Reviewer's report

**Title:** Comparison of ankle-brachial pressure index and pulse wave velocity as markers of cognitive function in a community-dwelling population.

**Version:** 1  **Date:** 12 February 2010

**Reviewer:** Franco Di Cesare

**Reviewer's report:**

**Major Compulsory Revisions**

1. Study objectives and design are not clearly stated and are ambiguously defined.
   Please, confirm whether the purpose of the study is "to compare" the Ankle-Brachial Pressure Index (ABPI) and Pulse Wave Velocity (PWV) as markers for cognitive decline. The study is also presented by the Authors "to determine the effectiveness of the ABI and the ba-PWV as markers of cognitive decline". Elsewhere in the paper, the study is described as "the first report to obtain a comparative data between the ABI and PWV as markers of cognitive function". In the Discussion, the research is considered as the first report suggesting the "usefulness of ABI and PWV as markers of cognitive function". The concept of usefulness should be clearly defined.

   Mini Mental State Examination (MMSE) total score is the indicator of cognitive functioning selected by the Authors. The MMSE includes 18 items that cover orientation, memory, attention, ability to follow commands, and copying a complex figure and yields a maximum total score of 30.

   MMSE total score distribution depends on age and education and reflects an observed level of cognitive impairment. MMSE cut-off score <24 is commonly accepted indicator of cognitive impairment. However, it is not a diagnostic indicator of progressive cognitive decline or dementia. The study design does not provide indicators allowing for adjustment for premorbid cognitive function.

   The concept of effectiveness needs a clear definition. Apparently, the study design as here has been presented is not adequate to evaluate the effectiveness of putative biomarkers.

   My impression is that the study is designed to determine the association of the 2 putative markers to cognitive impairment rather than to cognitive decline.

2. Results and Conclusions: the term "independent marker".
   The concept of "independent marker" should be defined. Biomarkers are usually classified as diagnostic or predictive or correlates, etc. Independent marker is an unusual terminology. Otherwise, confirm whether the term refers to the use of ABI and ba-PWV measures as independent factors in the multiple logistic regression analysis. Alternatively, if the term is here to be referred to as "independent risk factor".
3. Results: Sample characteristics.

It is stated that "ABI tended to decrease in subjects with poor cognition than those in control group." Notably, the level of significance reported on Table 1 was p<.01. I would suggest to keep consistency in the presentation and discussion of the study data. Consistently with what you stated in the statistical analysis plan, a value of p<0.05 is "considered significant". In this case, your statement on ABI differences between groups should read as not significant. In case you wish to comment on measures approaching but not reaching the level of significance p<.05, this should be extended to all variables. An example could be the Habitual Alcohol Intake which is higher in the clinical group with poor cognition and has significance value very close to p<.05 (data not shown on Table 1).

4. Discussion: the statement "the result of this study, which showed cognitive decline in subjects with lower ABI, suggest the solid predictive value of ABI" is not substantiated by study data.

5. Referenced articles. Please, check that all statements in your paper reliably report paper authors' opinion, comments, view, and data. I would suggest to pay particular attention to articles referenced as: 4,8,9,10,12,13,14,15,16,17,18,21,24,25,26) Find here below some examples of statements in your paper that, in my opinion, do not truly represent authors' statements.

The statement "Other cohort studies including the Edinburgh Artery Study and the Honolulu-Asia Aging Study, showed that a lower ABI caused the cognitive impairment (4)and increased the incidence of dementia (9)".

Apparently this statement is not consistent with what reported in the article referenced as 4 by Price, JF et coll. Ankle Barchial Index as a Predictor of Cognitive Impairment in the General Population: Ten-Year Follow-Up of the Edinburgh Artery Study. (JAGS 54:763-769, 2006). At page 768, the Authors state that "the study was not designed to determine the cause of the association between ABI and the subsequent cognitive impairment". They indicated that the results of the study support the initial hypothesis that "individuals with a low ABI represent a high-risk group in terms of the development of cognitive impairment." They state that low ABI "may also help predict future risk of cognitive impairment".

The study referenced as 9 by Laurin and coll, Ankle-to-Brachial Index and Dementia: The Honolulu-Asia Aging Study, Circulation 2007;116;2269-2274 reports: "a low ABI was related to an increased risk of total dementia and VaD." This comment is substantially different from your statement that "a lower ABI increased the incidence of dementia".

Please verify the statement "in a larger US community-based study (8), a low ABI predicted the decline of cognitive function over a period over a 7 years follow-up". The study was not designed to validate low ABI as predictive marker of cognitive decline rather to explore associations among cognitive functioning in the elderly
and subclinical cardiovascular disease and diabetes.

The Authors (Haan MN, Shemanski L, Jagust WJ, Manolio TA, Kuller L. The role of APOE epsilon4 in modulating effects of other risk factors for cognitive decline in elderly persons. JAMA. 1999 Jul 7;282(1):40-6.) report at page 43 that the presence of low ankle-arm blood pressure was associated with greater declines in both measures of cognition, a Modified Version of the MMSE (3MSE) and the Digit Symbol Substitution (DSS) Test. "A person with an ankle-arm blood pressure of less than 0.90mmHg experienced a 4.62-point decline on his or her 3MSE score over the 7 years and a 2.73-point decline in the DSS score vs #0.66 and #0.39, respectively, for those with an ankle-arm blood pressure of at least 0.90mmHg." They made no statement suggesting (and no compelling data are shown in the article substantiating) low ABI as predictive of cognitive decline.

6. Methods. Please, provide an accurate description of the statistical methods and analysis. Please provide more details on how the distance between brachium and ankle was estimated.

7. The content of the abstract should be modified accordingly.

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I declare I have no competing interests.