Reviewer's report

Title: Augmentation index assessed by applanation tonometry is elevated in Marfan Syndrome

Version: 1 Date: 7 June 2007

Reviewer: Patrick Segers

Reviewer's report:

General

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

This is an interesting and well written manuscript on pressure wave reflection (assessed via the augmentation index) in patients with Marfan disease. The main limitation of the work is the small size of the control (n=10) and patient population (n=11), but the strong point is that the population is well matched for height. Were subjects matched one-on-one, i.e., for a patient of a given age, sex and height there is a perfectly matched control?

The authors should consult Segers et al., Am J Physiology 290:2385-2392, 2006. In that study, wave reflection was addressed in a Marfan population (n=26) via the augmentation index and using wave reflection analysis. They found no overall differences in AIx between patients and control, but AIx appeared to be higher in younger subjects. It would therefore be very interesting to see the AIx data plotted as a function of age as well. The same also accounts for PWV.

Given the large age range and the large effect of age on most cardiovascular parameters, analysis of covariance (with age as covariant) is most relevant. What was the correlation between aortic root size and age? Are the correlation coefficients given in Table 4 univariate correlations? It is likely that blood pressure (PP) is relatively invariant with age in this population. As AIx and PWV are driven by age, it is possible that the association between these indices and aortic root size is predominantly driven by age.

The authors should provide more detail on some technical issues:
• When calculating AIx, how were P1 and P2 determined? Using automated algorithms or on sight? Was the person doing the analysis blinded to the clinical data?
• When calculating the transfer function, the time-alignment of the signal is potentially important, especially to calculate the phase. From Figure 1, the phase is positive for the low harmonics, which would indicate that pressures at the radial and carotid were not perfectly aligned; one would expect negative phase angle to account for the time delay that exists between the carotid and radial artery.
• What distance was used to calculate carotid-femoral PWV?

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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)

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Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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