Author's response to reviews

Title: Treatment with betablockers is associated with higher gray-scale median in carotid plaques.

Authors:

Giuseppe Asciutto (giuseppe.asciutto@med.lu.se)
Nuno V Dias (nunovdias@gmail.com)
Ana Persson (ana.persson@med.lu.se)
Jan Nilsson (jan.nilsson@med.lu.se)
Isabel Gonçalves (migvdias@gmailc.om)

Version: 5
Date: 9 August 2014

Author's response to reviews: see over
Dear Editors,

We would like to thank the editor and the reviewers for the valuable comments and suggestions on our article. We have improved the manuscript in accordance with the suggestions. Please find enclosed the answers to the comments and the revised manuscript.

We hope that the revised version is acceptable for publication in your prestigious journal.

Sincerely

The authors

Malmö, 2014-07-10
REVIEWER 1

Major Compulsory Revisions]

1. Tables for simple and multiple linear regressions and logistic regression analysis; Researchers addressed that "simple and multiple linear regressions were used to explore the relationship between two or more continuous variables, while logistic regression was used in case of dichotomous variables" on the line 164 ~ 166 in method section of the manuscript. However, there were no tables of simple and multiple linear regressions and logistic regression analysis in the manuscript. The tables for the simple and multiple linear regressions and the logistic regression analysis should be included in the article.

We included 4 new tables (2 to 5) for simple and multiple linear and logistic regression. The regression models were built based on the results of the simple regression analysis (p <.200). The decision to use non-relevant variables was done based on what reported in the literature about their possible influencing effects on atherosclerosis.

2. Variables which were included in the regression model: BMI was one of the variables which showed significant difference between two groups (Table 1). Furthermore, BMI influenced on the disease outcome including atherosclerosis. However, BMI was not included in the regression model (line 166 ~ 167). What were the criteria for the judgement to select the variables which were included in the regression model? It should be clarified in the method section.

BMI is now included in the regression models.
[Minor Essential Revisions]

1. Since this is a cross-sectional study, it is appropriate to refrain from using terms of beneficial or stabilizing effect, and rather use terms such as association. Similarly, it is appropriate to refrain from using term of "study cohort" on the line 181, and rather use terms such as "study population".

We changed the text according to your suggestion.

2. Table 1. The results of GSM in two groups should be included in Table 1.

We changed table 1 according to your suggestion.

3. Discordance between Fig Legends and Fig. Fig 1 & 2 in Figure legends Fig 1, 2, & 3 in Figure

We changed the text according to your suggestion and eliminated fig. 2 as suggested by REVIEWER 2

Major Compulsory Revisions

1. To evaluate the treatment effect of betablockers to GSM, the randomized double-blinded trial should be selected. The cross-sectional design of the present study is a serial shortcoming.
We agree that a randomized double-blinded trial could better answer the question on the possible protective effects of betablockers. However, as we had to do mainly with patients who have suffered neurological symptoms because of their carotid plaques, we could not feel to justify such a study design and analysed our patient population in a retrospective way. We see it also as a limitation of the study and therefore mentioned it as a pitfall of our investigation at the end of the Discussion section (lines 278-286).

2. The information concerning the types of betablockers should be given.

We completed the text with this information for betablockers and statins (lines 180-184)

3. The treatment durations of betablockers, statins, and antiplatelet drugs should also be clarified.

We included treatment duration for betablockers and statins in the text (lines 180-184). Unfortunately we do not have information about treatment duration for antiplatelets.

4. In multivariate analysis, BMI should be included as a covariate.

BMI is now included in the new 4 tables.

Minor Essential Revisions
1. Ref 4 and 5 did not report the relationship between GSM and cardiovascular disease (Introduction, third paragraph). The authors should cite adequate references.
We apologize for this error. We changed our formulation and reviewed the reference list.

2. *Some parts of Introduction in fourth paragraph should be described in Discussion.*

We completed the Discussion as suggested (lines 221-235)

3. *Figure 2 is not informative. I think it should be discarded.*

We removed Fig. 2 as suggested.

4. *I think that simple and multiple linear regression analyses were not performed in this study* (Methods, Statistical analysis, second paragraph).

We included the respective regression tables.