Reviewer's report

Title: Observational Dutch Young Symptomatic Stroke Study (ODYSSEY): study rationale and protocol of a multicentre prospective cohort study.

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Reviewer: alessandro pezzini

Reviewer's report:

In the present manuscript the Authors report on rationale and protocol of a multicentric study aimed at investigating the etiology, trigger factors, and prognosis of stroke patients aged 18 to 49 years. The topic is of interest because of the scarce information available on stroke at young age.

I have the following comments for the Authors to consider:

1. Because of its characteristics of methodologic paper, the Authors should provide more detailed definitions.

Patients
- TIA: “...(symptoms) lasting less than 24 hours” and “...with corresponding DWI-positive lesion on MRI-scan”. What about patients with the same clinical presentation and DWI-negative scan? What about the diagnostic work-up for these patients: will all subjects undergo a standard (imaging) protocol? If this is the case, what imaging procedures are included (for patients with ischemic stroke and for those with a TIA)?

Exclusion criteria
- 4. Intracerebral hemorrhage due to a known ruptured aneurysm: what about the other (true) vascular malformations (i.e., arteriovenous malformations)?
- What about intracerebral hemorrhages due to transformation of an infarct (is this classified as infarction or hemorrhage)?

Controls
Please, explain how these subjects will be selected: in particular, how 250 stroke-free subjects are planned to match 1,500 patients? It is likely to be 1 control subject per 6 stroke patients: if this is the case, Authors should exactly report how they will match the two groups (i.e., by sex and mean age? other?)

Classification of TIA or stroke: etiology...
- Please, provide the exact criteria for the etiologic classification of intracerebral hemorrhage
- “In addition, hematoma volume will be calculated”: what criteria for volume calculation?

Course of the disease
- Myocardial infarction: please, define

Measures – Follow up
- Occupation: how will the Authors sub-categorize this variable?

Additional files
- “Furthermore migraine…[58]”: I suggest to adopt the most recent criteria for migraine definition

Minor:
- Background: “Young stroke is generally…of 50 years”. Please, delete this sentence. The cut-off of age is arbitrary.
- Ref 26 is no more “in press”.

Overall, it is a bit difficult for the reader to follow the study description in the way the Authors present their protocol. I would suggest to report the different phases of the study in the text and to summarize all the procedures and variable definitions in a separate (supplemental?) part of the manuscript.

A paragraph should be included in which all the diagnostic (in particular, imaging) procedures are described, in which it is explicitly stated whether all the patients will undergo a standard diagnostic protocol (if this is the case, this should be reported in details) or not, and who will be in charge with clinical and follow up evaluations (physicians, study nurses, others…).

**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