Reviewer's report

Title: Does the Sex of Acute Stroke Patients Influence the Effectiveness of rt-PA? Experience from the TCD Multicenter Study

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Reviewer: Timothy Kleinig

Reviewer's report:

Al-hassain and colleagues report on a population of tPA-treated stroke patients studied with TCD, and seek to determine whether sex influences the response to treatment. In general, the study could be an interesting one - especially in determining whether the likelihood of acute recanalisation is higher in females, but the article has ambitions rather higher than its data allow. I would suggest it should be retitled 'Female gender does influence early recanalisation rates following RTPA: experience etc'

1. Major compulsory revisions

The flow of the introduction is not sufficiently logical and is unnecessarily discursive. The main author may wish to read their co-author's (A Alexandrov's) excellent article on scientific writing (Cerebrovasc Dis. 2004;18(2):135-8.)

Paragraph one is fine (if over-referenced). Paragraph two could be shortened to

1) Some studies have suggested females have a poorer prognosis following stroke

2) Conversely, female gender seemed to be a positive prognostic factor in pooled analysis of TPA trials (Kent) as well as showing a positive trend in IST-3 (Sandercock).

3) One possible explanation could be that females are especially more likely to recanalise or recanalise earlier following TPA

We therefore tested this hypothesis in a TCD-monitored thrombolysis cohort

I don't think that any functional outcome data from this study carry any weight at all compared with the RCTs, and this should be de-emphasised, both in the introduction, the methodology and the conclusion. Any functional outcome conclusions are also severely curtailed by incomplete follow-up

2) The population studied is not clearly delineated.

Who exactly was studied? In some places it appears to suggest that only CLOTBUST (Ref 21) patients were studied, but this was 126 patients and the data include many more. It appears (reading between the lines) that the study included the 126 CLOTBUSTER patients as well as 243 patients entered into a prospective database. If this is the case, it should be made more explicit. And were patients consecutively treated TPA patients with vessel occlusion, or were patients opportunistically included (raising possibility of selection bias).
3. Discussion needs rewriting

Again, would recommend Alexandrov's guide. Paragraph one should not be a treatise on PAI-1. I would place their results in the context of the large RCTs (which give a far purer population, if artificial) rather than Shobha's paper. I would de-emphasise the outcome data, which is in a relatively small population and confounded by incomplete follow-up. Limitations are well-canvassed.

The conclusion could be 'Our study did not demonstrate better or faster recanalisation in r-TPA -treated females with ischaemic stroke. Reported differential clinical responses to rTPA may be mediated by other factors' (which could be mentioned in the discussion.

Minor revisions

1 How was sICH defined?

2. Tenses should not be mixed (e.g. consent section in methods)

3. Statistically significant differences in age should be commented upon

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

**Quality of written English:** Needs some language corrections before being published

**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 interest, but should disclose that I am a Site PI for CLOTBUSTER