Reviewer’s report

Title: Cholecystectomy versus central obesity or insulin resistance in relation to the risk of nonalcoholic fatty liver disease: the third US National Health and Nutrition Examination Survey

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Reviewer: Roger Gutiérrez-Juárez

Reviewer's report:

In this manuscript Yue and collaborators investigated the contribution of cholecystectomy either independently or combined with central obesity/insulin resistance (IR) to nonalcoholic fatty liver disease (NAFLD) risk. To this aim the authors performed a cross-sectional analysis of data from the third U.S. National Health and Nutrition Examination Survey (NHANES III), for which ultrasonography was available. Based on their analysis of the data the authors estimated Odds ratios (ORs) and 95% confidence intervals for NAFLD using a logistic regression approach. The authors found that cholecystectomy was associated with a higher prevalence of NAFLD when compared with gallstones among participants regardless of whether or not they were centrally obese. Interestingly, the presence of gallstones was associated with a higher prevalence of NAFLD only if central obesity was also present. The risk of NAFLD with cholecystectomy increased to a lesser extent compared with the larger risk increase observed with IR or metabolic syndrome. The authors concluded that the risk of NAFLD contributed by cholecystectomy was comparable to that of central obesity in combined analyses. Furthermore, the contribution of the association with IR or metabolic syndrome was higher than with cholecystectomy alone. The role of cholecystectomy and other factors in NAFLD has been already established, what appears to be new here is the comparison between cholecystectomy and central obesity as factors contributing to NAFDL with the same "stregth". Although in general the manuscript is well written and data analyses seem straightforward, there are some points that deserve further discussion. These are described below.

Main issues:

1. To assess the extent by which central obesity contributes to NAFLD the authors use only waist circumference (WC) determinations. Is that enough to state that the "magnitude of the association of NAFLD with cholecystectomy was similar to that with central obesity" (p. 13, lines 274-275)? What else would need to be done to further strengthen this conclusion?

2. On page 10, lines 208-210, the authors state that "... the effects of gallstones on NAFLD were mediated primarily by the presence of central obesity, IR or MetS." Can the authors elaborate
on how exactly they propose that gallstone effects would be mediated by central obesity, IR or MetS?

3. Besides being more aware of the effect of cholecystectomy on the development of NAFLD, is there something that the authors would suggest regarding the treatment of gallstones, especially in people with other risk factors?

4. Do the authors think that a refinement in the detection of NAFLD (i.e., people with less than 30% fat infiltration of the liver) has the potential to influence their conclusions?

Minor issues:

1. There is a number of English language issues throughout the manuscript that need to be corrected by someone familiar with the language.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

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