

ANSWER TO THE REVIEWERS

This is an excellent review about the role for detection of ischemia in non-infarcted related artery after acute myocardial infarction. This manuscript is nicely structured and well written. I have no question about this manuscript.

Thank you very much for your revision and comments

The authors attempted to review a role for ischemia detection in multivessel disease after an acute myocardial infarction. This topic is very actual and clinically relevant. I have no additional comments for this editorial.

Thank you very much for your revision and comments

This is an interesting and timing review of the literature on the usefulness of non-invasive testing in post-AMI (both STEMI and NSTEMI) patients. The use of non-invasive testing in post-AMI patients remains reserved only to selected subjects with multi vessel disease. However, non-invasive testing, as Authors demonstrate is an excellent gate-keeper to further revascularization and is also an excellent risk-stratifier. The manuscript reviews the main studies and results on this issue providing a balanced view on advantages and limitations. There are, however, some, issues left unaddressed: 1. Exercise and pharmacologic testing do identify patients at different risk of future events. It is well established that those who cannot exercise show a significantly worse outcome. Please comment. 2. Not all tests are created equal and stress echocardiography has advantages and limitations over perfusion testing. This should be discussed. 3. There is no mention to the potential role of more advanced stress echo techniques such as the assessment of coronary flow reserve or GLS. 4. There is no mention of the potential role of CT scanning in this setting. 5. Please address the widespread use of testing these patients on medical therapy and the potential drawback of false negative results in this setting. 6. It would be very valuable for the readership of the journal to have a paragraph on the clinical implications of these results and on the approach of these authors to their real clinical world. Minor There are a few typos throughout the manuscript that should be corrected. Please note that dipyridamol should read dypiridamole.

Thank you very much for your revision and comments

- 1. Exercise and pharmacologic testing do identify patients at different risk of future events. It is well established that those who cannot exercise show a significantly worse outcome. Please comment.**

We cannot agree more completely with this statement. However, our aim in this editorial was to discuss an approach based on ischemia for revascularization in comparison to the classical approach based on angiography/revascularization. So, we have pointed to this issue, instead of discussing which could be the best technique or method to detect ischemia, in order to not lose focus.

- 2. Not all tests are created equal and stress echocardiography has advantages and limitations over perfusion testing. This should be discussed.**

We agree completely, although in the real world one or another of these non-invasive methods is available in the different centers. So, in the end, expertise in the technique is the matter.

Having told this, the purpose of this review was not the comparison between the different techniques for ischemia detection (otherwise it would be more extensive), but rather the comparison between invasive and less-invasive approaches. Nevertheless we state that MIBI SPECT is a very sensitive technique when it came to discuss the VANQUISH trial and we put stress echo, myocardial perfusion imaging and MR as reliable and reasonable techniques for ischemia detection at the end of the paper.

3. There is no mention to the potential role of more advanced stress echo techniques such as the assessment of coronary flow reserve or GLS.

We agree that coronary flow reserve may be interesting for some patients in expert hands. Also, future development in the use of GLS at high heart rates might do the method interesting during stress.

Having told this, our aim in this editorial was to discuss an approach based on ischemia for revascularization in comparison to the classical approach based on angiography/revascularization. So, we have pointed to this issue, instead of discussing which could be the best techniques or methods to detect ischemia, in order to not lose focus.

4. There is no mention of the potential role of CT scanning in this setting.

CT, as a mainly anatomic technique was not addressed in this editorial because our aim was to discuss an approach based on ischemia for revascularization in comparison to the classical approach based on angiography/revascularization. On the other hand, as most centers have availability of any kind of functional imaging (stress echo, myocardial perfusion...), functional assessment with CT-FFR, on the contrary, is not widely available yet.

5. Please address the widespread use of testing these patients on medical therapy and the potential drawback of false negative results in this setting.

We have not commented specifically on “false negative” studies, but we have discussed through the paper the fact that these subjects with CAD and absence of ischemia actually have good outcome.

6. It would be very valuable for the readership of the journal to have a paragraph on the clinical implications of these results and on the approach of these authors to their real clinical world.

According to your suggestions and those of the Editorial Office, we have added a conclusion section in which we state that:

“In patients with acute myocardial infarction and multivessel disease ischemia detection may be useful for clinical decisions. In non-ST elevation myocardial infarction or acute coronary syndrome the ultimate role of ischemia detection for clinical decision making process in the current era of modern imaging and new drugs and stents is pending.”

Also according to your comments, we have added a sentence stating that the current approach in our center for patients with STEMI and multivessel CAD disease is based on ischemia (page 2)

Minor There are a few typos throughout the manuscript that should be corrected. Please note that dipyridamol should read dypiridamole.

This has been corrected. Thank you.

The manuscript by Peteiro and Bouzas-Mosquera discusses a topic undergoing intense study and interest at the present time, namely the role for ischemia detection after an acute myocardial infarction. The writing is clear. There are only some minor concerns related to the paper. Firstly, an abstract should be provided along with the manuscript core tip. Secondly, the latest ESC/EACTS guidelines on myocardial revascularization should be cited (Neumann, Franz-Josef, et al. "2018 ESC/EACTS guidelines on myocardial revascularization." European heart journal 40.2 (2018): 87-165.).

Thank you for your revision and comments.

We are providing an abstract in the new version of the paper

Also, the reference by Neumann has been added, according to your suggestion