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ANSWERING REVIEWERS - Comments in Blue

PEER-REVIEW REPORT

Name of journal: World Journal of Cardiology

Manuscript NO: 41450

Title: Safety and efficacy of frequency-domain optical coherence tomography in the evaluation and treatment of angiographically-intermediate coronary artery lesions

Reviewer's code: 03414056

Reviewer's country: Spain

Science editor: Fang-Fang Ji

Date sent for review: 2018-08-14

Date reviewed: 2018-08-20

Review time: 6 Days

SPECIFIC COMMENTS TO AUTHORS

This paper entitled "Safety and efficacy of frequency-domain optical coherence tomography in the evaluation and treatment of angiographically-intermediate coronary artery lesions" attempted to assess the safety and efficacy of frequency-domain optical coherence tomography (FD-OCT) in the evaluation and treatment of angiographically-intermediate coronary lesions (ICL). The authors showed that doing FD-OCT is safe and effective in the evaluation and treatment of ICL with a short sample of patients. This is an interesting paper in the current context with an increased use of the new devices and strategies to evaluate ICL, the study lacks of some details in the analysis that could of importance, that I will mention through the review: 1. The introduction is well written. 2. A methodology section there is an important detail

missing that is the power calculation or the sample size calculation, also minor details are 1) it's good to know how the follow up was performed (in person, by telephone...), 2) which was the minor bleeding definition in the secondary endpoint 3) how was unstable angina defined 3. The results are well presented 4. In the discussion section, the value of the results is clearly shown but I miss some referral to ORBITA substudies on the importance of medical therapy compared with ICP 5. The limitations section is clear but I found that some aspects could be included as the sample size is not calculated

AUTHORS' REBUTTAL NOTE - Reviewer's code: 03414056

The study lacks of some details in the analysis that could of importance, that I will mention through the review:

1. The introduction is well written.

2. A methodology section

- there is an important detail missing that is the power calculation or the sample size calculation.

We have made appropriate changes as required. (please refer to Statistical Analysis paragraph)

also minor details are

- 1) it's good to know how the follow up was performed (in person, by telephone...) - **We have made appropriate changes as required.**

- 2) which was the minor bleeding definition in the secondary endpoint - **We have made appropriate changes as required.**

- 3) how was unstable angina defined – **We have made appropriate changes as required (and we included how SA, NSTEMI and STEMI were defined as well)**

3. The results are well presented

4. In the discussion section, the value of the results is clearly shown but I miss some referral to ORBITA substudies on the importance of medical therapy compared with ICP - **We have made appropriate changes as required.**

5. The limitations section is clear but I found that some aspects could be included: as the sample



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PEER-REVIEW REPORT

Name of journal: World Journal of Cardiology

Manuscript NO: 41450

Title: Safety and efficacy of frequency-domain optical coherence tomography in the evaluation and treatment of angiographically-intermediate coronary artery lesions

Reviewer's code: 03493974

Reviewer's country: Bulgaria

Science editor: Fang-Fang Ji

Date sent for review: 2018-08-14

Date reviewed: 2018-08-20

Review time: 6 Days

SPECIFIC COMMENTS TO AUTHORS

The manuscript presented by Khurwolah et al. touches an important topic in interventional cardiology. It is associated with the management of angiographically intermediate coronary lesions. Providing a tool for accurate assessment of those is of great importance to the appropriate management of these “borderline” cases which are frequently under- or overtreated. In their study the authors show that using QCA leads to overestimation of lesion severity in comparison to FD-OCT. This is a prerequisite for overtreatment. On the other hand, the results show that OCT-guided decision making seems to be safe. The population with intermediate coronary lesions is largely underrepresented across different randomized trials. Therefore, despite the relatively small sample size this prospective single centre interventional study adds a lot of important data to the topic. However, there are some specific remarks that are worth mentioning: 1. The definition of the primary efficacy endpoint is somewhat vague. One

usually expects to define a primary endpoint with the occurrence of some clinical event or a surrogate to assess important clinical events. This should be rethought and reworked before considering the manuscript again for publication. 2. Page 11, paragraph FD-OCT findings, line 5 needs some clarification. The text states the reference area derived from was smaller in the PCI group compared to OMT group while based on the results pointed out on Table 3 and cited in the text the reference area is not significantly different. 3. As the sample size is relatively small the results on safety endpoints in terms of MACE should be interpreted with great caution and stating that clearly in the text is highly recommended.

AUTHORS' REBUTTAL NOTE - Reviewer's code: 03493974

However, there are some specific remarks that are worth mentioning:

1. The definition of the primary efficacy endpoint is somewhat vague. One usually expects to define a primary endpoint with the occurrence of some clinical event or a surrogate to assess important clinical events. This should be rethought and reworked before considering the manuscript again for publication.

We believe that this study, which is a first of its kind in terms of its specific aim that translates inherently into its study design and methodology, in that it concerns the evaluation of the safety and efficacy of OCT (not PCI) as a diagnostic tool in assessing the stenosis severity of ICLs (borderline stenotic lesions), the primary efficacy endpoint needs to deal specifically with how effective, as an diagnostic tool, OCT is in evaluating the ICLs. Saying so, the best way to achieve this is to demonstrate that the ultra-high diagnostic resolution provided by OCT is the primary efficacy factor, mediated by its superiority over 2D-QCA in terms of accurate evaluation of MLA and % AS. In this specific setting, it is not possible to assess the primary efficacy endpoint by means of a particular clinical event or a surrogate to assess important clinical events. The reason for this is that OCT is a primarily a diagnostic (and not an interventional) tool, and therefore it is not possible to assess its efficacy based on clinical events such as MACE, recurrent episodes of angina, recurrent hospitalization, etc... We are here assessing the



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efficacy of OCT, and not PCI (efficacy of PCI can assessed using clinical events, but that is not the case here as we are assessing the efficacy of OCT). We have significantly rethought about the argument laid out by the reviewer in question, but found that there is no better way in which we can define our primary efficacy end-point, and that the best way to assess the efficacy of OCT in this particular study is by the specific manner in which we defined our primary efficacy end-point.

2. Page 11, paragraph FD-OCT findings, line 5 needs some clarification. The text states the reference area derived from was smaller in the PCI group compared to OMT group while based on the results pointed out on Table 3 and cited in the text the reference area is not significantly different. - **We have made appropriate changes as required.**

3. As the sample size is relatively small the results on safety endpoints in terms of MACE should be interpreted with great caution and stating that clearly in the text is highly recommended. - **We have made appropriate changes as required.**



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PEER-REVIEW REPORT

Name of journal: World Journal of Cardiology

Manuscript NO: 41450

Title: Safety and efficacy of frequency-domain optical coherence tomography in the evaluation and treatment of angiographically-intermediate coronary artery lesions

Reviewer's code: 03702209

Reviewer's country: Greece

Science editor: Fang-Fang Ji

Date sent for review: 2018-08-14

Date reviewed: 2018-08-23

Review time: 8 Days

SPECIFIC COMMENTS TO AUTHORS

Criteria Checklist has been performed and were found relevant to the journal requirement 1. This is a very interesting study assessing the safety and efficacy of frequency-domain optical coherence tomography (FD-OCT) in the evaluation and treatment of angiographically-intermediate coronary lesions (ICL). The primary efficacy endpoint was to demonstrate the superiority and higher accuracy of FD-OCT compared to 2D-QCA in evaluating stenosis severity in patients with ICL. The primary safety endpoint was the incidence of 30-day major adverse cardiac events (MACE). Secondary endpoints included MACE at 12 months and other clinical events. 2. the present study is of significant value as it is the first one ever to investigate both the efficacy and safety of FD-OCT in evaluating and guiding the optimal treatment of patients with angiographically-borderline coronary artery lesions and also the superiority and higher accuracy of FD-OCT compared to 2D-QCA in evaluating stenosis severity in patients



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with ICL. 3. However, other safety endpoints such as duration of the procedure, fluoroscopy time, amount of contrast media used, and radiation dose delivered were not formally evaluated by our study. Also, the sample size was relatively small and it was a non-randomized study as the subjects were assigned to either arm based on specific predetermined OCT criteria. SMALL CORRECTIONS: 1. In the abstract section please make clear that the recurrent episodes of angina did not differ between the treatment groups 2. In page 4 (core tip):.....the benefits of this imaging modality over its procedural risks...: please add appropriate references 3. in table 5 please add p values, although the differences seem non significant

AUTHORS' REBUTTAL NOTE - Reviewer's code: 03702209

SMALL CORRECTIONS:

1. In the abstract section please make clear that the recurrent episodes of angina did not differ between the treatment groups – **We have made appropriate changes as required.**
2. In page 4 (core tip):...the benefits of this imaging modality over its procedural risks...: please add appropriate references - **We have made appropriate changes as required.**
3. in table 5 please add p values, although the differences seem non significant - **We have made appropriate changes as required.**