

Response to Reviewers

Manuscript title: Diagnosis and Management Challenges of In-Stent Restenosis in Coronary Arteries

Manuscript number: 31719

We thank the reviewers for their thoughtful review and comments on the manuscript titled “Diagnosis and Management Challenges of In-Stent Restenosis in Coronary Arteries”. Below is the point-to-point revision of the manuscript as suggested by the reviewers.

We would like to alert the editorial office that we made changes in the authors list that is shown in the new version of the manuscript.

Thank you,

M Chadi Alraies, MD

Reviewer 1:

This is an interesting and important overview on diagnosis and challenges of in-stent restenosis in coronary arteries. However, there are several important issues to be considered for further improvement of the paper with respect to readability, scientifically critical assessments and actuality

1. Formal issues: give a list of all abbreviations

This was addressed and we added a full page with abbreviations that are listed in the manuscript

2. Shorten the paper: Especially shorten the chapter dealing with restenosis treatment starting with line 240.

This was addressed and the treatment section was summarized.

3. Do not simply report all the single results of numerous restenosis studies rather than give and comprehensive overview referring to the actual meta-analyses.

This was addressed and practical summary was added at the end of each section.

4. The number of figures showing clinical examples (coronary angiograms) should be reduced. Only take examples representing the highest clinical and illustrative impact

This was addressed and we reduced the number of cases to 3 cases only.

5. Scientific considerations: unfortunately, the review more or less restrains on local mechanisms of restenosis and technical issues with regard to stenting or re-stenting with different devices. Potential effects of more or less adherence to secondary prevention measures/activities (e.g. smoking, cholesterol lowering, exercise training, risk diseases like diabetes, adherence to medication etc.) have not been addressed at all. It is a "must" to critically include such considerations.

This is very valid point that we didn't address in the initial submission. We have added these recommendation to the new manuscript

6. Restenosis also strongly may depend on the morphologic conditions of the first PCI (e.g. high risk intervention? diffuse three vessel disease? acute or elective intervention? etc.). Especially the readiness for risk interventions of the interventional cardiologist may influence the outcome. The authors should critically reflect this point.

This is very valid point. We add few comments to address this recommendation. At the same note, we are addressing ISR presenting with stable symptoms.

7. Actuality: the estimation of bioresorbable scaffolds should be updated by citing the results of the ABSORB-II-Study. These results did not fulfill the primary expectations so far.

This is very valid point and we agree that BVS should not be address in ISR topic since the primary endpoint was not met for primary lesions. We decided to take this section off to agree with the reviewer viewpoint.

Reviewer 2.

No changes were required.

Editorial changes:

1. We listed all authors names in the references
2. The style of the reference number have been changed to be between two square brackets and before the full stop.
3. Added the Pubmed PMID number was added.