Author’s response to reviews

Title: The correlation between serum lipid profile with carotid intima-media thickness and plaque

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Author’s response to reviews: see over
Dear Mr. Gilbert Tacbobo,

Many thanks for providing us an opportunity to revise the manuscript “The clinical significance of serum lipoprotein ratios in assessing early-stage atherosclerosis” (MS1594268620141861). We appreciate for your important decision and the reviewers’ constructive comments. The manuscript has been revised according to the reviewers’ comments. In this version, the concerns raised by the reviewers have been addressed carefully on a point-by-point basis. We believe that the revision has significantly improved the quality of the manuscript and hope that the revised manuscript is acceptable for publication.

Thank you.

With best wishes,

Yours sincerely

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Responses to the comments raised by reviewer SHINJI MAKITA:

Major compulsory revision

#1. Line 61, in the abstract, they described that TC/HDL-C ratio (OR; 1.367, 95%CI; 0.975-1.917, p<0.05) were significantly associated with the presence of carotid plaque after adjustment of age. In line 196, the presence of carotid plaque was significantly and independently predicted by TC/HDL-C ratio (OR; 1.367, 95%CI; 0.975-1.917, p<0.05). On the other hand, in the Table 4, LDL-C/HDL-C ratio was included by stepwise analysis with the data of OR=1.367, 95%CI 0.975-1.917, p=0.037. Does this value show the data of TC/HDL-C? If so, no data of LDL-C/HDL-C are shown. Furthermore, “95%CI 0.975-1.917” is NOT significant level, and does not respond to “p=0.037”, because the range is across the level of 1.000.

RE: Thanks for pointing our mistakes. We are very sorry for our wrong writing. “TC/HDL-C ratio” in line 61 and 196 should be “LDL-C/HDL-C ratio”. “OR; 1.367, 95%CI; 0.975-1.917” is not the data of LDL-C/HDL-C ratio and the correct is “OR; 1.535, 95%CI; 1.047-2.124”. However, the p value is right. Thank you for your serious correction, and we have amended all the mistakes in the article.

#2. In the ROC curve analysis, it seems that TC/HDL-C ratio is the best predictor for the presence of plaque than (or as well as) LDL-C/HDL-C ratio. I cannot understand their main conclusion from these statistical data.

RE: Sorry for the unclear statement. In the ROC curve analysis, we examined not only each of the 7 lipid parameters, but also the combination model established by
multiple logistic regression analysis, including LDL-C/HDL-C ratio and HDL-C. When each of the 7 lipid parameters was separately used, TC/HDL-C ratio was the best predictor for the presence of plaque as well as LDL-C/HDL-C ratio. However, the combination model showed the largest area under the curve, which implied that LDL-C/HDL-C ratio combined with HDL-C was better than TC/HDL-C ratio itself. The manuscript have been revised as “Serum LDL-C/HDL-C ratio ... may be a useful marker for predicting the presence of carotid plaque in the Chinese general population combined with HDL-C level”.

**Minor essential revision**

#1. Diabetes or uncontrolled hypertension were excluded in the present analysis. Why these were excluded? Please explain.

**RE:** The purpose of this study aimed to investigate associations between conventional lipid parameters and lipid ratios with carotid IMT and plaque in Chinese general population without apparent diseases. Therefore, diabetes and uncontrolled hypertension were excluded. In addition, according to the diagnostic criteria of atherosclerotic carotid artery disease in China, carotid IMT greater than 1.4mm may indicate atherosclerosis, thus the subjects with carotid IMT greater than 1.4mm were also excluded in this study (line 110).

#2. They mentioned that non-HDL-C level failed to be an independent index for predicting early-stage atherosclerosis in present study. It seems that this sentence is not necessary to describe in the conclusion section, because non-HDL-C had some
significant relationships with carotid atherosclerotic findings. Furthermore, lack of statistical power such as small number of population may cause this negative data.

**RE:** Thank you for your comment. We have modified the conclusion section as suggested.

#3. All p values should be described as actual value, not use p<0.05.

**RE:** We have changed all the p values into actual value according to your suggestion.

Special thanks to you for your constructive comments.
Responses to the comments raised by reviewer Po-Yuan Chang:

1. The authors used several lipid markers in this study. They also described “lipoprotein” markers, but I cannot find any “lipoprotein” in the manuscript. Lipoproteins include LDL, HDL, etc, which are different from LDL-C, HDL-C. The definition should be clarified.

RE: Thanks for your suggestion. It is really true as you mentioned that the definition of lipoprotein should be clarified. We have changed “lipoprotein ratio” into “lipid ratio” in the article.

2. Carotid Intima-media thickness (IMT) has been used as an indicator of atherosclerosis for decades. Therefore the originality and novelty of this study is low.

RE: Thanks for the comments. As you describe, carotid IMT has been used as one of the most reliable markers of atherosclerosis, so we use the index as the golden standard for assessing atherosclerosis. Firstly, carotid IMT is performed to diagnose atherosclerosis. The subjects with carotid IMT greater than 1.4mm, which meet the diagnostic criteria of atherosclerosis, have been excluded in this study. Secondly, the present study investigates the correlation between lipid parameters changes with carotid IMT in order to find the associations between lipid variation and early-stage atherosclerosis in arterial wall.

3. The definition of “early-stage” atherosclerosis is lacking.

RE: We are sorry for the unclear description. The present study focuses on the
associations between conventional lipid parameters and lipid ratios with early-stage atherosclerotic intimal changes in general people (clinical healthy population). We clarified that subjects with diagnosed atherosclerosis (carotid IMT > 1.4mm) were excluded in this revision (line 110).

4. There is no difference in IMT among the study population. The presence of a “plaque” in vascular walls cannot be used as sole evidence of atherosclerosis.

RE: We are sorry for unclear description of “early-stage atherosclerosis”. The present study aimed to investigate the associations between lipid parameters with early-stage atherosclerotic intimal changes in arterial wall in general people, not diagnosed atherosclerosis patients.

5. More discussions should be made on the novel markers for “early-stage” atherosclerosis.

RE: Thanks for your comment. We have modified the discussion section as suggested (line 214-222).

Special thanks to you for your constructive comments.