Author's response to reviews

Title: Gender differences in adiponectin level and body composition in older adults: Hallym Aging Study

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Version: 2 Date: 5 November 2013

Author's response to reviews: see over
Response to Review

November 04, 2013

Dear BMC Geriatrics reviewers and editorial staffs:

We would like to express our sincere gratitude for your consideration and thorough scrutiny of our manuscript. We greatly appreciate the referees’ specific suggestions and constructive comments. According to the provided suggestions, we have made corrections and clarifications in the manuscript and have enclosed our revised manuscript together with point-by-point responses to the referees’ comments.

We guarantee the accuracy of our references. We hope our revisions will be considered and accepted in the affirmative air during the further review process. Once again, we appreciate your consideration and look forward to hearing good news from you soon.

Thank you.

Sincerely,

Dong-Hyun Kim. MD, PhD.
TITLE: Gender differences in adiponectin level and body composition in older adults: Hallym Aging Study

[Comments for formatting changes]

1. Please include an Acknowledgement section in the main manuscript and transfer the funding statement to this section.
2. Please also remove the language revision statement included at the end of the manuscript.

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Reviewers’ Comments to the Author and Author’s reply

[Reviewer: Lei Chen]

Major Compulsory Revisions:

1. The conclusion section says “The present study shows gender differences were associated with body composition and adiponectin concentration in older adults”. This conclusion is not clear. Per the results, I assume the author is intending to say “gender may be an effect modifier for the relationship between body composition and adiponectin concentration”
We appreciated your important review and comments. As your suggestion, we corrected this sentence in our manuscript.

**Minor Essential Revisions**

2. Table 2: the header of “mean (95% CI)” is misleading. I assume the authors refers to the mean of regression coefficient

Thank you for your comment. As your suggestion, the header for the most of data of this section of table 2 is “Correlation Coefficient (95% CI)”. However, some of data of this section were presented in categorical variable, and the header for them was “mean (95% CI)”. Therefore we presented it in the footnote.

3. Results section: per Table 2, the most pronouncing correlations are between adiponectin and HDL-C, triglyceride, HOMA-IR. This is worth some description in the results section, as well as discussing it's implication

We included the description about the correlations between adiponectin and HDL-C, triglyceride, HOMA-IR in the result and discussion section.

4. Discussion section: the authors acknowledged that “the weakness of the study is small sample size”. Is there any other limitations? Could the sampling method impact the generalizability of the conclusion?

Thank you for your advice. To redeem the limitation from small sample size, the participants were selected by systematic sampling from 200 areas which were randomly selected in Chuncheon, a small city in South Korea. However, the sampling method cannot overcome the
limitation from small sample size thoroughly. Compared to other populations, the
collection of body fat and muscle to the adiponectin level in an older population was
shown to be very small or insignificant after multiple regression analysis. Therefore, a larger
study population is needed to determine the small but significant contribution of body fat and
muscle to the adiponectin level in an older population. We included it in the discussion
section.

5. Introduction section: next to the last sentence of the second paragraph. It says “With age,
body composition, especially visceral adiposity and muscle mass, change.” This is not a
complete sentence, please revise.

Thank you for your correction. The sentence meant that “Body composition changes with
aging.” We revised the sentence in the manuscript.

6. Statistical analysis section, it says “In the linear regression, the dependent variables were
natural log (loge) transformed …”. Besides adiponectin, are there any other dependent
variables?

Thank you for your comment. Adiponectin, insulin, HDL, TG and HOMA-IR were log
transformed because they were not normally distributed. We clarified and revised the
sentence in the manuscript.

7. Discussion section, page 8, 5th to the last line: it says “However, our results suggested that
gender difference was not merely a confounding factor but a disease modifying factor in
older adults”. Do the authors want to say “gender …is an effect modifier “? Thank you for your correction. We revised the sentence in the manuscript.

**Discretionary Revisions**

8. Discussion section: page 8, 4th and 3rd lines: it says that adiponectin is negative related with ARM BMC in male, but not in female; conversely, adiponectin is negatively related with LEG BMC in female, but not male. It is hard to understand the gender difference here, and would be worth some discussion for the possible cause of this, could this be a spuriously finding?

In univariable analysis, adiponectin is negative related with ARM BMC in male, but not in female; conversely, adiponectin is negatively related with LEG BMC in female, but not male. However, in multivariable linear regression models, bone mineral content was not associated with adiponectin in both sexes. We revised the discussion section of our manuscript.

**[Reviewer: Mario Luca Morieri]:**

**Major Compulsory Revisions:**

1) Discussion on testosterone: 2nd paragraph is unclear and need correction,

1a. Following sentences are divergent: “Interestingly, an inverse correlation was found between testosterone and adiponectin in males and females. … …

However, the correlation between testosterone and adiponectin in males was positive,
although insignificant. The results of our study suggested that hormonal changes according to age and gender, especially change of testosterone in females, could be an important factor influencing the paradoxical finding of adiponectin in older adults."

1aa. This data are statistically insignificant, thus it should not be so emphasized.

1b. Statistical analysis need correction: Table 3 “Multiple linear regression analysis of the relationship between adiponectin concentrations and body composition”, in this Multivariable associations also testosterone was included, without metabolic variable. Testosterone should be analyzed with other metabolic variable.

1c. Authors should compare their findings with other work (e.g. GA Laughlin et al. Sex-specific determinants of serum adiponectin in older adults: the role of endogenous sex hormones. International Journal of Obesity (2007) 31,457–465.)

1d. Abstract conclusion: author asses that hormonal change can influence the adiponectin paradox in older adults; this is not reported in the “abstract results” and furthermore finding from this work is not statistically significant.

We appreciated your specific suggestions and constructive comments.

1a. & 1aa. As you pointed out, the data were statistically insignificant. Therefore we revised the paragraph about testosterone in the discussion section.

1b. Thank you for your constructive comments. In Table 3, we re-analyzed the data and testosterone was analyzed with other metabolic variables in model 4 of the multivariable analysis as follows. We revised the manuscript also according to the results.

Table 3. Multiple linear regressions of adiponectin (dependent variable) with age, body composition for older men and women:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Men Model1</th>
<th>Model2</th>
<th>Model3</th>
<th>Model4</th>
<th>Women Model1</th>
<th>Model2</th>
<th>Model3</th>
<th>Model4</th>
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(Intercept)  0.082  2.089  2.766  -1.500  1.308  3.711  1.088  1.343
Age  0.026\textsuperscript{b}  0.018\textsuperscript{o}  0.018\textsuperscript{o}  0.024\textsuperscript{o}  0.014  0.004  0.001  0.011
Body Fat\% -  -0.021\textsuperscript{b}  -0.020\textsuperscript{b}  -0.013\textsuperscript{a}  -  -0.011\textsuperscript{b}  -0.011\textsuperscript{b}  -0.003
Arm SM (g) -  0.000  0.000  0.000  -  0.000  0.000  0.000
Arm BMC (g) -  -0.002  -0.001  -0.001  -  0.000  0.000  0.000
Leg SM (g) -  0.000  0.000  0.000  -  0.000  0.000  0.000
Leg BMC (g) -  0.000  0.000  0.000  -  -0.001\textsuperscript{a}  -0.001\textsuperscript{a}  -0.001
Waist/Height -  -0.712  -0.496  0.955  -  -1.565\textsuperscript{a}  -1.424\textsuperscript{a}  -0.516
Albumin -  -  -0.200  -0.251\textsuperscript{a}  -  -  -0.041  -0.009
Testosterone -  -  0.027  0.028  -  -  -  -0.630  -0.412
HOMA-IR -  -  0.008  -  -  -  -0.172\textsuperscript{b}
HDL-Cholesterol -  -  0.876\textsuperscript{c}  -  -  -  -  0.423\textsuperscript{a}
Triglyceride -  -  -0.127  -  -  -  -  -0.153
Model adjusted R\textsuperscript{2}  0.056  0.152  0.167  0.322  0.011  0.136  0.142  0.285

Abbreviations: SM, skeletal muscle mass; BMC, bone mineral content HDL, high-density lipoprotein; HOMA-IR, Homeostasis Model Assessment Insulin Resistance. Values are standardized \(\hat{\beta}\)-coefficients.

Model 1 includes age. Model 2 includes Model 1 variable plus body composition parameters and waist/height ratio. Model 3 includes Model 2 variables plus albumin and testosterone. Model 4 includes Model 3 variables plus metabolic variables. \(0.05>P \geq 0.01\). \(0.01>P \geq 0.001\). \(P<0.001\). - indicates not included in model.

Adiponectin, HOMA-IR, HDL and triglycerides were log-transformed for analyses.

1c. Thank you for your specific comment and reference. We compared our findings with other works as follow in the discussion section.


1d. As your suggestion, we corrected the sentence of our abstract conclusion.

2) Author should better explain the association of leg bone mineral content with adiponectin in the discussion. Please compare this work with others with similar and different result (e.g. Basurto L et al. Eur J Endocrinol. 2009 Feb;160(2):289-93. Adiponectin is associated with low bone mineral density in elderly men)

Thank you for your specific comment and reference. We compared our findings with other work in discussion section

3) Methods, Study population: If survey is not included in this study, authors should explain better when they have collected samples and performed the data collection (at baseline?) and why/how only 320 participants were selected.

We revised the study population and data collection, questionnaires and measurements section in the method of our manuscript according to your suggestion.

4) To this reviewer table 2 is unclear when reporting comorbidities on treatment. Authors should clarify how it was obtained.

The data about comorbidities on treatment were obtained from structured questionnaires. Questionnaires were administered face-to-face by trained interviewers. We clarified it in the data collection, questionnaires and measurements section in the method of our manuscript and the footnote of tables.

Minor Essential Revisions

1) Introduction: “Some researchers reported that not only visceral adipose tissue but also subcutaneous adipose tissue are both associated with adverse cardiometabolic risk”. Author should change the sentences as follow: “...but also abdominal subcutaneous adipose tissue are both…”
Thank you for your comment. We changed the sentence as follows: “Some researchers reported that not only visceral adipose tissue but also abdominal subcutaneous adipose tissues are both associated with adverse cardio metabolic risk”

2) Introduction: “With age, body composition, especially visceral adiposity and muscle mass, change.” At least one reference should be added.

We revised the sentence and added the reference as follows; Body composition changes with aging. (Ref; St-Onge MP et al. Body composition changes with aging: the cause or the result of alterations in metabolic rate and macronutrient oxidation? Nutrition. 2010;26(2):152-155)

3) Table 1. Body composition is reported in gram, whereas body fat is reported as percentage. Author should report all data on body composition in the same method.

Thank you for your advice. We added “fat mass in gram” in the Table 1 and 2.

In Table 3 (multiple linear regression), the adjusted R-square for models including fat percentage was higher than the adjusted R-square for models including fat mass in gram. Therefore we presented the models including fat percentage.