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OPEN PEER REVIEW

Effect of High-intensity Interval Training on Endothelial Function in Type 2 Diabetic Females

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This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

1 comment · 17 Feb 2021

Ebrahim Norouzi Reviewer

MAJOR REVISION 17 Feb 2021

Dear Author,
The manuscript entitled "Effect of High-Intensity Interval Training on Endothelial Function in Type 2 Diabetic Women" presents a topic that may interest readers of the "Asian Journal of Sports Medicine". Although I consider the topic interesting, I would like to make some comments about the present manuscript below:

1. The quality of the English writing is NOT good, and it is really difficult for me to understand the text. There are a number of grammatical errors in the manuscript. The authors may wish to have the manuscript proofread for clarity by a native English speaker.
2. It is documented that high-intensity interval training would be harmful to the patient population. Heart rate variability during this training is not only unhelpful but can also increase health problems. Based on previous studies, balance and sensory functions are impaired in patients with diabetes. Why did you not focus your training on these factors? Furthermore, and most concerning, women with type 1 diabetes usually also have depression. Have you measured their depression levels?

major concerns:
introduction:
1. In the introduction, the authors need to be more explicit about the real justifications for the review. Also, why is a study on this topic essential? Why high-intensity interval training and not other exercises?
2. In the introduction, there is a sudden discussion about Flow-mediated dilatation (FMD) and Type 2 diabetes (T2D). You should define metabolic problems and mention the types of metabolism-related illnesses, such as diabetes. Further, define diabetes and provide epidemiological information about it. Lastly, identify the negative effects of diabetes on women's health. After that, you can describe methods of diabetes control and treatment, such as exercise-based interventions, aerobic or resistance training, dietary interventions, etc. Then you can discuss high-intensity interval training.

Method:
1. Please explain the sampling method clearly.
2. Inclusion and exclusion criteria were not mentioned. Please provide the complete criteria for inclusion and exclusion of participants. Did you check your participants' physical activity levels? Did you check which medications your participants had used?
3. For how many years have the participants had diabetes?
4. A flowchart is needed!
5. You say nothing about the intervention in detail! The control group should serve as a wait-list control group or do something. In your study, they do nothing and just participate in your study!

Results:
6. ANOVA with repeated measurements should be used, not ANOVA. Moreover, Shapiro Wilk should be used to test for normality because your sample size is just 30!
7. You should not use just a paired t-test to determine interaction effects; you should also use the independent t-test.

Discussion:
1. In the end, the discussion is very vague. Could the authors please lengthen this section and add some thoughts to ensure that the discussion adds novelty to the manuscript?

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear editor,

We would like to thank you and the team of reviewers who found our study interesting and gave valuable comments. The manuscript had some deficiencies that we tried to correct according to the logical expert reviewer's comments. We did revise with our best try to consider all the comments as specific as possible.

We hope that the reviewers will find our responses satisfactory. Please find below a detailed point-by-point response to all comments. Please kindly note that all the revised parts within the revised manuscript are highlighted for your convenience of re-reviewing.

Reviewer 1:

1. *The quality of English writing is NOT good and it is really difficult for me to understand the text. There are a number of grammatical errors in the manuscript. The authors may wish to have the manuscript proofread for clarity by a native English speaker*

   Thank you for your concern. We did the grammatical revision thoroughly and got help from an English-speaking person.

2. *It is documented that high-intensity interval training would be harmful for the patient population. The heart rate variability during this training not only is not helpful but can increase health problems. Based on previous studies, balance and sensory functions are impaired in patients with diabetes, why did you not focus your training on these factors? further and most concerning, women with type 1 diabetes usually also have depression, have you measured their depression levels?*

   We thank the reviewer for raising this important issue that encouraged us to rewrite the last paragraph of the background section. In this paragraph, we tried

to clarify the issue that HIIT could be safe for diabetic patients and cited relevant references to support the above-mentioned claim (Refs 27-29). However, regarding depression of diabetic patients, we did not measured any depression level or other psychological variables.

Introduction:

1. *In the introduction, the authors need to be more explicit about the real justifications of the review. Also, Why is essential a study this topic? Why high-intensity interval training and not others exercise?*

Thank you for your comment. We have almost rewritten the background section and tried to consider this comment in the revised manuscript.

2. *In the introduction, there is a sudden discussion about Flow-mediated dilatation (FMD) and Type 2 diabetes (T2D). you should mention metabolism problem definition and the types of metabolism-related illnesses such as diabetes. Further, define diabetes and provide epidemiological information about it. In last, identify diabetes's negative effects on health among women. After that, you can describe methods of control and treatment in diabetes like exercise-based interventions, aerobic or resistance training, diet intervention, and etc. then you can discuss high-intensity interval training.*

According to your valuable suggestion, the introduction is restructured and reordered compared to the previously submitted version. We tried to consider your suggestion in the first and second paragraph of the introduction.

Method:

1. *Please explain clearly the sampling method.*

Following your suggestion, we added the sampling method (second line of participants and the study design subsection).

2. *Inclusion and exclusion criteria were not mentioned. Please mention the criteria for inclusion and exclusion of participants completely. do you check your participants about their physical activity levels? Do you check your participant about the medicine which they have used?*

We have included additional information concerning the inclusion and exclusion criteria in the method section. Regarding participants' physical activity levels, we do not have detailed information; but none of them had any training program from at least six months before the beginning of the study (this is mentioned as an exclusion criterion in the revised version of the manuscript). Concerning medicine usage, all the participants continued their prior regimen with metformin (this is also mentioned in the new version of the manuscript).

3. *How many years the participants have diabetes?*

We pointed it out in the third line of the method section that participants had at least two years history of diabetes.

4. *Follow chart is needed!*

As is mentioned in the method section of the revised manuscript, we used convenience-sampling method and then 30 participants were randomly assigned into two equal groups of HIIT and control. Fortunately, we did not have any withdrawal and all the participants were included in the data analysis. Therefore, if you agree, we would like not to use any follow chart.

5. *You say nothing about intervention in detail! The control group should be as waited-list control or do something. in your study, they do nothing and just participate in your study! it is not ethical.*

We have added further detail, and a better structure, to explain the intervention. Concerning the control group, even though the participants were encouraged to maintain the activities of daily living without any training program, however they continued their prior medication regimen during the study period, as is mentioned in the new manuscript. Besides, all the ethical issues were considered according to the declaration of Helsinki and an official Ethics Committee approved the trial.

Results:

6. *ANOVA with repeated measurements should be used not ANOVA. moreover, Shapiro Wilk should be used for normality because your sample is just 30!*
7. *you should use not just a pair t-test for knowing interaction effects, you should also use the independent t-test.*

Thank you for your valuable comment. Agreeing with your viewpoint, we had already used ANOVA with repeated measurements! However since the ANOVA with repeated measurement is one of the various forms of ANOVA, we had written just “ANOVA” in the previous version of the manuscript. However, it is corrected in the revised manuscript.

With respect to your comment about the independent t-test, in the case of using ANOVA with repeated measurements in a 2×2 design (like our design), the p value of the interaction effect in output of the SPSS software will be exactly the same as p value of the independent t-test (when it is used to compare the deltas for knowing interaction effects). Because we have already reported the interaction effects, we did not performed the independent t-test. Nevertheless, if you prefer, we can perform the independent t-test and report its results too.

Discussion:

1. *In the end, the discussion is very vague; please could the authors lengthen this section and add some thoughts to ensure the discussion is added novelty to the manuscript.*

We have followed this useful suggestion and have updated the discussion. We have tried to rephrase some of the concepts covered in the discussion to make them more concise and easier to comprehend.

***Reviewer** 2:*

Thank you for the pleasure of reviewing this article. The authors have described a randomised trial assessing the role of HIIT on FMD and other biochemical variables. Overall the quality of writing is fine and the groups appear to be well balanced. Their measurements section is also well detailed. However, there are several crucial parts of this study that are missing (please see comments).

We thank the reviewer for the positive feedback.

How were patients randomised? If you are randomizing, you should offer a clear protocol. Not all methods of randmoisation are equal.

We thank the reviewer for raising this question. Thus, we have added appropriate text to the "*participants and study design"* subsection (2nd paragraph) and tried to explain the randomization method: "participants were randomly assigned into two equal groups of HIIT and control using permuted block randomization"

Why is there no limitations section? There are likely several important limitations to this study that the authors should explore.

Thank you for pointing this out. According to your helpful comment, we added additional paragraph at the end of discussion for this purpose.

There results are not very clearly presented, and I would ask that the authors revisit this section to make it easier for readers.

According to your suggestion, the first paragraph of the results is restructured. We would like you to kindly take a look at the figure 1. We think that the significant changes are easy to recognize in this figure. Nevertheless, if you suggest any additional correction, we will welcome it.

Please change wording of women to females as you are referring to gender. May I also ask why the authors specifically chose to study females? There appears to be no introduction of this.

In accordance with your comment, we replaced women with females. Regarding females as participants, we have included additional information in the first paragraph of the introduction that indicate females may have higher risk for some chronic disease than males. However, if you suggest, we can mention this issue as a limitation in the discussion section, too.

Other comments:

1. Please add 'mellitus.' This is important so that future literature reviews can identify this article.

We would like to thank you for your valuable suggestion. We added "Mellitus" to the keywords for future scientific searches. However, because of more common use of T2D in the literature, we would prefer not to change it in the text of the manuscript.

2. 'Hyperglycemia and insulin resistance are major causal factors that increase cardiovascular disease risk" - Please cite evidence for this being part of the causal pathway.

We appreciate the precise comment and apologize for any confusion. We should have already corrected this. As another reviewer also has concerns in regards to both content and structure of the introduction, we have amended the manuscript according to both reviewers' suggestions. Even though, the relationship between insulin resistance and hyperglycemia is reported in the literature

(https://doi.org/10.1186/s12933-018-0762-4), we preferred not to mention it in the revised version of the manuscript.

3. The 20-44 group seems to be very young for a population who have had DMT2 for 2 years? Please clarify why these ages were chosen and the bias this would have as well as the external validity of your findings.

People in this age group are classified as early (20-29 years old) and middle (30-44 years old) adulthood, according to the ACSM stage of aging (ACSM' resource manual for guidelines for exercise testing and prescription, Seventh edition. Page 92). Therefore, there is a standardized classification for that. However, regarding the population and T2D, we agree that T2D most often develops in people over age 45, but more and more young adults are also developing it (https://www.cdc.gov/diabetes/basics/type2.html). An important reason to choose younger females for our study was the high-intensity training intervention that we wanted to conduct.

4. I do not require you to change this, but for future reference, my understanding is that the Shapiro-Walk test would be more suitable test for normality for your sample character.

Thank you for your helpful recommendation. We run also the Shapiro-Wilk test and replaced it, accordingly.

5. "Our results are consistent with previous reports regarding the greater efficiency of the HIIT than traditional exercise protocols on glycemic control in people with T2D" - Sorry, is this my misunderstanding? how can you declare this if your study compared HIIT versus controls… it did not compare HIIT versus traditional exercise protocols.

Thank you for your correct comment. We did not compare the HIIT versus traditional exercise protocols. Therefore, we have followed this useful suggestion and have revised the sentence: "Our results are consistent with previous studies regarding the efficiency of the interval training programs on glycemic control in people with T2D (33, 34)"

2 Revision 1

0 comments

No public comments in this round.