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Name of Journal: *World Journal of Cardiology*

ESPS Manuscript NO: 21567

Manuscript Type: ORIGINAL ARTICLE

REPLY TO REVIEWERS' COMMENTS:

REVIEWER #1 (227531):

We wish to thank this reviewer for his/hers constructive comments on our work, which we believe have led to significant improvements.

The authors studied a group of 70 patients with CAD by means of coronary flow reserve and several indexes related to arteriosclerosis (peripheral arterial tonometry, pulse waveform analysis, carotid to femoral pulse wave velocity) and to inflammation (Lp-PLA2). As expected these indexes were impaired in patients with lower coronary flow reserve. The weakness of the study is the confirmatory nature of the findings, the strength the well done design.

I have the following concerns:

1) The authors state that the subjects studied were patients with CAD successfully revascularized, but in no place within the manuscript is explained which types of revascularizations were performed.

Reply: We acknowledge this reviewer's point. Following the reviewer's request, we have now clarified that all the patients have had significant LAD disease and have undergone PCI into their LAD with placement of DES or with CABG (PCI: n=64, CABG: n=6). This is now stated on page 6 para 1 as follows: "*All the patients had undergone successful*

revascularization (PCI, n=64 or CABG, n=6) into their LAD within a year before inclusion in the study."

2) Also, explain how successful revascularization was defined.

Reply: Following the reviewer's request, we have now clarified that as successful revascularization is defined as the reduction of a minimum stenosis diameter to <20% with a final TIMI flow grade 3 without side branch loss, flow-limiting dissection, or angiographic thrombus (as visually assessed by angiography) according to the last proposed criteria [Levine GN, et al; 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention. J Am Coll Cardiol. 2011;58:e44-122.]

The above are now stated in page 6 para 1 ."*PCI was considered successful when there was remained reduction in the caliber of the stenotic artery to <20% with a final TIMI flow grade 3 without side branch loss, flow-limiting dissection, or angiographic thrombus (as visually assessed by angiography[16])"*

As a result, a new relative reference has been included additionally in the revised reference list (Reference #16 in the revised list of references).

3) Figures showing graphics for some of the techniques employed would be great to the readership. I suggest to do it for peripheral tonometry and for carotid to femoral PWCC assessment.

Reply: Following the reviewer's suggestion we have now added graphics showing the representing the most significant differences in mean value \pm SD of PWVc, AIx, DAI, DSA in patients with CFR<2.5 versus patients with CFR \geq 2.5.

This is appeared now in the manuscript as Figure 1

4) The authors state that choosing a cut-off value of 2.5 was based on previous publications (page 9). Please report these publications.

Reply: We apologize for this omission. We have now added the relative references 6, 19. (page 9, para2) We have also replaced the previous ref#33 with a novel reference (# 19 in

the new reference list) [**Rigo F.** Coronary flow reserve in stress-echo lab. From pathophysiologic toy to diagnostic tool. Cardiovascular Ultrasound 2005;**3**:8. [PMID: 15792499, DOI:10.1186/1476-7120-3-8]]

5) Please report how many patients were excluded due to unfeasible CFR study.

Reply: Following the reviewer's request, we have now clarified that 1 patient was excluded due to unfeasible CFR study (feasibility of the method greater than 98 %).

This is now stated in the section of Methods (page 9, first para revised version) as follows:

"The feasibility of the method was greater than 98% for all indices in our study cohort (initially 71 patients were recruited, but one patient was excluded due to unfeasible CFR study) "

REVIEWER #2 (225335):

We wish to thank this reviewer for his/hers constructive comments on our work, which we believe have led to significant improvements.

Some comments on it:

1) Authors need to state who performed the echocardiographic examinations. And also provide the assessor's experience.

Reply: Following the reviewer's request, we have now stated that Ass Professor Ignatios Ikonomidis has performed the echocardiographic examinations with more than 5500 studies the last 10 years and several publications using echo assessment of CFR (see ref 5,8,14) This now stated in page para as follows: *"Dr Ignatios Ikonomidis, counting more than 5500 CFR echo studies the last 10 years, has performed the echocardiographic examinations and the CFR measurements for this study[5,8,14]"*

2) Study limitations should be moved before the conclusions.

Reply: Following the reviewer's request, we have now moved the section of «Study Limitations» before the «Conclusions»

REVIEWER #3 (211908):

We wish to thank this reviewer for his/hers constructive comments on our work, which we believe have led to significant improvements.

Comments on the manuscript: ESPS Manuscript NO: 21567 with the Title: Association of abnormal aortic wall properties and arterial wave reflections with impaired coronary flow reserve in coronary artery disease patients after successful revascularization, written by Tritakis et al.

This observational study is very interesting and is well conducted. Only few minor corrections:

1) Page 5: Line 28: Please consider "-- may determine" instead of "-- may determines".

Reply: We apologize for this typo. It has been corrected in the revised version.

2) Page 11: Line 8: Please consider "Finally we" instead of "Finally with"

Reply: We apologize for this typo. It has been corrected in the revised version.

3) Page 11: Line 12: Do you mean with coronary reserve "coronary flow reserve"

Reply: We apologize for this typo. It has been corrected in the revised version.

REVIEWER #4 (214291):

We wish to thank this reviewer for his/hers comments on our work.

Interesting manuscript !