

ANSWERING REVIEWERS

Dear Editor,



Please find enclosed the edited manuscript in word format (file name: 20416-Review.doc).

Title: Neoatherosclerosis: Coronary stents seal atherosclerotic lesions but result in making a new problem of atherosclerosis

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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:

Reviewed by 00571492

(1) This review discusses the recent phenomena of neoatherosclerosis. Overall this review was well structured, presented the relevant information and discussed the topic adequately. The primary issue with the manuscript is the poor grammar and sentence structure which can be remedied by a native English speaker. Some further queries and suggestions follow.

Response: Firstly we thank for reviewer's favorable comments.

The manuscript will be checked by native speaker of English and we will submit with English accreditation.

(2) Intro: Could be more concise, for example remove or shorten the history of balloon and stent procedures. More focus could be given to introducing the new concept of neoatherosclerosis and outlining its definition.

Response: We thank for reviewer's important comment. Because the "Intro" section precedes "Vascular response after PCI" section which mentions series of PCI procedures including POBA and stent implantation, we believe the need of history of POBA and stent procedures. To focus on the neoatherosclerosis, we added a sentence.

(3) Throughout the manuscript the authors refer to 'ISR' and 'VLST' a lot, and interchange it with 'neoatherosclerosis' making it difficult for the reader to interpret.

Response: We thank for reviewer's important comment.

As we previously mentioned, a part of neoatherosclerosis can cause ISR and VLST. Because the pathophysiology of ISR or VLST is multifactorial and which may depends on DES type, we used the term "ISR or VLST" to match with individual contexts.

(4) Vascular response after PCI: What is the relevance or causal relationship between the initial

PCI injury and neoatherosclerosis? How does the initial damage to the vascular wall, and cellular changes influence neoatherosclerosis development? If there is no clear link then the section could be made shorter and more focused on neoatherosclerosis.

Response: We thank for reviewer's important comment.

As we mentioned in the "Vascular response after PCI" section, any interventional procedures such as PCI can cause denudation of endothelium. The apparent linkage between initial vascular damage and neoatherosclerosis is not clear so far, even in POBA can cause atherosclerotic change in the vessel. Stent implantation causes perturbation of coronary blood flow which promotes inflammation leading to neoatherosclerosis.

(5) Neoatherosclerosis in BMS: The authors state: "BMS showed late luminal re-narrowing beyond 4 years was common" but then say "ISR and VLST are not frequent clinical events after stent implantation" is this not in disagreement?

Response: We thank for reviewer's important comment.

According to the reviewer's comment, we omitted the following sentence to avoid to confuse.

(6) Why does neoatherosclerosis only occur in a few patients following BMS implantation?

Response: We thank for reviewer's important inquiry.

As we mentioned in page 9 line 10, histopathological study of BMS implanted coronary artery showed neoatherosclerotic change. Neoatherosclerotic change could be seen in not a few patients but in almost all BMS implanted coronary artery.

(7) The natural progression of BMS is provided including early and late stages, but what signifies neoatherosclerosis exactly? Need a definition.

Response: We thank for reviewer's important inquiry.

As we mentioned in the context in page 9 line 13, chronic inflammation by stent itself and subsequent macrophage recruitment with strong collagen degrading matrix metalloproteinase expressing vulnerable plaque forms neoatherosclerosis.

(8) Are there any theories why some patients may get neoatherosclerosis sooner than others, or not get it at all?

Response: We thank for reviewer's important inquiry.

As we mentioned in pag 11 line 22, neoathersclerosis occurs more rapidly in DES than BMS might be due to the eluted drug prevents endothelial cell proliferation and viability, migration which allows infiltration of lipid-laden foamy macrophage into the vessel. We also mentioned the association between patients' background and neoatherosclerotosis in page 14 line 4.

(9) In several sentences facts have been provided without a relevant reference.

Response: We thank for reviewer's important comment.

We added reference in some sentence (page 9 line 11, page 9 line 23, page 10 line 3, page 10 line 15).

(10) The manuscript would be significantly improved if it was edited by a native English speaker.

Response: We thank for reviewer's important comment.

The manuscript was checked by native.

(11) The picture quality of Figure 1 appears to be too low and not focused.

Response: We thank for reviewer's important comment.

To our great regret, we cannot improve the image quality of the picture in Figure 1 because the picture was taken at the maximum pixel of coronary angioscopy. To improve the quality of the

pictures and to focus on it, the smaller sizing of the pictures will be suitable.

(12) Figure legends: Need to explain all abbreviations in the figure legends.

Response: We thank for reviewer's important comment.

We rephrased abbreviations in the figure legends.

Reviewed by 00214259

(1) It is a good review about basic and clinical studies about problems of neoatherosclerosis correlating with coronary stenting. The review is complete.

Response: Firstly we thank for reviewer's favorable comment.

(2) I think that a section containing a discussion or integration should be added.

Response: We thank for reviewer's important comment.

We state in the conclusion paragraph as integration of the context.

(3) Introducing BRS in table1 should be considered.

Response: We thank for reviewer's important comment.

We added the column of BRS in the table.

(4) Language polishing should be done.

Response: The manuscript will be checked by native speaker of English and we will submit with English accreditation.

(5) More specifically:

Page 8 line 21: VLST.s ?(s is needed?).

Response: We rephrased.

Page 11 line 5: Sentence should be rephrase.

Response: We rephrased.

Page 11 line 13: Sentence should be rephrase.

Response: We rephrased.

Page 12 line 10: Sentence should be rephrase.

Response: We rephrased.

Page 12 line 12: Sentence should be rephrase.

Response: We rephrased.

3 References and typesetting were corrected.

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