OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

International Journal of Endocrinology and Metabolism
Article DOI: 10.5812/ijem.109285
Published in: International Journal of Endocrinology and Metabolism: 19(4); e109285

Peer Review Report for "Anthropometric Indices and Age at Natural Menopause: A 15-Year Follow-up Population-Based Study"

Author(s): Maryam Farahmand, Fahimeh Ramezani Tehrani , Maryam Rahmati, Fereidoun Azizi

Review Timeline:

Submit Date: 9 Sep 2020
Revised Date: 2 Feb 2021
Accepted Date: 19 Apr 2021

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | Revision (0)

22 Oct 2020

Dear AE,
- Anthropometric indices and age at natural menopause: A 15-year follow-up population-based study
- Introduction: the gap of the study is not clear, why have the researchers done this study?
- Material and methods: Exclusion and inclusion criteria are not clear.
- How many years have people been pursued? Which phase(s)? The figure should be completed. Material and methods should be completely reported; this section is very vague.
- Results: Please provide the characteristics of participants according to “Reached menopause at the
end of follow-up” and “not Reached menopause at the end of follow-up” as well as change of the variables such as BMI, WHR, WHtR, and ABSI in these two groups.
- In the introduction, the researchers provide information regarding ABSI, BRI, VAI, LAP, and their relation to ANM, however, no results were provided in this manuscript. Please report the association between these variables with ANM. In addition change of these variables and their relation to ANM should be reported.
- In addition please provide the HR for the association between these variables and the risk of ANM.

- Discussion: Please provide a mechanism of anthropometric indices associated with ANM.
Thanks.

Sima Nazarpour: Reviewer | **Revision** (0) 3 Nov 2020

Dear AE,
The study entitled “Anthropometric indices and age at natural menopause: A 15-year follow-up population-based study” aimed to investigate the ability of Anthropometric Indices (AI) in predicting ANM. This is a well-designed and well-written study with an interesting subject. However, this study has some concerns which should be addressed before publication. The followings are suggested:
Title
- The title reflects the content appropriately
Abstract
• Please add a sentence about the importance of menopausal age.
• Please indicate the type of study in the method section.
• Keywords: “Anthropometric Indices” is not in the mesh, please change it to “anthropometry”. Also, “Age at Natural Menopause” is not in the mesh, please change it to “Menopause”
Background
- The statement of objective at the end of the background does not require a subtitle.
Methods
• You stated that “our study population included all the women who aged >20 years old and met the eligibility criteria. Please indicate the eligibility criteria and exclusion criteria.
• Please indicate the type of study in the method section.
• How do you ensure that your sample size is sufficient for this study? Please provide sample size justification.
• It is necessary to define the terms of “the visceral adiposity index (VAI) and lipid accumulation product (LAP)”.
• The design of the study is not sufficiently described and needs to be explained in more detail.
• Please explain ethical considerations
Results:
• Results recorded appropriately.
• In the sentence "The mean (SD) BMI, WHR, WHtR and ABSI were 27.0 (5.1), 0.8 (0.1), 0.5 (0.1) and 0.75 (0.05), respectively." please mention the unit of BMI.
Discussion
• If possible, please provide some underlying pathophysiologies related to the findings.
• What further studies are recommended in this area?
• Please add some clinical use for the findings of this study for clinicians.
Thanks.

REFEREE: Reviewer | **Revision** (0) 15 Dec 2020

Dear AE,
Title: Anthropometric indices and age at natural menopause: A 15-year follow-up population-based study

In this manuscript the authors have tried to associate some anthropometric indices with natural menopause in a cohort study. My comments are as below:
1. Page 3, Definitions: the formulas for Anthropometric Indices have some typo errors. Brackets and parentheses should be placed in their correct positions. For example correct formula for LAP is: [WC (cm)-58] * TG (mmol/l) instead of [WC (cm)-58*TG(mmol/l), i.e. the bracket after 58 is missing that changes the result significantly. Other formulas have similar typo errors, please recheck all of them.
2. What were the inclusion and exclusion criteria of this study? Please define precisely. The only criterion set for the study is age>20 years at recruitment. Were there any menopause women at the beginning of the study? What was the age range at the enrolment? What was the minimum and maximum time to menopause?
3. Please give justifications for using Accelerated Failure Time (AFT) model in this study. What is the reason for applying such a model among varieties of existing survival models?
4. Page 4, Statistical analysis section: Based on which criterion, Weibull distribution has been found as the best distribution fitted to the time to menopause onset?
5. Table 2: Time ratios (TRs) are all very close to one (ranges between 0.98 to 1.01), so despite some significant TRs, their effect sizes are very small and negligible. For example for one standard deviation of BMI (i.e. 5 Kg/m2) we have TR=1.01 and significant (p=0.02). Apart from its significance, this is not a considerable association. So, it is recommended to be cautious on discussion and conclusion. For example stating that “the studied indices are most useful new AIs for the assessment of ANM” need to be modified accordingly.
6. Please report the fitting indices of the models in table 2? What is the prediction power of the models?
Thanks.

REFEREE: Associate Editor | **Revision** (0) 27 Dec 2020

Dear EIC,
The manuscript needs major amendments.
Thanks.

Fereidoun Azizi & Dr. Azita Zadeh-Vakili: EIC | **Revision** (0) 27 Dec 2020

Dear Author,
The reviewers' comments are mentioned. Please correct the details as mentioned above carefully according to reviewers' request.
Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear Editor-in-Chief, Professor **Fereidoun Azizi**

Greetings,

We appreciate your considering our manuscript entitled **“Anthropometric indices and age at natural menopause: A 15-year follow-up population-based study”,** and the constructive comments of the reviewer, based on which we have revised the manuscript with **point-by-point responses** (R) to his/her comments (C).

Attached herewith the revised version of manuscript; awaiting your reply at your earliest convenience.

Thank you

Sincerely

REVIEWERS' COMMENTS:

Point to point responses (R) to reviewer comments (C):

Reviewer 1:
The study entitled "Anthropometric indices and age at natural menopause: A 15-year follow-up population-based study" aimed to investigate the ability of Anthropometric Indices (AI) in predicting ANM. This is a well-designed and well written study with an interesting subject. However, this study has some concerns which should be addressed before publication. The followings are suggested:

Title
(C) The title reflects the content appropriately

(R) Thank you for your positive consideration.

Abstract
(C) Please add a sentence about the importance of menopausal age.

(R) Agreed, a sentence added text. (Abstract, Background)

(C) Please indicate the type of study in the method section.

(R) Agreed, added. (Abstract, Methods)

(C) Keywords: "Anthropometric Indices" is not in the mesh, please change it to "anthropometry". Also, "Age at Natural Menopause" is not in the mesh, please change it to "Menopause"

(R)Agreed, these keywords changed.

Background

(C)The statement of objective at the end of the background does not require a subtitle.

(R) This section has written based on the format of the **Journal.**

Methods

(C) You stated that "our study population included all the women who aged >20 years old and met the eligibility criteria. Please indicate the eligibility criteria and exclusion criteria.

(R) Due to the limited number of words in the journal format, this section was shown in Figure 1, but, it was given in the text according to the reviewer's comment as follows:

Our study population included all the women aged >20 years who participated in the TLGS (n= 5405). Menopausal women at baseline were excluded (n=125) and those with missing data (322) those with met the eligibility criteria including lack of a history of surgical menopause or any other ovarian surgery at all of the follow-ups (n=183), and lost to follow up (n=899). Finally, 3876 women completed follow up (fig1).

(Methods, page 2,lines 13-18)

(C) Please indicate the type of study in the method section.

(R)Agreed and added.

(Methods, page 2, line 8)

(C) How do you ensure that your sample size is sufficient for this study? Please provide sample size justification.

(R) Thank you for your valuable comment. We calculated our sample size using the formula provided in *Hsieh's, Philip's, and Lavori's* .

The formula was as below:

$$D=(Z_{1-\alpha}+Z_{1-\beta})^2/\sigma^2(\log\Delta)^2$$

$$N=D/\rho$$

$$\alpha=0.05\ \beta=0.2\ \sigma=5\ \Delta=0.95\ \rho=0.38$$

Where σ^2 is the variance of BMI and Δ is the log hazards ratio associated with a one-unit change in BMI obtained from previous studies. D is the required number of menopause events, ρ is the overall menopause rate in this study and N is the needed sample size. Therefore, the required number of menopause events would be 517 and a sample size of 1361 is needed. So, *our* sample size is sufficient for this study.

(Methods, page 3, lines 1-9)

(C) It is necessary to define the terms of "the visceral adiposity index (VAI) and lipid accumulation product (LAP)".

(R)These terms were highlighted in the definition section.

(Methods, page 2, lines 24-26)

(C) The design of the study is not sufficiently described and needs to be explained in more detail.

(R) It has already been explained that word limitation prevents the explanation of details, but according to the reviewer's comment, we explained in more detail.

(Methods, page 2, lines 13-18 & page 3, lines 15-19 & lines 1-9 & page 4, lines 1-13)

(C) Please explain ethical considerations

(R)Agreed, ethical considerations added as follows:

Before, doing the study informed consent was obtained from all participants in the study, and all procedures were approved by the ethical committee of the Research Institute for Endocrine sciences.

(Methods, page 4, lines 10-12)

Results:
(C) Results recorded appropriately.

(R) Thank you for your positive consideration.

(C) In the sentence "The mean (SD) BMI, WHR, WHtR and ABSI were 27.0 (5.1), 0.8 (0.1), 0.5 (0.1) and 0.75 (0.05), respectively." please mention the unit of BMI.

(R)Agreed and added.

(Results, page 4, line 22)

Discussion

(C) If possible, please provide some underlying pathophysiologies related to the findings.

(R) Due to the limited number of words, as much as possible was added details of pathophysiology.

(Discussion, page 5, lines 11-12, 16-17, 20-23& page 6, lines 1-3)

(C) What further studies are recommended in this area?

(R) Agreed, we added this subject in the text.

(Discussion, page 6, lines 25,26)

(C) Please add some clinical use for the findings of this study for clinicians.

(R) Agreed, we added this subject in the text.

(Discussion, page6, lines 22-24)

Reviewer 2:
Anthropometric indices and age at natural menopause: A 15-year follow-up population-based study

(C)Introduction: the gap of the study is not clear, why have the researchers done this study?

(R) Agreed, the gap of this study added

(Background, page 2, lines 3-6)

Material and methods: (C)Exclusion and inclusion criterial are not clear.

(R) Due to the limited number of words in the journal format, this section was shown in Figure 1, but, it was given in the text according to the reviewer's comment.

(Methods, page 2, lines 14-19)

(C)How many years have people been pursued? Which phase(s)? Material and methods should be completely reported; this section is very vague.

(R) As mentioned in the result section, the median (interquartile range) of the survival time (years) was 12.5 (7.9-15.8) years. They pursued from phase 1 to phase 6.

(Methods, page 4, lines 20-21) and fig.1

Results: (C)Please provide the characteristics of participants according to "Reached menopause at the end of follow-up" and "not Reached menopause at the end of follow-up" as well as change of the variables such as BMI, WHR, WHtR, and ABSI in these two groups.

(R*)* Thank you for your precise comment, the characteristics of participants according to "Reached menopause at the end of follow-up" and "not Reached menopause at the end of follow-up"were added to table 1. However, change of the variables such as BMI, WHR, WHtR, and ABSI as well as cardiometabolic variables in these two groups have been reported on another prepared paper which is under reviewed.

(Page 8)

(C) In the introduction, the researchers provide information regarding ABSI, BRI, VAI, LAP and their relation to ANM, however no results were provide in this manuscript. Please report the

association between these variables with ANM. In addition change of these variable and their relation to ANM should be reported.

(R) Thank you for your precise comment. The association of these variables with ANM was provided by an accelerated failure time model by reporting time ratio in table 2. According the result section, increasing ABSI and LAP is related to earlier ANM while increasing BMI postpones the ANM. Moreover, change of the variables such as BMI, WHR, WHtR, and ABSI as well as cardiometabolic variables in these two groups have been reported on another prepared paper which is under reviewed.

(C) In addition please provide the HR for the association between these variables and risk of ANM.

(R) Although using Cox proportional hazard model as a semiparametric model and reporting HR has come to the fore by most researchers in medical fields, results of accelerated failure time models have often been more valid and have had minor bias since these models have better fitness in similar conditions due to a specific statistical distribution for the survival time and their not having need to PH assumption. Although the PH model specifies that the effects of the covariates act multiplicatively on the hazard function, the AFT model regresses the logarithm of the failure times over the covariates, postulating a direct relationship between failure time and the covariates . When survival time has a specific statistical distribution, the statistical power of parametric survival model is higher than Cox

model which is a semiparametric survival model. In this study, we used a parametric approach and reporting HR is out of scope of the study.

(Methods, page 3, lines 15-19 & page 4, lines 1-5 & page 4, lines 7-9)

(C) Discussion: Please provide mechanism of anthropometric indices that associated with ANM.

(R) Agreed, the mechanism explained in discussion.

(Discussion, page 5, lines 11-12, 16-17, 20-23& page 6, lines 1-3)

Reviewer 3:
Title: Anthropometric indices and age at natural menopause: A 15-year follow-up population-based study
In this manuscript the authors have tried to associate some anthropometric indices with natural menopause in a cohort study. My comments are as below:

*(C)1. Page 3, Definitions: the formulas for Anthropometric Indices have some typo errors. Brackets and parentheses should be placed in their correct positions. For example correct formula for LAP is: [WC (cm)-58] * TG (mmol/l) instead of [WC (cm)-58*TG(mmol/l), i.e. the bracket after 58 is missing that changes the result significantly. Other formulas have similar typo errors, please recheck all of them.*

(R)Agreed, all of the formulas rechecked, and if necessary modified.

(Methods, page 2, lines 25-27)

(C)2. What were the inclusion and exclusion criteria of this study? Please define precisely. The only criterion set for the study is age>20 years at recruitment. Were there any menopause women at the beginning of the study? What was the age range at the enrolment? What was the minimum and maximum time to menopause?

(R) Due to word limitations, the inclusion and exclusion criteria of this study have shown in full in figure1 but, were given in the text according to the reviewer's comment. All non-menopause women aged 20 to 60 years old (mean (SD)= 33.9 (8.9)) were included in this study. The minimum and maximum time to menopause was 1 and 18 years respectively.

(Methods, page 2, lines 14-19)

(C)3. Please give justifications for using Accelerated Failure Time (AFT) model in this study. What is the reason for applying such a model among varieties of existing survival models?

(R) The AFT model can be rewritten specifying a direct relation between the logarithmof the survival time and the explanatory variables and with considering a parametric distribution, the statistical power of AFT model is higher than Cox model which is a semiparametric survival model. Although using Cox proportional hazard model has come to the fore by most researchers in medical fields, results of accelerated failure time models have often been more valid and have had minor bias since these models have better fitness in similar conditions due to a specific statistical distribution for the survival time and their not having need to PH assumption.

(Methods, page 3, lines 15-19)

(C)4. Page 4, Statistical analysis section: Based on which criterion, Weibull distribution has been found as the best distribution fitted to the time to menopause onset?

(R) The Exponential, Gompertz, lognormal, log logistic regression, and Weibull regression models were checked, and their goodness of fit was compared using Akaike Information Criterion (AIC). Weibull showed lower AIC than other AFT models.

(Methods, page 4, lines 3-5)

(C)5. Table 2: Time ratios (TRs) are all very close to one (ranges between 0.98 to 1.01), so despite some significant TRs, their effect sizes are very small and negligible. For example for one standard deviation of BMI (i.e. 5 Kg/m2) we have TR=1.01 and significant (p=0.02). Apart from its significance, this is not a considerable association. So, it is recommended to be cautious on discussion and conclusion. For example stating that "the studied indices are most useful new AIs for the assessment of ANM" need to be modified accordingly.

(R) Agreed, this sentence changed.

(Discussion, Page 6, lines 15-17& 21,22)

(C)6. Please report the fitting indices of the models in table 2? What is the prediction power of the models?

(R) The strategy of including the variables in the AFT model of this study was confirmatory and we aimed to see if included anthropometric indices (addition to some adjusted variables like *age, age at menarche, education, parity, smoking, and physical activity at baseline*) could affect ANM. However, we reported the fitting indices of the models based on AIC in table 2 in each separated model.

(Page 9)

OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (1) — 2 Apr 2021

Dear AE,
All the comments have been answered.
Thanks.

REFEREE: Reviewer | **Revision** (1) — 10 Apr 2021

Dear AE,
With many thanks to the authors for considering comments raised in my previous revision of the manuscript, the only point left is that some formulas in the definition section have not been yet corrected. My previous comment was:
“Page 3, Definitions: the formulas for anthropometric Indices have some typo errors. Brackets and parentheses should be placed in their correct positions. For example correct formula for LAP is: [WC (cm)-58] * TG (mmol/l) instead of [WC (cm)-58*TG(mmol/l), i.e. the bracket after 58 is missing that changes the result significantly. Other formulas have similar typo errors, please recheck all of them”
Thanks.

REFEREE: Reviewer | **Revision** (1) — 12 Apr 2021

Dear AE,
Thanks for responding to the questions and addressing all comments.
Regards.

REFEREE: Associate Editor | **Revision** (1) — 19 Apr 2021

Dear EIC,
The revised manuscript is acceptable for publication.
Thanks.

REFEREE: EIC | **Revision** (1) — 19 Apr 2021

Dear Author,
The document is reviewed carefully by the reviewers. According to their comments and your revisions as requested, this manuscript is accepted.

Thanks.