Reviewer’s report

Title: CARDIOVASCULAR RISK REDUCTION OVER TIME IN PATIENTS WITH DIABETES OR PRE-DIABETES UNDERGOING BARIATRIC SURGERY: DATA FROM A SINGLE-CENTER RETROSPECTIVE OBSERVATIONAL STUDY

Version: 2 Date: 22 Oct 2018

Reviewer: Mario Luca Morieri

Reviewer’s report:

I thank the Authors for their response to my previous comments, I found the new version of the manuscript improved.

However, there are still some comments, in particular in the results section that required further revision to allow sufficient clarity, transparency, and interpretation of the analysis done by the Authors.

Previously point Point 2), Authors have modified the sentence as follow:

"Higher glucose levels at baseline were clearly associated with a higher CVD risk (OR = 4.35 [2.73, 6.99], p < 0.001) and the effect. The difference between baseline and month 12 was also statistically significant (OR = 0.31 [0.26, 0.36], p < 0.001). Nevertheless, after the intervention all patients reached similar levels of CVD risk regardless of their previous status. Therefore, patients with higher fasting glucose levels are the ones that benefit the most from the intervention regarding CVD risk (OR = 0.44 [0.27, 0.71], p < 0.001)"

New comments: While the text is now much clearer than before, the numbers in the brackets are still not clinically interpretable, and requires more details described in the methods. Usually, Odds Ratio are used for their easy interpretation. Please specify in the brackets how to interpret this OR or maybe consider to report the estimates (logOR) that might be easier to understand "e.g. for each mg/dl increase in glucose there was an … increase risk of having one higher unit (%) of CVD risk)" or otherwise these numbers are useless and create confusion. Similarly the effect on changes between baseline and 12-month, elaborate in the methods how the analysis was done and clarify in the text how to interpret those numbers. (as suggested also by the STROBES guidelines).

Point 3)

The authors modified the sentence as follow:

"At baseline, patients with type 2 diabetes showed a statistically significant higher CVD risk compared to patients with pre-diabetes (OR 3.23 [2.32, 4.50], p<0.001). Patients with pre-
diabetes showed a significant reduction in risk (OR: 0.49 [0.40, 0.60], p<0.001) 12 months after surgery, compared to their baseline risk. Nevertheless, at that time point (month 12), patients with type 2 diabetes showed a larger reduction in CVD risk than those with pre-diabetes (OR 0.40 [0.30, 0.63], p<0.001)."

New comment:

Similarly to what specified above, while the text is clear, these results and numbers can't be understood by the readers.

Eg. In the first sentence, if authors say: "at baseline patients with type 2 diabetes showed a statistically significant higher CVD risk compared to patients with pre-diabetes" then they report an Odds ratio, but readers can't understand if this is to % CV point or to presence of high CV risk (cut-off of 20%).

This is highly confusing. Please either report the mean CV risk % the two groups and the P value for the difference between them. Or if they want to report OR then clarify the text. For example "Diabetes status, as compared to prediabetes, was associated with a higher risk of having a CVD risk above 20% (OR …)".

Similarly, in the sentences on changes from baseline to 12 month, it is much easier to report the mean difference % with C.I. from baseline to 12 months instead of an O.R. that is really hard to understand clinically. How was it estimated?

Additional point:

Regarding this previous comment and answer regarding OSA:

Please define cut-off used to define OSA. Did all patients underwent polysomnography before and after surgery? please clarify.

Answer:

All the patients underwent polysomnography before surgery. After surgery, resolution of OSA was considered if CPAP (Continuous Positive Airway Pressure) was removed by the physician pneumologist.

New comment: If I understand your answer, you consider only OSA patients if on CPAP treatment. Regardless of index (e.g. Apne/hypopnea index). Anyway, please specify the definition you used in the methods.

Regarding this previous comment and answer:
Results: in the following sentence pg 6-7: "Higher glucose levels at baseline were clearly associated with a higher CVD risk (OR= 4.35 [2.73, 6.99], p < 0.001)." It is unclear the unit for the reference, to which unit is the OR referred to? Please specify.

Answer:

Since we are using fasting glucose levels as a continuous variable in the logarithmic scale, the OR refers to an increase of one unit (in the log scale) in these levels. (odds(x+1)/odds(x)).

New comments: As stated above, these Odds Ratio have almost no meaning clinical interpretation (moreover if you performed the analysis in the log scale of glucose levels). Please consider expressing these analyses in different ways. Or alternatively, for clarity and transparency, elaborate this in the text so that readers can understand the meaning of your results i.e. the O.R.

Additional point:

As specified by reviewer 1.

Among the limitations helpful for discussion and interpretation of this paper, it should be specified that your primary outcomes (CV risk estimated with FRS) is strongly influenced by the presence of diabetes. Thus much of the higher benefit of bariatric surgery found from the studies among subjects with diabetes Vs those without is derived from the remission of diabetes status. While changing in other metabolic trait were similar in the two groups.

Clearly specify in the text of figure legend to what the P values in the Figures are referred to.

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

No

**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

**Quality of written English**

Please indicate the quality of language in the manuscript:

Acceptable

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