Reviewer's report

Title: The effect of long-term homocysteine-lowering on vascular structure and function in stroke: a randomized controlled trial and meta-analysis

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Reviewer: Jan Auke Rauwerda

Reviewer's report:

The authors performed a well designed randomized controlled trial. They also compared their results with a meta-analysis. However, there are still some questions, raised from the manuscript, which has to be answered.

Participants with previous stroke or TIA. Of the 532 patients included in the protocol, recruitment was done in resp. 169 en 174 patients, only resp. 86 en 87 attended the follow-up. Even less could be analysed. The authors stated that the exclusion was the same in both arms. Looking at the numbers that is correct, however, looking at the groups of no response cq declined: is there any information about the reason for no response or decline?

The second point is the small groups of patients with hemorrhage or a stroke of unknown reason: a hemorrhage could also be caused by the burst of a small aneurysm, a totally other disease than an ischemic stroke. Why did the authors include this category?

Medication shown in Table 1: the optimal treatment of TIA's cq ischemic infarction also included statines. We also know that statines had some influence on plaque regression and for that reason also possible on the FM or CIMT. Information about the use of statines is not within their manuscript.

Initial treatment of TIA or stroke: the severity of carotid artery disease could be of reliable measurement of the carotid intima and medial thickness measurement. An other interesting point is the reliability of patient whom suppose to be refrain from smoking, drinking coffee as well as alcohol, 6 hours prior to the study. Did the authors measure one of these parameters? Duplex measurements were done by a single observer. In the manuscript, no intraobserver variability was mentioned. Are there data?

The study was stopped for two years. How sure were the authors, that the patients used their medicine (placebo or vitamins)?

On page 13, the authors describe no adverse events. We know the chronic use of vitamin B can lead to a neuropathy. Did they look for it?

The authors say nothing in their discussion about food intake. We also know that eating habits are baseline characteristics.

Nice conducted study, should be accepted with minor essential revisions.

Level of interest: An article of insufficient interest to warrant publication in a
scientific/medical journal

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

I declare that I have no competing interests