

To the Editors of the World Journal of Diabetes

Re: MS 67081 – resubmission #1

We thank the Editors and Reviewer for providing us with the opportunity of resubmitting our work to the World Journal of Diabetes. We have revised the manuscript according to the Reviewer's and Editor's comments. Following is a point-by-point response (blue font).

3 SCIENTIFIC QUALITY

Please resolve all issues in the manuscript based on the peer review report and make a point-by-point response to each of the issues raised in the peer review report. Note, authors must resolve all issues in the manuscript that are raised in the peer-review report(s) and make point-by-point responses to each of the issues raised in the peer-review report(s), which are listed below:

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: It is a pretty neat study to show that the younger patients with worse metabolic status after bariatric metabolic surgery had lower weight loss. The correlation of ketogenesis with respect to weight loss is very well stated. The study also correlated the ketogenesis with age of the patients which was also an interesting research area.

We thank the reviewer for these comments.

4 LANGUAGE QUALITY

Please resolve all language issues in the manuscript based on the peer review report. Please be sure to have a native-English speaker edit the manuscript for grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability, so that the manuscript's language will meet our direct publishing needs.

All language issues raised in the peer review report have been resolved (Abstract: those with ketosis; and, ~~thereby as in a vicious cycle~~, Methods [page 4]: KETO-BMS-~~e~~ (you mean KETO-BMS) study)

5 ABBREVIATIONS

In general, do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition. Certain commonly used abbreviations, such as DNA, RNA, HIV, LD50, PCR, HBV, ECG, WBC, RBC, CT, ESR, CSF, IgG, ELISA, PBS, ATP, EDTA, and mAb, do not need to be defined and can be used directly. Now we list the abbreviations rules as follows.

(1) Title: Please spell out any abbreviation in the title. Abbreviations are not permitted.

No abbreviations are included in the title.

(2) Running title: Please shorten the running title to no more than 6 words. Abbreviations are permitted.

Running title is 5 words.

(3) Abstract: Abbreviations must be defined upon first appearance in the Abstract. Examples: Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (*H. pylori*).

All abbreviations have been defined upon first appearance in the Abstract.

(4) Key words: Abbreviations must be defined upon first appearance in the Key words.

There are no abbreviations in the Key words.

(5) Core tip: Abbreviations must be defined upon first appearance in the Core tip. Examples: Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (*H. pylori*)

All abbreviations have been defined upon first appearance in the Core Tip.

(6) Main Text: Abbreviations must be defined upon first appearance in the Main Text. Examples: Example 1: Hepatocellular carcinoma (HCC). Example 2: *Helicobacter pylori* (*H. pylori*)

All abbreviations have been defined upon first appearance in the Main Text.

(7) Article Highlights: Abbreviations must be defined upon first appearance in the Article Highlights. Examples: Example 1: Hepatocellular carcinoma (HCC).

Example 2: *Helicobacter pylori* (*H. pylori*)

Article Highlights have been added to the main text. All abbreviations have been defined upon first appearance in the Highlights.

(8) Figures: Please verify the abbreviations used in figures and define them (separated by semicolons) at the end of the figure legend or table; for example, BMI: Body mass index; CT: Computed tomography.

All abbreviations used in the figures have been verified.

(9) Tables: Please verify the abbreviations used in tables and define them (separated by semicolons) at the end of the figure legend or table; for example, BMI: Body mass index; CT: Computed tomography.

All abbreviations used in the tables have been verified.

6 EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor: 1 Scientific quality: The manuscript characterizes the relationship between ketonic bodies production, weight loss and metabolic changes following bariatric surgery. The topic is within the scope of the WJG.

We thank the Science Editor for the time and effort spent reviewing our work.

(1) Classification: Grade B;

(2) Summary of the Peer-Review Report: The authors show that the younger patients with worse metabolic status after bariatric metabolic surgery had lower weight loss. The correlation of ketogenesis with respect to weight loss is very well stated. The study also correlated the ketogenesis with age of the patients which was also an interesting research area. The questions raised by the reviewers should be answered;

We have made the requested edits/additions, as listed below:

- All abbreviations have been defined upon first appearance in the Abstract (ketone bodies, body mass index).
- In the introduction (page 3), a reference (Boyers D, et al. "Cost-effectiveness of bariatric surgery and non-surgical weight management programmes for adults with severe obesity: a decision analysis model") has been added to support the statement that "Bariatric metabolic surgery (BMS) offers a unique opportunity to study nutritional ketosis, avoiding the complexity of a nutritional intervention such as VLCKD that would need greater effort from patients and also greater costs".
- In the introduction (pages 3-4), we have elaborated on the statement "However, not all subjects respond to a similar extent (*please elaborate if it is with regards to Diabetes or any other thing in specific*)", specifying that "those with cardiometabolic abnormalities such as diabetes (especially when long-standing or poorly controlled) and arterial hypertension exhibiting poorer weight loss after surgery". Two references have been added to support this statement (Cottam S, et al. "The Use of Predictive Markers for the Development of a Model to Predict Weight Loss Following Vertical Sleeve Gastrectomy" and Muraca E, et al. "Metabolic and psychological features are associated with weight loss 12 months after sleeve gastrectomy").
- In the Methods (page 4) we have corrected "KETO-BMS-o", which is now "KETO-BMS"
- In the Methods (page 4) we have specified that patients move to solid foods after the first 8 weeks from surgery.
- As for the question "Does it take into account any physical activity differences between younger and older adults?" (page 7) relating to 12-month weight loss, we did not formally assess the level of physical activity throughout follow-up. This is now listed as a limitation of the study in the Discussion (page 10). We also argue that changes in physical activity are small in the first months after surgery (Herring LY, et al. Changes in physical activity behaviour and physical function after bariatric surgery: a systematic review and meta-analysis), and therefore are unlikely to significantly affect our primary outcome (weight loss at 6 months). However, we cannot exclude that changes in physical activity during the following months influenced WL at 12 months.
- As for the comment "All these results correlate well with the figure, However the values listed in Table 2 can confuse the reader as they somewhat are misleading and confusing. Please do list it with a better explanation so that it doesn't confuse the readers" (page 7), we have clarified (Table legend) that values

listed in Table 2 relate to pre-operative characteristics, so that the readers do not confuse these values with those relative to the 6-month timepoint depicted in Figure 2. For consistency, we have changed the legend to Table 1, as we realized that the term “baseline” had been used to indicate both the pre-operative and the first post-operative assessments. The term “baseline” was also changed to “pre-operative” in the Methods (page 5).

- As for the comment “Another limitation to be listed would be that the sample size is small” (page 10), we have listed the relatively small sample size as a limitation of the study (page 9).

- As for the comment “The error bars for the weight loss in patients with ketosis after 6 months and 12 months seem to be very long. Why is there such a big variation because the baseline is somewhat similar for both sets of patients. Does this large variation show any effect on the accuracy??”: considering the mean percent weight loss, standard deviations are actually similar between groups, and smaller at the time of the primary endpoint (WL at 6 months: 27.5 ± 5.1 vs. 23.8 ± 4.3 in the KB+ vs the KB- group, respectively; $p=0.035$) than at baseline (12.3 ± 3.7 vs. 11.3 ± 3.6 in the KB+ vs the KB- group, respectively; $p=0.438$). Variability increases slightly at 12 months (33.2 ± 7.9 vs. 28.4 ± 4.6 in the KB+ vs the KB- group, respectively; $p=0.067$), likely because data at this timepoint were available for a subgroup of 35 patients (89.7% of the total, 24 in the KB+ group and 11 in the KB- group), which might explain the lack of a statistically significant difference at the 12-month timepoint. It should also be noted that, despite the relatively small sample size, data were normally distributed and there was homogeneity of variance, as assessed by the Levene's test. We have added the exact number of subjects for each group in the Results (page 6) and listed the small sample size and the availability of data on WL at 12 months only for a subgroup of patients as limitations of the study (page 9).

(3) Format: There are 3 tables and 2 figures;

(4) References: A total of 45 references are cited, including 7 references published in the last 3 years;

As mentioned above, we added 4 references in the revised version of the manuscript. The number of references is now 49, 9 of which published in the last 3 years (2019-2021).

(5) Self-cited references: Self-cited references are not detected because the references are not complete with all authors.

We apologize for this oversight. The bibliographic references have been completed with the addition of all authors.

(6) References recommendations: The authors citation is an acceptable range.

We thank the Science Editor for this comment.

2 Language evaluation: Classification: Grade A. A language editing certificate issued by AJE was provided.

3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the signed Informed Consent Form, and the Institutional Review Board Approval Form is correctly provided. No academic misconduct was found by the Google/Bing search. However, the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement is not provided.

The signed Conflict-of-Interest Disclosure Form and Copyright License Agreement have been provided.

4 Supplementary comments: This is an invited manuscript. No financial support was obtained for the study. The topic has not previously been published in the WJG.

5 Issues raised:

(1) A re-review of the manuscript is required

(2) The “Author Contributions” section is missing. Please provide the author contributions;

We have provided the author contributions.

(3) PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;

We apologize for this oversight. PMID and DOI numbers have been added to the reference list, and all authors have been listed.

6 Re-Review: Required.

7 Recommendation: Conditional acceptance

(2) *Company editor-in-chief:* I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Diabetes, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office’s comments and the Criteria for Manuscript Revision by Authors.

We thank the Editor in Chief for the time and effort spent reviewing our work.

The following new/revised files have been uploaded:

(1) Manuscript File (Auto-edited)

(2) 67081-Answering Reviewers

(3) 67081-Audio Core Tip

(4) 67081-Conflict-of-Interest Disclosure Form

(5) 67081-Copyright License Agreement

(6) 67081-Image File

(7) 67081-Table File

Best regards,

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