Reviewer's report

Title: Association between different measurements of blood pressure variability by ambulatory blood pressure monitoring (ABPM) and ankle-brachial index

Version: 2 Date: 27 May 2010

Reviewer: Beth Weatherley

Reviewer's report:

Major compulsory revisions:
1. The statement regarding exclusion of 3 subjects from linear regression should be moved to the statistical methods section.

2. Rather than separate linear regressions of the left and right legs, I would suggest either a model of the lower ABI (one measure per subject) consistent with the logistic regression models or a mixed model that includes both measures and accounts for the within-subject correlations. Separate models would be appropriate if side of the body were a major modifier of the association between the BP variability measure and ABI, but this does not appear to be the case. In any individual, either side may have a greater degree of atherosclerosis and it would seem more appropriate to model taking this into account.

3. The analysis including the pulse pressure is fine, and the sentence added to the results sufficient.

4. Although only 3 subjects had high ABI, I would suggest excluding them from the logistic regression models and re-running. It is not universally agreed that these values represent ‘abnormal’ ABI in the same sense as a low ABI, and the inclusion of these values may introduce noise into the analysis. Depending on the results, a statement that the exclusion of these subjects did not substantially change the results could be included or the results of the models excluding the subjects could be presented.

5. The linearity of the association of continuous predictors with ABI in the models should be checked. This could be done one-at-a-time, for example, by including polynomial terms (quadratic and cubic) and testing for their significance. A linear model with >400 subjects should accommodate 40 predictors and a logistic regression model with almost 60 ‘events’ should accommodate 6 predictors, therefore, the inclusion of 3 terms in a model, testing for the simultaneous significance of 2 of these, should not pose any major difficulty.

Minor essential revisions: None

Discretionary revisions:
1. Regarding the additional utility of BP variability above the BP itself, the c index – which represents the area under the ROC curve – is readily computed from
logistic regression. (This is provided as part of standard output for logistic regression in SAS, and may be available in SPSS.) The c indexes from the models including BP with and without the time-rate index could be presented. Although these models are not prognostic of cardiovascular outcome directly, and the addition to the Discussion is good, the ABI is being evaluated as a sort of surrogate for outcome in this study and more information could be provided.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.