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: 1 Date: 20 Sep 2018

Reviewer: Mario Luca Morieri

Reviewer’s report:

Dear Editor and Authors,

I’ve read with interest this paper aiming to compare the CVD risk reduction between obese patients with type 2 diabetes and prediabetes, before and after bariatric surgery. To reach their goal the authors did a retrospective longitudinal study of 105 subjects, with a follow-up of up to 5 years.

The paper has the following strengths

- Adequate number of patients with a long follow-up
- Prediabetes status has been evaluated with an oral glucose tolerance test
- It covers an interesting topic, it is overall well written, except for the results that need editing

And limits:

- While the background, discussion, and methods are well written, the results section require more attention and different paragraphs are not understandable to this reviewer
- Additional analyses (see below) are required to test some of the main hypothesis of the paper
- Some conclusions are slightly exaggerated and should be modified

These are the specific comments:

Major comments:
1) Please reconsider this conclusion "the state of prediabetes should become a criterion to be considered in metabolic surgery in patients with BMI ≥ 35 in the future" that is far beyond the degree of evidence suggested by this retrospective study. Furthermore, the study is focused on the effect of bariatric surgery in subjects with diabetes Vs those with prediabetes, while to draw similar conclusions the design of the study should have compared subjects with prediabetes that underwent medical treatment+bariatric surgery Vs medical treatment alone. Please correct throughout the manuscript.

It should also be noted that in their current presentation (although additional analyses have been suggested, see below) the data reported by the authors show a greater benefit among subjects with diabetes as compared to those with pre-diabetes, and this should be adequately highlighted in discussion and in the abstract.

2) Methods: To this reviewer is unclear why Authors tested "The association of glycemic status with CVD risk was assessed using a beta regression model including the interaction between fasting blood glucose levels and time in order to study the different trends over time between patients with high and low glucose levels". But they did not formally test the association between diabetes/prediabetes status and CVD risk reductions (testing the null hypothesis that are similar). Indeed, since the main goal of the paper is to compare diabetes Vs pre-diabetes, authors should formally test (eg. with regression model) if the CVD risk reduction from baseline to 12-months is different in the two groups. For example, such models, might be as simple as a linear regression (or beta regression if preferred) testing the association of diabetes/prediabetes status with CVD risk at 12 months (dependent variable), adjusted for CVD risk at baseline (and other covariates if needed).

3) Also related to the point 2: in the results, the following sentence (page 7) is unclear to this reviewer. "patients with type 2 diabetes experienced a clear benefit after the intervention compared to prediabetes (Figure 2), with a large reduction in CVD risk at 12 months compared to the baseline risk (OR =3.22 [2.33, 4.46], p < 0.001). Although the great benefit appeared in diabetic patients, a significant decrease in CVD risk was observed in prediabetic patients 12 months after surgery, compared to the their baseline risk (OR=0.49 [0.40, 0.59], p < 0.001)." The reported Odds Ratio are confusing. To what is referred the OR of 3.22 ? it is the association of prediabetes compare to diabetes with CVD risk reduction? Which is the unit of the dependent variable, single % point of CVD risk? Or CVD below-above the cut-off of 20%? Please clarify both the text in the results and methods.

Minor comments:

The following sentences are unclear to this reviewer, please rephrase them:
Introduction: "Due to prediabetes is an intermediate metabolic state between normoglycemia and type 2 diabetes, to explore if bariatric surgery can reduce cardiovascular disease risk would be interesting."

Methods: "Body fat percentage was measured by bio-electrical bio-impedance (Bodystarâ 1500) once a year and high body fat percentage was considered > 25% in men, respectively, >33% in women."

Discussion: "Our results showed a high type 2 diabetes remission rate (92%) 5 years after surgery but it is specially highlighted no prediabetic patient developed type 2 diabetes."

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

One decimal is more than sufficient for BMI and waist circ measures.

Since you have roughly 100 patients overall, please report the N of patients in the text together with % value (that can be rounded to integer number).

Numbers at the beginning of a sentence should be spelled out.

Table 1 and table 2: please consider to report decimal only when meaningful, to this reviewer most of the values could be rounded to integer or single digit decimal. Furthermore please use numbers of decimal consistently for measures in the same line. This will improve the readability of tables.

Table 1, please consider adding a column with a P-value for differences between the two groups might help the reader.

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

In the section "Evolution of the different secondary clinical parameters after surgery", since the main goal of the paper is to compare the effect of bariatric surgery among subjects with diabetes Vs prediabetes, it might be very useful to test whether the evolution is different in the two groups. Can authors run an exploratory analysis to test this within models including the "diabetes/prediabetes status" by "time" interaction term in the mixed model?

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.

No

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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