Format for ANSWERING REVIEWERS

September 27, 2013

Dear Editor,

Please find enclosed the edited manuscript in MS format (file name: Hiroki Teragawa-2013.09.27-WJC No 4900).

Title: Positive influence of aspirin on coronary endothelial function—Importance of the dose

Author: Hiroki Teragawa, Naoya Mitsuba, Ken Ishibashi, Satoshi Kurisu, and Yasuki Kihara

The manuscript has been improved according to the suggestions of reviewers:
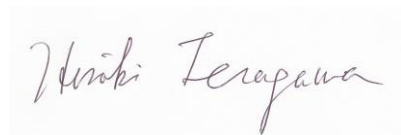1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer
   (1) We have addressed the definitions of coronary vascular function in the "Methods" section.
   (2) We have corrected several mistakes seen in the original manuscript.
   (3) We have specified the role of author contribution in the last author.

Thank you again for publishing our manuscript in the *World Journal of Cardiology.*

Sincerely yours,

Hiroki Teragawa, MD, PhD

Dept. of Cardiovascular Medicine,
Hiroshima General Hospital of West Japan Railway Company
3-1-36 Futabanosato, Higashi-ku,
Hiroshima 732-0057 Japan
Tel No. +81-82-262-1171
Fax No. *81-82-262-1499

To Reviewer #1

Thank you for your comments. We have revised our manuscript accordingly. Our responses are outlined below.

1) The authors keep referring to vasodilation as coronary endothelial function. They should explain why, as vessel diameter is determined by the tone of smooth muscles around it, rather than by the endothelium.

Based on your comments, we have added the definitions of coronary vascular function especially in coronary endothelial dysfunction in the "Methods" section.

2) The statement on p. 14 "However, changes in coronary artery diameter in response to ACh infusion were reduced in Group Ia compared with those in Group Ib (p = 0.0231)" contradicts statements elsewhere in the manuscript and the data in Table 4, which imply that patients receiving lower dose of aspirin (Group Ia) were more responsive to ACh. This appears to be a typo that must be corrected.

Based on your comments, we have swapped "Group Ia" and "Group Ib".

3) Contribution statement says: "Y. Kihara approved the final version of the manuscript". Is this sufficient for the authorship?

Based on your comments, we have specified that Y. Kihara both revised and approved the manuscript.

To Reviewer #2

Thank you for your comments. We have revised our manuscript accordingly. Our responses are outlined below.

1) In the introduction or method section, it should have some background about endothelium-dependent and -independent vasodilation, so that readers from other fields can understand the meaning of all these measurements and their relationship to endothelial function.

Based on your comments, we have added the definitions of coronary vascular function especially in coronary endothelial dysfunction in the "Methods" section.

2) The sample size for each group in the Abstract does not match that in the Methods and result section. For example, in the Abstract, group I has 61 patients (Ia: n=48), and group II has 75 patients. However, in the methods section, group I has 63 patients (Ia: n=50), and group II has 76 patients. This would clearly influence all the subsequent measurements and statistics. Please double check the numbers and make corresponding corrections.

Based on your comments, we have corrected the patient numbers in the Abstract. The patient number in the Methods section and the statistics were correct in the original manuscript.

3) Table 3: Ach should be written as ACh.

Based on your comment, we have changed Ach to ACh in Tables 3 and 4.

4) Page 13 line 14. "Changes in coronary artery diameter in response to ACh infusion were reduced in Group II compared with those in Group I (p = 0.0043)." Please clarify ACh infusion rate for the change. The p value (0.0043) does not match that in Table 3 (0.0030). Please explain the mismatch.

P value (p = 0.0043) in Figure 1 was obtained from the significant difference between the serial changes in response to ACh infusions using one way analysis of variance, while p value (0.003) in Table 3 was obtained from the significant difference between the percent changes in coronary artery diameter at a dose of ACh 30 μg/min using the contrast analysis. Therefore, two p values were different.

5) Page 14, lines 3-4. "However, changes in coronary artery diameter in response to ACh infusion were reduced in Group Ia compared with those in Group Ib (p = 0.0231)". This statement is incorrect. Group Ia and Group Ib should be swapped, and the p value does not match that in Table 4 (0.0123), and also please specify the ACh infusion rate and percent change.

Based on your comments, we have swapped "Group Ia" and "Group Ib".

The P value (p = 0.0231) in Figure 2 was obtained from the significant difference

between the serial changes in response to ACh infusions using one way analysis of variance, while p value (0.0123) in Table 4 was obtained from the significant difference between the percent changes in coronary artery diameter at a dose of ACh 30 μg/min using the contrast analysis. Therefore, two p values were different.