Reviewer's report

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

**Version:** 3 **Date:** 24 September 2013

**Reviewer:** LEONARD YEO

**Reviewer's report:**

This is a well written article and deals with a subject that is clinically relevant. Physicians who treat acute stroke patients will be able to derive practical and useful information from the article.

However there are several minor points:

(Minor Essential revisions)

1) Page 6 under "patient and clinical assessments"

patients were either continuously monitored with TCD for 2 hours BEFORE starting IV rt-PA bolus or underwent....

I believe this should be changed to AFTER IV rt-PA bolus as it would not be ethical to delay the initiation of treatment for 2 hours, and i do not believe the author's institution has done so.

2)The abstract states that the patients were treated at 3 hours but 21 patients were included up to 4 hours. either keep to 3 hours or change the abstract.

(Discretionary Revisions)

3)there was a large proportion of patients with cardioembolic source of stroke and a correspondingly high NIHSS. However the presence of absence of AF or embolic source was not used as a factor in the univariate or multivariate analysis. Although there was not much difference in incidence between the sexes in table 1, there was not much information on outcomes and cardioembolism. wonder if there would be any change if it was included in the analysis.

4) We clinically treat patients up to 4.5 hours, to represent a more real-life scenario, i think including patients up to 4.5 hours is more accurate. is there any reason why the manuscript keeps to a 3 hour limit?

5) The relationship between gender and outcomes after systemic thrombolysis remains poorly understood. Generally, the outcomes among female AIS patients without thrombolysis are expected to be worse than their male counterparts.1-3 Some small studies that seem to indicate better outcomes in women after intravenous thrombolytic therapy for AIS.2-6 Kent et al's nullification theory that the poorer natural history of stroke in women who are not treated with thrombolysis are “nullified” by the increased effectiveness of intravenous tPA in
females compared to males.7 The author’s findings that gender does not predict recanalization or 3 month outcomes should be tempered with the fact that females who do not receive tPA have worse outcomes as well as the fact that the recent studies show females are less likely to receive tpa.

There should be some mention in the article that females in the therapeutic window should be managed more aggressively to achieve better outcomes with intravenous thrombolysis. Although this is equal to males, it still significantly improves their outcomes compared to conservative treatment without IV rTPA.


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

**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