Reviewer's report

Title: Flow Mediated Dilation of the Brachial Artery: An Investigation of Methods Requiring Further Standardization

Version: 1 Date: 12 January 2007

Reviewer: Michiel Bots

Reviewer's report:

General

The study deals with methodological aspects of the FMD measurement using ultrasound. The paper is well written. The study is done in a single center, with a single dedicated sonographer for the FMD assessment, with one off line reader dedicated to FMD measurement. The analyses are done according to the highest standards. The results are well displayed. The conclusions are based on the results presented in the paper.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

My main comment involves the discussion part of the part and the inference the authors make. In their study in one center, with one well trained and dedicated sonographer well educated in providing the best images, with one off line reader, again well trained, and trained in all ins and outs of the measurement, with sufficient time dedicated the job, in all healthy subjects, the reproducibility at different time points is very modest with Intraclass correlation coefficients of 0.6. In this study the FMD measurement is probably the best you can get.

There are many other single center and multicenter studies published that report coefficients of variation of FMD measurements of 25-50%. Also in these studies dedication was present, yet the imaging technique or the off line measurements was less than what has been reported here or there were more technicians involved, clearly leading to increased measurement error.

Therefore, my recommendation is to address this further in the discussion on the relevance of the FMD measurement or measurement of change in FMD in multicenter studies, or in studies with more technicians. To me these results, and those of other indicate that either very large sample sizes are needed, or multicenter studies should be abandoned.

Also, the authors may want to discuss the value of having duplicate measurements in a study as a potential means to reduce part of the measurement error.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

none.

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Discretionary Revisions (which the author can choose to ignore)

none.

What next?: Accept after minor essential revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

'I declare that I have no competing interests'