Reviewer’s report

Title: The changes in clot microstructure in patients with ischaemic stroke and the effects of therapeutic intervention: a prospective observational study

Version: 2
Date: 22 November 2014

Reviewer: Anetta Undas

Reviewer’s report:

The paper by Stanford S. et al. presented that stroke patients had unfavorably altered clot properties including higher fibrinogen concentrations and the effect of thrombolysis on clot microstructure was more prominent than antiplatelet therapy. The paper showed in the Introduction the current knowledge about the links of thrombus structure and ischemic stroke. The paper is of interest and yields new insights into the pathophysiology of stroke, however the interpretation of the data presented is hard given several confounders and imprecise clinical information.

1. Patient characteristics should be detailed. The definitions of all the clinical states, e.g. hyperlipidemia were not provided. The term “antiplatelets” is unclear. Are any medications other than “antiplatelets or statins used? At least antihypertensive agents were probably used; ACE inhibitors, for instance, have been reported to alter plasma fibrin clot properties. A few basic laboratory tests are missing. Given available data, apart from fibrinogen, some other laboratory test are likely to alter clot parameters, such as creatinine, glycemia, C-reactive protein (see the latest reviews on fibrin clot properties in thromboembolism). Given the topic I would expect at least D-dimer levels.

2. Stroke severity should be presented. Were there any associations between for example the modified Rankin scale and rheometric tests?

3. Aspirin exerts several antithrombotic effects other that of COX-1 acetylation, including decreased thrombin generation. Given the fact that a small effect of rtPA on clots is surprising compared with a more potent effect of aspirin this issue needs more attention in the Discussion.

4. In the Introduction more information on the factors that determine clot structure and function in acute ischemic stroke is needed. Are there any differences between patients with acute ischemic stroke and those with hemorrhagic stroke? Could we expect any differences between acute myocardial infarction versus acute ischemic stroke in terms of fibrin parameters? Please comment on it in the Discussion.

Minor comments

“real-time clot formation time” – this parameter has not been mentioned in the abstract. Data on the age, sex and mode of therapy are needed in the Abstract. Moreover, it should be clearly stated which clot parameters were changed following stroke therapy with rtPA. In the data presentation, stroke patients...
should be highlighted, not healthy controls. The last sentence of the Abstract could be deleted.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.