Reviewer's report

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

Version: 1 Date: 17 April 2010

Reviewer: Beth Weatherley

Reviewer's report:

The authors examine which of three blood pressure variability measures derived from ambulatory blood pressure monitoring is most related to the ankle-brachial index, a marker of macrovascular atherosclerosis, in 425 hypertensive patients included in the MONITOR clinical study.

Major compulsory revisions:

1. In the introduction, the authors state that whether these variability measures add substantial information over BP values has not been shown, but analyses do not appear to directly address this question. The predictiveness (AUC or c index) for a model including, for example, only age, diabetes, and BP over 24 hours could be compared with the value for a model that further includes one or more measures of BP variability.

2. Modelling the association with ABI as a dichotomous variable assumes that both high and low ABI are associated with higher BP variability. Was this assumption checked? High ABI has not been consistently shown to represent high risk of cardiovascular outcomes (in the ARIC study it was not). High and low ABI values may represent differing underlying pathophysologies, therefore, it would seem prudent to examine the associations separately with high and low ABI. For example, Table 1 could present characteristics of patients with low, normal, and high ABI. Logistic regression models could either exclude those with high ABI, and compare low with normal ABI, or include ABI as a 3-category outcome. A plot of BP variability versus ABI would show whether both low and high ABI values are associated with higher BP variability.

3. Modelling the association with ABI as a continuous outcome and, presumably, each measure of BP variability as a linear predictor, assumes that the association is linear, e.g., BP variability increases with decreasing ABI. This would seem contradictory to considering both high and low ABI as ‘abnormal’ in the logistic regression models, with the expectation that increased BP variability is related to both low and high ABI. This relationship could be explored by modelling the BP variability as a non-linear function of the ABI, to see if indeed both low and high ABI values are associated with increased BP variability.

4. The BP variability may reflect arterial compliance. The addition of pulse pressure to the models might clarify the independence of effects of the BP variability itself from compliance.
Minor essential revisions:
1. ABPM should be spelled out at first occurrence in abstract, and should be noted following first full reference in the introduction.

2. In table 1, the row label ‘No antihypertensive’ should be clarified, as it is not clear what the numbers represent.

Discretionary revisions:
1. Is there a theoretical reason why the time rate index should be more highly correlated with abnormal ABI than the other two measures? If so, this should be included in the discussion.

**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.

**Declaration of competing interests:**

I declare that I have no competing interests.