Author's response to reviews

Title: Could the Sasang Constitution Itself be a Risk Factor of Abdominal Obesity?

Authors:

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Author's response to reviews: see over
Answers to the editor’s and reviewers’ comments

We appreciate the editor and reviewers for their thoughtful comments on our work and for the effort and time they put into the review of our manuscript. The editor and reviewers raised several issues that required revision of the manuscript. We have addressed these issues in the revised manuscript as follows.

1. Reviewer’s comments.

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<td>1)</td>
<td>It is generally believed that Sasang Constitutions were formed mainly from inherited factors. So if the authors have done family survey, the data will make the conclusion more persuasive.</td>
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<td>2)</td>
<td>As the authors said, environmental factors may be the acquired risk factors for AO. So this is an important direction for future research.</td>
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Authors’ Answer

We highly appreciate your comment. We agree with your opinion. Family surveys and a gene level study could be good methods to demonstrate whether SC is an inherent risk factor for AO. However, our cross-sectional design did not enable us to analyze the association between inherent SC and AO. We described it as our limitation and, following your comment, we have added family SC research as a future direction to the discussion section.

Revised manuscript

Our study has several limitations. Previously, a large Korean family study suggested a significant association of chromosomes 8q11.22-23 and 11q22.1-3 with SC [23], and another study found that SC was associated with AO at the genetic level [32]. Family surveys and gene-level studies could be a good method to demonstrate whether SC is an inherent risk factor for AO. However, because our study had a cross-sectional design, we could not analyze the association between inherent SC and AO. In addition, we did not control for environmental factors, such as meals, lifestyle, and exercise habits, which are acquired risk factors for AO.

We believe that further studies on not only a direct comparison between constitutions considering acquired environmental factors for AO but also on inherent family SC are needed.
2. Reviewer’s comments

** General Comment
This is a data-based cross-sectional study among Korean people to evaluate whether SC type could be a risk for AO. Although this is an interesting piece of work, a few issues need to be addressed.

Authors’ Answer
Thank you very much for your kind comment. Based on your comments, we have revised the introduction, methods, results, discussion and reference sections.

1) Introduction.
- Explain the scientific background and rationale for the investigation being reported

Revised manuscript
The fundamental cause of AO is presumed to be a combination of environmental factors (inappropriate eating and physical inactivity) and the organism's genes, such as the 5-HT2A gene and glucocorticoid receptor (GR) gene in Western society [9-13].

According to SCM theory, lung hypo-function and liver hyper-function are related to a large WC, and the TE type is associated with hyperactive liver function and a developed waist area [14, 15]. We hypothesize that SC could be a risk for AO. Several family studies have been conducted to investigate the genetic evidence for SC, and they found that SC could be not only inherent but also a risk factor for obesity [22, 23]. However, there has been no clinical study to show that SC could be a risk factor for AO. In this study, we present indirect evidence of whether SC could be a risk factor for AO among Koreans.

2) Method/Design. The method section is insufficiently described.
- Participants: Give the eligibility criteria, and the sources and methods of selection of participants
- A flowchart to show the study design would be helpful
- Variables: Clearly define all outcomes, constitutional diagnosis, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
- Bias: Describe any efforts to address potential sources of bias
- Study size: Explain how the study size was arrived at
- Statistical methods: Explain how missing data were addressed.

Revised manuscript
- Eligible participant and data missing

The eligible subjects were recruited from KMCs among individuals over 30 years old whose constitution had been confirmed by experts in SC. Individuals with severe physical or mental illness or any deformation in the body trunk and pregnant women were excluded.

A total of 2,598 subjects (931 males and 1667 females) were recruited from 23 KMCs. Three of them were
excluded because of missing data. A total of 67 TY types were also excluded because of their low proportion in the Korean population. In total, 2,528 subjects (909 males and 1,619 females) were included in the final analysis. A flowchart of the study design is shown in figure 1.

- Study size

The study size was assumed from a Bernoulli distribution. We calculated a sample size of at least 600 subjects of each constitution on the basis of a 95% confidence interval and a 4% margin of error.

- Flow chart

![Flowchart of the study design](image)

- Variables

We collected WC measurements to determine the AO prevalence according to SC. We also collected data on age, sex, body mass index (BMI), and blood pressure and blood samples to control for the influence of confounding factors, which are important risk factors for AO [25, 26].

- Diagnostic Criteria

Hypertension was diagnosed by following the guidelines of the 7th Report of the JNC as ≥ 90 mmHg for diastolic pressure, ≥ 140 mmHg for systolic pressure or taking medicine for the treatment of high blood pressure [29]. DM was diagnosed with the ADA criteria as ≥126 mg/dl of fasting plasma glucose or taking medicine for the treatment of DM [30]. Hypertriglyceridemia was diagnosed as TG ≥150 mg/dl, and low HDL cholesterol was diagnosed as HDL cholesterol <40 mg/dl in males and <50 mg/dl in females. To diagnose AO as a disease, we followed the WHO Report of Asia-Pacific guidelines of WC ≥ 90 cm for males and ≥ 80 cm for females [31].

- Bias

WC was measured around the level of the umbilical scar of the subjects, who took their upper clothing off and stood in an erect posture with their arms folded in front of their chest [27]. BMI was indirectly calculated through the weight and height, and the blood pressure was measured from each subject’s left upper arm after enough rest. To reduce measurement bias among the KMCs, all instructors were educated by KIOM at least once per year, and KIOM monitored the progress of the data collection. All instructors followed a standard operation procedure (SOP) that was developed for the “Korea Constitution Multicenter Study” [27, 28]. Blood samples were collected after more than 12 hours of fasting, and the fasting blood glucose, triglyceride (TG) and HDL cholesterol levels were tested by an authorized institution.
3) Result
- Participants:
a) Give reasons for non-participation at each stage
b) Consider use of a flow diagram
- Main results: Make clear which confounders were adjusted for and why they were included

Authors’ Answer
We have described reasons for non-participation and constructed a flow diagram in the methods section. We have also explained the confounders in the methods section. To clarify the multiple logistic regression models considering confounders, we have also added detailed model explanations to the results section.

Revised manuscript
Table 3 shows a sequentially developed multiple logistic regression model of AO. Model 1 was crude, without adjustment, model 2 was adjusted for age and BMI, and model 3 was adjusted for age, BMI, hypertension, DM, hypertriglyceridemia, and low HDL cholesterol.

4) Discussion
- Key results: Summarize key results with reference to study objectives
- Limitations: Discuss both direction and magnitude of any potential bias
We summarize key results with reference to study objectives and also described the weak point and future direction

Revised manuscript
- Key results
This study suggested that SC may be a significant and independent risk factor of AO. Specifically, the TE type was associated with increased AO prevalence compared with the SE and SY types in males (OR 1.79; 95% CI 1.02-3.15, and OR 1.74; 95% CI 1.18-2.58, respectively) and females (OR 1.51; 95% CI 1.03-2.23, and OR 1.88; 95% CI 1.32-2.68, respectively), even after adjusting for age, BMI, hypertension, DM, hypertriglyceridemia, and low HDL cholesterol. This result means that the TE type could be more susceptible to AO than other types, which is similar to the trend found for hypertension, DM, and metabolic syndrome, which are associated with SC [17-21].

- Limitation and further direction
Our study has several limitations. Previously, a large Korean family study suggested a significant association of chromosomes 8q11.22-23 and 11q22.1-3 with SC [23], and another study found that SC was associated with AO at the genetic level [32]. Family surveys and gene-level studies could be a good method to demonstrate whether SC is an inherent risk factor for AO. However, because our study had a cross-sectional design, we could not analyze the association between inherent SC and AO. In addition, we did not control for environmental factors, such as meals, lifestyle, and exercise habits, which are acquired risk factors for AO.
We believe that further studies on not only a direct comparison between constitutions considering acquired environmental factors for AO but also on inherent family SC are needed.

5) Reference: Follow the guideline of reference

Authors’ Answer
Thank you very much for your kind comment.
We reformatted the references according to the guidelines for BMC CAM references.

** Specific Comments:
1) On page 4, the authors state, “the Sasang constitution (SC) has been found to be the inherent cause of obesity in Korean society,” but no references are provided.
2) On page 17, table 2, check the group sample size.
3) This manuscript should be rewritten with the help of native speaking scientist.

Authors’ Answer
Thank you for your detail review.
First, we revised that sentence, identified the reference study and provided the reference number. Second, we believe that there were some errors in the subject number in the process of making the table. We have corrected the sample size. Third, we requested language editing service to AJE translating company which is a well-known editing company in English manuscript. The certificate is annexed.

Revised manuscript
1) SC could be not only inherent but also risky for Obesity [22, 23, 32].
2) Table 2. Prevalence of Abdominal Obesity stratified by Gender and Constitution

<table>
<thead>
<tr>
<th>Variables</th>
<th>Constitution Type</th>
<th>Total</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TE</td>
<td>SE</td>
<td>SY</td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AO</td>
<td>259 (63.7)</td>
<td>28 (14.7)</td>
<td>102 (32.8)</td>
</tr>
<tr>
<td>NO</td>
<td>148 (36.4)</td>
<td>163 (85.3)</td>
<td>209 (67.2)</td>
</tr>
<tr>
<td>Total</td>
<td>407 (100)</td>
<td>191 (100)</td>
<td>311 (100)</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AO</td>
<td>530 (86.5)</td>
<td>184 (41.7)</td>
<td>292 (52.8)</td>
</tr>
<tr>
<td>NO</td>
<td>95 (15.5)</td>
<td>257 (58.3)</td>
<td>261 (47.2)</td>
</tr>
<tr>
<td>Total</td>
<td>613 (100)</td>
<td>441 (100)</td>
<td>553 (100)</td>
</tr>
</tbody>
</table>

Data are shown as the n (%). TE, Tae-eumin; SE, Soeumin; SY, Soyangin; AO, Abdominal obesity; NO, Non-obese

3) Certificate - appendix
3. Editorial comments

We recommend that you copyedit the paper to improve the style of written English. You may wish to ask a native English speaking colleague to assist you with this. If this is not possible, you may need to use a professional language editing service. For authors who wish to have the language in their manuscript edited by a native-English speaker with scientific expertise, BioMed Central recommends Edanz (www.edanzediting.com/bmc1). BioMed Central has negotiated a 10% discount to the fee charged to BioMed Central authors by Edanz. Use of an editing service is neither a requirement nor a guarantee of acceptance for publication. For more information, see our FAQ on language editing services at http://www.biomedcentral.com/authors/authorfaq/editing.

Authors’ Answer

We appreciate the editor for thoughtful comments on our work and for the effort and time they put into the review of our manuscript. The editor recommended us to improve the style of written English in the revision of the manuscript. We requested AJE translating company to edit the original manuscript one more time, which is also well-known to edit the English manuscript well.

The certificate is shown below and is annexed.