Author's response to reviews

Title: Feasibility and Diagnostic Power of Transthoracic Coronary Doppler for Coronary Flow Velocity Reserve in Patients Referred for Myocardial Perfusion Imaging

Authors:

   Eva Maret (eva.maret@lj.se)
   Jan Engvall (jan.engvall@lio.se)
   Eva Nylander (eva.nylander@lio.se)
   Jan Ohlsson (jan.ohlsson@lj.se)

Version: 2 Date: 11 March 2008

Author's response to reviews: see over
Regarding MS: 1236008936185019 Feasibility and Diagnostic Power of Transthoracic Coronary Doppler for Coronary Flow Velocity Reserve in Patients Referred for Myocardial Perfusion Imaging

Dear professor Picano,

We are grateful for the suggestions given to our manuscript and offer the following responses below (italicized).

With these changes added, we hope the manuscript will be acceptable for publication.

Reviewer 1
In the present study Maret et al describe the feasibility of transthoracic Doppler for coronary flow velocity reserve in patients with known or suspected CAD. The study confirms the ability of CFR to identify a subset of patients without disease with a high negative predictive value (88%). The study is interesting and the conclusions are sound, but there are a few issues that authors should address.

1. The feasibility of the technique is lower than any previous report. This is a major limitation of the study since a 70% feasibility would make the technique unsuitable for any routine clinical use. Several factors may affect the feasibility: technology employed, operator expertise and experience and type of stressor. Please address each single item.

Response: We have refrained from discussing equipment from different vendors since we only had access to Sequoia from Siemens. We mentioned briefly that we avoided external contrast agents because of reports of side effects. The operator experience has been further discussed page 12, line 1-2. The type of stressor is discussed page 11 line 9

2. CFR accuracy is not validated versus coronary angiography but vs. myocardial perfusion scintigraphy. Therefore, it is a concordance study between the two techniques. Both techniques suffer from the same limitation: they are unable to distinguish between micro and macrovascular coronary disease, making perfusion an imperfect gold standard for the recognition of CAD. More
appealing for clinical use would be the assessment of both wall motion and CFR. The assessment of CFR adds sensitivity for LAD disease with a modest loss in specificity. In reality, the inherently quantitative information of LAD flow reserve allows a stratification of the response, integrating many different tests into one: greatly reduced CFR (<1.5) yields extraordinary specificity whilst mildly reduced CFR (<2.0) offers outstanding sensitivity. Do authors have any data on wall motion analysis? Have they tried different cut-off values?

Response: Hyperpnea and problems in scanning is discussed page 11, line 15. We have not tried different cut-off values in this small population since CFVR>2 to us seemed rather well established.

3. Authors define as abnormal patients with fixed or reversible defects. It would be interesting to separate them and have the CFR measurements.

Response: The study had only 21% patients with coronary disease according to scintigraphy. We have performed that calculation (enclosed) but refrained from further dividing the material in small groups.

4. When authors in table define the actual number of CAD patients (CAD) how was diagnosis made: clinical history or coronary angiography?

Response: CAD was defined from hospital records of myocardial infarction or the patients having had coronary angiography performed.

5. Authors provide in figure 4 individual CFR in the population separating on the basis of normal and abnormal SPECT. The individual CFR largely overlaps in the two groups. Please provide mean values and statistical differences, if any.

Response: Mean value and p-value has been added, page 9 line 3

O, Topcu S, Yildirir A, Muderrisoglu H. Nebivolol improves coronary flow reserve in patients with idiopathic dilated cardiomyopathy Heart 2006; 93:319-24. Please specify medications at time of testing and discuss the potential advantages of a technique which is not influenced by anti.anginal therapy.

Response: Data on pharmacological treatment are given page 4 line 24. The advantage of discontinuing pharmacological treatment was discussed page 11, line 4.


Response: Reference no 3 (Froehlicher) has been omitted and the two suggested references in paragraph 7 added together with references suggested by reviewer 2.

8. The prognostic value of CFR has been recently demonstrated in diabetic patients and negative stress for wall motion criteria. This is one of the conditions in which CFR may be reduced in the absence of CAD.

Response: This interesting observation supports our findings.

Reviewer 2
A reasonably interesting study comparing an initial experience with coronary flow reserve with myocardial perfusion imaging.

Abstract. Background is too long (shorten to no more than 4 lines).

Response: Shortened to four sentences.

Discussion. On page 10, last para, you should acknowledge more explicitly that stress scintigraphy is a poor gold standard, especially in view of the low specificity – as also recognized in guidelines (Fox K, Eur Heart J 2006).

Response: Done. Reference added

Discussion. Be more quantitative on the radiation
burden of scintigraphy (10 mSv, about 500 chest x-rays): Picano E. Sustainability of medical imaging. BMJ. 2004;328:578-80).

**Response:** Mentioned in discussion, but reference not added

Update your reference list discussion article showing the high feasibility of coronary flow reserve with contrast (Rigo F et al., Transthoracic echocardiographic imaging of coronary arteries: tips, traps, and pitfalls. Cardiovasc Ultrasound. 2008;6:7).

**Response:** Done, page 11, line 18

Finally, a p-value was entered in table 2, for the calculation of Chi-square regarding the 2x2 table for TTDE vs MPI