Reviewer's report

Title: Thrombomodulin Ala455Val Polymorphism and the Risk of Cerebral Infarction in a Biracial Population: The Stroke Prevention in Young Women Study

Version: 1 Date: 26 August 2004

Reviewer: Arjen Slooter

Reviewer's report:

General

In this article, the authors investigate the association between a thrombomodulin polymorphism and ischemic stroke. The paper is well written, deals with a novel issue and is based on large numbers, taken into account the young age of the participants. There are however also weaknesses.

1. As the authors make clear, it is uncertain whether the studied polymorphism, THBD ala455val, is functional, e.g. associated with a change in the level of protein expression or associated with a different protein isoform, although there is some circumstantial evidence. The described observation may be a chance finding.
2. It is unclear why the authors did not study two other polymorphisms in thrombomodulin (arg385ser and pro477ser), that were shown to have functional consequences.
3. The quality of some confounding variables is poor. The presence of hypertension and diabetes was assessed by questionnaires; the authors did not review these data when participants of the study were seen for blood withdrawal.

None.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. The authors should describe in more detail which proportion of cases and controls from the original database are included in the present study.
2. Matching was performed (on age and residence), but the authors fail to adjust for both matching factors; additional adjustments should be made for residence.
3. Terms as ‘cohort’ and ‘baseline characteristics’ falsely suggest a (more solid) follow-up study. As this is a case control study, these terms should be omitted.

A paragraph on the clinical or public health implications would improve the manuscript.

What next?: Accept after minor essential revisions

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

Quality of written English: Acceptable
Statistical review: No

Declaration of competing interests:
None