

RE: ID bmjnph-2020-000183

Editor in Chief, *BMJ Nutrition, Prevention & Health*

Dear Dr. Martin Kohlmeier

I would like to thank you for your positive decision on our submission to *BMJ Nutrition, Prevention & Health*, bmjnph-2020-000183, entitled ""The impact of supervised beego, a traditional Chinese water-only fasting on thrombosis and hemostasis"" by Yixuan Fang, Yue Gu, Chen Zhao, Yaqi Lv, Jiawei Qian, Lingjiang Zhu, Na Yuan, Suping Zhang, Li Wang, Mengli Li, Qing Zhang, Li Xu, Wen Wei, Lei Li, Li Ji, Xueqin Gao, Jingyi Zhang, Yueping Shen, Zixing Chen, Guanghui Wang, Kesheng Dai, and Jianrong Wang from Soochow University.

We also thank the referees for their suggestions and comments, which are very helpful for us to improve our manuscript. We found several statistical mistakes in our initial submission, and have now corrected in Figure 1 and Supplementary Figure 1 (verbal changes are highlighted in yellow).

We have now revised the manuscript to reduce redundant information and also modified our description (highlighted in yellow) to make our contention more acceptable as the reviewers kindly suggested.

We have also provided our answers to the reviewers point by point in the following pages. We hope that this revised version will be suitable for publication in BMJ NPH.

Since this is the first report on beego study and its methods are described in detail. This makes the manuscript longer than usual.

Sincerely,

Jianrong Wang, PhD

Professor of Hematology, Hematology Center of Cyrus tang Medical Institute, Soochow University, China.

Reviewer(s)' Comments to Author:

Reviewer: 1

Comments to the Author

1. Please describe in detail how supervisions were conducted during beego. How were the 7 day or 14 day fasting chosen?

RE: For supervision during fasting, medical professionals including clinic doctors (periodically) and nurses (all the time) were present in the location where beego was collectively conducted in the first 4-day fasting. Thereafter, Wechat or phone communication remains constant when the participates went at home in office for continued fasting. Blood pressure, pulse, blood glucose and weight were measured by the professionals along with other measurements every day. Emergency rescue kits were provided in the beego location. The information for the supervision has now been more detailed the beego protocol.

The subjects were free to chose 7 day or 14 day fasting regime based on their willingness and safety evaluated by professionals using daily records on health.

2. Please indicate whether the participants were allowed to interact socially with the nonparticipants freely or not. Were all the experiments performed at about the same dates. What were the dates of the experiments? What was the average temperature in the day and in the evening during beego?

RE: Yes, the participants were free to interact with their relatives or friend visitors in the first four-day fasting in the hotel where they conducted fasting regime. They then did the rest of the fasting at home or in office when they may be able to do some light work at home or in office and regularly come back to our Campus hospital for collecting blood samples and regular health check.

All the measurements and laboratory tests were performed in one trial at the same dates, specifically for the period November 14-17 2019 collectively in the hotel and November 18-28, 2019 at home or in office.

Fasting in the first four days is critical when Glucogenesis–Ketogenesis transition is initiated and ongoing. It largely determines how far a subject may be able to proceed with the fasting. Therefore, the fasting experiments of the first four days were conducted in the hotel nearby our University campus. During the period, courses including human physiology, psychological induction, light excises, etc., were provided to facilitate the fasting process.

The average outdoor temperature in the day was around 15–20°C and 5–10°C in the evening during the beego practice. The temperature information in Suzhou city where the beego was practiced are given below:

Date	Temperature (°C)	
	Highest	Lowest
Nov 14, 2019	18	10
Nov 15, 2019	21	12
Nov 16, 2019	24	16
Nov 17, 2019	24	11
Nov 18, 2019	11	5
Nov 19, 2019	13	5
Nov 20, 2019	15	11
Nov 21, 2019	16	11
Nov 22, 2019	21	16
Nov 23, 2019	23	16
Nov 24, 2019	20	8
Nov 25, 2019	10	6
Nov 26, 2019	12	8
Nov 27, 2019	9	7
Nov 28, 2019	10	6
Nov 29, 2019	12	9
Nov 30, 2019	13	8
Dec 01, 2019	9	4
Dec 02, 2019	9	0
Dec 03, 2019	10	3
Dec 04, 2019	12	3

3. Please indicate whether the participants recorded their sleeping patterns during the fasting period.

RE: Yes. The participants recorded their sleeping patterns using Fitbit Inspire HR during the fasting period. We have data on sleeping quality (status

per minute) for 25 participants, heart rate per second for 27 participants. It appears that beego improves their sleeping patterns, in particular the beego subjects responded positively with their sleeping quality. We will publish it separately, when data for large volume of participants is available.

4. Please indicate what would be the major difference in method between Beego and other forms of fastings recorded in the literature

RE: The major difference between beego and other forms of fastings recorded in the literature are: 1) No food including meal, supplements, fruit juice, soda, etc., were taken except water. 2) The participants are instructed to have psychological induction to overcome the feeling of hunger. 3) Refeeding program is critical for the safety of beego, and proceeds strictly step by step to ensure gut function recovery.

Reviewer: 2

Comments to the Author

This paper reports the results of a pilot study of beego, a form of intermittent fasting. No prior scientific publication has performed an analysis of this form of fasting. This is not a randomized trial and no parallel control arm is present. The participants were given the option of engaging in a 7-day or a 14-day fasting period, thus some preference of the participants went into the allocation to the two different regimens. As a pilot study, though, this is a well-performed study and the results are interesting and important in the field. Some of the findings, such as elevation of cholesterol and LDL-C during the fasting period and eventual return to baseline of those parameters after feeding resumes replicates one of my 2013 papers that I have seen very few studies that have provided data to answer whether that was correct, so this is an interesting and important feature in my mind that helps to validate that the other findings of the study are correct. The findings should be replicated in future research, but this serves as an important paper to describe the beego regimen and its health effects. I suggest some minor revisions, but eventual acceptance.

Fang and colleagues evaluated the effect of an unrandomized beego intervention on risk of thromboembolism and cardiovascular outcomes in a pilot study. This is an interesting fasting regimen and the first of its kind for describing beego. The inclusion of meditation and other psychosocial support for successful adherence to the regimen is an interesting addition in the field of intermittent fasting.

Major comments:

1. The Results section has some redundancy in the text in that it provides, perhaps as a reiteration, some of the Methods that were described in the Methods section. This makes the paper somewhat more difficult to read and longer than it needs to be. Making the Results section more succinct would be beneficial. In general, focusing the text of the paper to be more succinct throughout including in the Discussion would be helpful. The paper provides results on a substantial amount of data, thus being succinct is important for the reader.

RE: We thank the reviewer for the important suggestion, and have simplified the descriptions in the Results and Discussion Sections.

2. Because this is a non-randomized study with no parallel control group, the paper should take care to avoid overstating the findings. It would be good to soften the claims in the Conclusion and throughout so that the findings do not claim more than they show in a sample size that is <50 subjects.

RE: We thank the reviewer for his/her suggestion, and have modified our contentions throughout the manuscript.

Editor(s) Comments to Author: Associate Editor

Comments to the Author:

This pilot study using beego, a form of intermittent fasting, together with meditation and other psychosocial support as the intervention is interesting and presents some novel results regarding a special fasting regimen on risk of thromboembolism and cardiovascular outcomes. However, it is an unrandomized trial with no parallel control and <50 subjects, which generates concerns about the scientific value of the findings. Please answer the reviewers' questions and revise the manuscript according to the reviewers' comments.

RE: We thank the Associate Editor' s comment. We have softened our conclusion in the revision.