatology and Surgery, The Second Affiliated Hospital, College of Medicine, Xi'an Jiaotong University, Xi'an, China*
Address: Department of Hepatology and Surgery, The Second Affiliated Hospital, College of Medicine, Xi'an Jiaotong University, 157 Xi Wu Road, Xi'an, Shaanxi 710004, China. Tel.: +86 29 87678006; fax: +86 29 87678634
*Corresponding author.
*E-mail address*: Izf2568@gmail.com

# Regular coffee: A magic bullet or a naked gun? Regular coffee but not espresso drinking is protective against fibrosis in NAFLD

*To the Editor:*

We read with interest the article by Anty *et al.* [1] reporting that consumption of regular coffee but not of espresso is an independent protective factor for liver fibrosis, in severely obese European patients. Effects of coffee and caffeine on liver disease, including NAFLD, cirrhosis and HCC, have been reported over several years, with different methodological approaches and non-univocal results [2–4]. We appreciate the great effort that the authors have put, working with an extremely selected population, and using very careful tools for the assessment of steatosis and fibrosis. Nonetheless, it appears useful to challenge the effective reliability of the methodology they have chosen for reaching their results and conclusion. The enthusiasm of the conclusion is perhaps not adequately supported by consistent data and is misleading for readers: "*Consumption of regular filtrated coffee but not espresso was independently associated with a lower level of fibrosis in morbidly obese European patients. The finding that some compounds in coffee can protect from liver fibrosis is of potential pharmacological interest. As sugar could decrease the beneficial effect of coffee, coffee consumption, particularly regular coffee, could be encouraged but without sugar addition!*" [1]. The authors [1] describe coffee both as a nutrient and as a blend of drugs, and also as different recipes. Why not as a high quality beverage? Looking at the statements of the conclusion, some details are not available: which espresso? Which pharmacological effect? From where does the sugar appear and is there any information on sugars in this study? Moreover, the predictive models used are not clearly described. Actually, it seems that only four of the six statistically different measures in the two groups are used (AST, caffeine from regular coffee, HOMA-IR and NASH) skipping ALT and quantity of regular coffee consumed (ml/wk). It is reasonable, in our view, that challenging and showing (if the current table refers to a stepwise regression) a more extended model could be possible and useful. In the data analysis, it is not clear if the overlap of use of different coffee beverages has any effect: the calculation of the overall content of caffeine appears very conjectural due to the obvious diversity of different coffee recipes. Essentially, 38 subjects (19.5%) drank only regular coffee, 76 (39%) only espresso: perhaps a plain comparison of these two "almost-pure" groups, as these are, could help. Information on regular coffee and caffeine intake relies entirely on self-reporting of the subjects and, much more important, depends on the quantity accounted for in this way. On this basis, the conclusion that different coffee recipes and preparations really have a homogenous content of caffeine is quite difficult to confirm or accept. Even the definition of "espresso" cup adopted by Anty *et al.* [1] is very far from what the word really represents [5]: the current quantity of a cup of espresso [5] is almost 10–15% of the quantity stated by the authors in the table available as Supplementary material of the article [1]. There is also a different perspective: it is possible, if not likely, that the nutritional behavior of obese people using regular coffee – any quantity – is different from the nutritional and lifestyle behavior (including physical exercise) of obese people drinking espresso coffee. Unfortunately, in this study, we do not have any information on the nutritional profile of this population and of the two main subgroups. No information is available on their physical exercise habits, socio-economical status and other factors that could affect food intake and obesity. Last but not least, no definition of "malnutrition" and of related markers is considered: it should be considered and could be a useful issue in dealing with obesity, steatosis and fibrosis in liver disease. Overall, several major confounders are not sufficiently taken into account in this study, as it is currently presented: interpretations should have been more carefully reviewed by the authors and, particularly, some reappraisal of correlations introduced. The latter as presented and interpreted, may be confusing if not misleading. The article is still lacking reliable nutritional information in the prevention or treatment, if any, of fibrosis and NAFLD, and we need consistent evidence and less conjecture.

## Conflict of interest

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

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Guglielmo M. Trovato*
G. Fabio Martines

# Reply to: "Regular coffee: A magic bullet or a naked gun? Regular coffee but not espresso drinking is protective against fibrosis in NAFLD"

*To the Editor:*

**Filtered, ristretto, lungo and what else?**

We have read with interest the comments and criticisms made by Trovato and colleagues concerning our recently published study [1]. We would like to clarify a number of specific points.

Firstly, we agree that our study population – morbidly obese patients referred for bariatric surgery – is a very particular group; morbidly obese subjects represent one percent of the French population. Our patients were consecutively enrolled in the bariatric program and agreed to complete a detailed questionnaire, given by a trained interviewer, assessing their coffee and caffeinated drink consumption. For each patient, a liver biopsy was obtained and assessed by validated classification. This histological analysis remains the gold standard to determine the various elementary lesions of NAFLD and NASH. This method is reliable and allowed us to differentiate pure steatosis, NASH, and the various degrees of fibrosis, in contrast to the use of only non-invasive methods such as liver ultrasound, as in the study by Catalano *et al.* [2].

Secondly, as we stated in the Discussion, we do not know why the consumption of filtered regular coffee and not the consumption of espresso was associated with less fibrosis, in our cohort of morbidly obese patients. An initial hypothesis is that these two high-quality beverages are different in their composition because of their specific manufacturing processes. Another hypothesis is that regular and espresso drinkers have hidden, intrinsic differences. For example, espresso drinkers could use a higher quantity of sugar or use special forms of sugar (enriched in fructose for example). In our study, we found a positive correlation between the consumption of espresso and the number of parameters of the metabolic syndrome, the level of triglycerides, and a negative correlation with the level of HDL cholesterol. We must keep in mind that if 6 g of sugar (the usual amount of sugar served with an espresso in France) is added to an espresso of 50 ml, the concentration of sugar (120 g/l) is slightly higher than a typical cola-based soft drink (35 g of sugar for 330 ml, i.e., 106 g/l). As we stated in the Discussion, we did not take into account the amount and type of sugar added to coffee in the questionnaire, and the last sentence of our paper was intended as a joke! Studies including more detail concerning consumption should answer this question, as was done in the Nutrinet study in France [3].

Our study probably reflects the current mode of consumption of coffee in France. The espresso drunk by our patients is essentially home-made using small machines, which are becoming more and more popular. The obtained beverages are different from the filtered coffee and possibly from the espresso made in coffee shops [4]. The volume obtained with these machines can vary from "ristretto" (25 ml), standard "espresso" (40 ml) to "lungo" (110 ml). Moreover, in the case of the "espresso" made by professionals, the quality of the obtained beverage can be very different, depending on the coffee shop, in terms of caffeine, chlorogenic acid and probably in the content of other compounds [5]. So the term "espresso" designates different beverages, and the delicious "ristretto espresso" made in a traditional Italian coffee shop is probably different from the beverage currently obtained at home in France with a small coffee machine.

Thirdly, a questionnaire is an imperfect way of collecting information but has been used extensively and validated in epidemiological studies on coffee that include cohort studies [5]. With respect to our patients, it appeared that the daily consumption of coffee was regular over time and generally well recalled.

The multivariate analysis has been performed using standard statistics. For logistic regression, non-redundant parameters that are significant in univariate analysis were selected. The quantity of regular coffee consumed and the approximate amount of caffeine from regular coffee were the same variable expressed in a different way. The patients were asked the volume of the various kinds of coffee and other caffeinated drinks consumed. A conversion table automatically converted the amount of each drink into the amount of caffeine consumed. This is why only the equivalence in caffeine consumption was finally retained for multivariate analysis. Similarly, AST and ALT were linked together. We chose AST because it is also a marker of fibrosis. In a model including AST and ALT, we obtained a similar result for regular coffee consumption (OR = 0.76, 95% CI: 0.58–0.99, $p = 0.041$).

Fourthly, we recognize that we did not provide a complete nutritional and lifestyle assessment in our study. However, known confounders for coffee association, alcohol and tobacco use were assessed and were similar in patients with and without significant fibrosis.

Finally, our study is in accordance with the recent results of Molloy *et al.* who found a beneficial effect of filtered coffee consumption on the level of fibrosis of morbidly obese American patients [6]. As observed in our study, no effect was seen on