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OPEN PEER REVIEW

Acute Effects of Smoking on Diastolic and Systolic Cardiac Function of Healthy Smokers according to 2D Speckle Tracking Echocardiography

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SUBMITTED	REVISED	ACCEPTED
1 Apr 2022	26 May 2023	25 Jun 2023

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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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Contents

1 **Original submission** Referee 1, Referee 2, Associate Editor, Editor-in-Chief 2
2 **Revision 1** Associate Editor, Editor-in-Chief 3
Authors' reply to reviewers 4
Reviewer and editor comments 9

1 Original submission

4 comments · 1 May 2023 – 24 May 2023

Referee 1 Reviewer

ACCEPT 1 May 2023

This manuscript is accepted and can be published.

Referee 2 Reviewer

MINOR REVISION 20 May 2023

The revisions must be incorporated into the manuscript. The format of the charts is not appropriate. The charts should be based on the study objectives.
Why have charts based on age, sex, etc., been included? Did you have a sufficient sample size?
The charts should be bar charts with 95 percent confidence intervals.

Associate Editor

MINOR REVISION 24 May 2023

Needs revision.

Editor-in-Chief

MINOR REVISION 24 May 2023

Please make the revisions based on the comments.

2

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 Dr. Zibaeenezhad,

Editor-in-Chief,

International Cardiovascular Research Journal,

Greetings

We highly appreciate the time and effort that you and the reviewers dedicated to providing feedback on our manuscript and are grateful for the insightful comments on and valuable improvements to our paper. Here, we have provided a revised version based on the editor and reviewers' comments, along with a point-by-point response. We hope the responses meet their expectations. Please do not hesitate to let us know if any further changes are required; your comments are always welcome.

Yours sincerely

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"Acute effects of smoking on diastolic and systolic cardiac function using 2D speckle tracking echocardiography in healthy smoker people"

Please find below a point-by-point response to the comments along with the changes in the revised manuscript outlined by "highlights" in MS Word of the manuscript.

Comments and responses:

Reviewer comments:

1. *This manuscript is accepted and can be published.*

Response: Dear reviewer, thanks so much.

2. *The format of the graphs is not appropriate. The graphs should be based on the study objectives. The graphs should be bar charts with 95% confidence intervals.*

Response: With thanks for the respected reviewer's comment, the graphs were designed as bar charts with 95% confidence intervals, in accordance with the comments and suggestions and based on the main objectives and parameters of the study, and were replaced.

3. *What is the reason for presenting graphs based on age, sex, etc.?*

Response: Regarding the effect of sex, a significant difference in diastolic dysfunction assessed by the 2D SPECKLE TRACKING ECHOCARDIOGRAPHY method has been reported between men and women (1). In addition, the effect of increased sympathetic system activity following smoking has been suggested, which itself may be considered one of the possible mechanisms in the occurrence of the acute effects of cigarette smoking on systolic and diastolic cardiac function (2). On the other hand, in studies conducted to date, a significant difference between women and men in terms of autonomic nervous system activity and sympathetic and parasympathetic balance has been observed (3). Therefore, unlike the very limited studies conducted on the acute effects of cigarette smoking on the systolic and diastolic function of the cardiac ventricles, which were performed only on male populations (4), or which, despite the presence of women and men in the study, did not consider or examine the difference in the changes of echocardiographic parameters between women and men (5), our study analyzes the systolic and diastolic cardiac function parameters by sex, and the results show that the

changes in PASP and GLS, despite being significant in both sexes, are more marked in women than in men following smoking.

Regarding the effect of smoking intensity, in studies conducted to date, smoking intensity in terms of pack-years has shown a significant difference in the occurrence of various complications, including cardiovascular complications. In this regard, in previous studies, the classification of smoking intensity in terms of pack-years as <10, 10 to <25, 25 to <40, and ≥40 pack-years has been used (6). Therefore, given the unknown acute effect of smoking intensity on the acute effect of cigarette smoking on systolic and diastolic cardiac function, the first classification category used, i.e., smoking of 10 pack-years, was considered as the cut-off point for evaluating this issue. Accordingly, the result of this analysis showed that the greater change in PASP and the E/A ratio in participants who smoke less than 10 pack-years is more noticeable than in the group who smoke 10 pack-years or more. In other words, in individuals with lower smoking intensity, the acute effect of smoking each cigarette on pulmonary artery pressure and the E/A ratio (as a measure for evaluating left ventricular diastolic function) is more noticeable.

It should be noted that the graph related to the analysis of differences at the age cut-off of below and above 30 years was removed, in accordance with the respected reviewer's opinion regarding focusing on the main objectives of the study and the lack of sufficient evidence on the necessity of performing this analysis.

4. *The corrections should be applied in the text of the article.*

Response: With many thanks for the valuable comments of the respected reviewers toward improving the quality of the article, the above points and further explanation regarding the reason for the analysis by sex and smoking

intensity were added to the text and have been highlighted. In addition, a strengths and weaknesses section was also added at the end of the discussion section of the article.

5. Did you have an adequate sample size?

Response: Yes. It should be noted that the sample size, based on the limited previous studies conducted (5), taking into account a standard deviation of lv GLS equal to 2.8, a precision of 0.65 and a 95% confidence level (α error equal to 0.05), was calculated using the following formula:

$n= Z^2_\alpha * \sigma^2 / d^2$

n = sample size

standard deviation $\sigma=2.8$

precision of estimate d = 0.65

for a 95% confidence level $Z_\alpha = 2$

Therefore: $n= 2^2 * 2.8^2 / 0.65^2 = 31.36 / 0.42 = 74.67$

Thus, the sample size was calculated as about 75 persons, and considering the possibility of sample attrition during the stages of the study, 80 persons were considered for greater assurance.

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3. Koenig J, Thayer JF. Sex differences in healthy human heart rate variability: a meta-analysis. Neuroscience & Biobehavioral Reviews. 2016;64:288-310.
4. Alshehri AM, Azoz AM, Shaheen HA, Farrag YA, Khalifa MAA, Youssef A. Acute effects of cigarette smoking on the cardiac diastolic functions. Journal of the Saudi Heart Association. 2013;25(3):173-9.
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6. Ding N, Sang Y, Chen J, Ballew SH, Kalbaugh CA, Salameh MJ, et al. Cigarette smoking, smoking cessation, and long-term risk of 3 major atherosclerotic diseases. Journal of the American College of Cardiology. 2019;74(4):498-507.

2 Revision 1

2 comments · 7 Jun 2023 – 25 Jun 2023

Associate Editor

ACCEPT 7 Jun 2023

accept

Editor-in-Chief

ACCEPT 25 Jun 2023

accept