Reviewer’s report

Title: Asymmetrical Bioimpedance in the Anterior Circulation for Urgent Stratification of suspected Stroke (ABACUS Stroke): study protocol for a diagnostic accuracy study

Version: 0 Date: 23 Sep 2019

Reviewer: Johannes Reitsma

Reviewer's report:

Nice to see a protocol for a dedicated diagnostic accuracy study. Below are my comments focusing of completeness & clarity of the protocol and the rationale behind choices in the design and analyses.

1. Title

I would add "…urgent stratification of patients suspected of stroke" to highlight the correct population.

2. Abstract: use of "double bind"

Double blind is a confusing term even in the context of RCTs, but even less useful in a diagnostic accuracy study. I would rather describe what information was available to the readers of the Cerebral Bioimpedance Asymmetry (CBA) measurement and whether the result of the CBA measurement was used in the further work-up.

3. Abstract: index test results

Please add what type of result the CBA measurement produces (binary, ordered categories, continuous) and whether any predefined threshold exist.

4. Background, page 4, line 79 following

The current information about the treatments is rather uninformative. Please provide the absolute risks for the outcome for these interventions in relation to the absolute risk in the control groups. Furthermore, is the outcome long-term disability only or a composite including death as well?

5. Background, page 8, second bullet

I would rephrase as: To explore whether key clinical characteristics and radiological features are associated with the diagnostic accuracy of CBA


See previous remark about double blinding.
7. Methods page 9, line 217 and following about inclusion criteria and study flow

The intended use in practice will be that CBA measurement is performed first followed by further investigations and management. The protocol now allows for imaging to be performed first. The danger becomes that performing the imaging or any findings on imaging will influence the decision to do the CBA measurement. The study population will then not be the correct reflection of the suspected population. Ideally perform the CBA before the imaging, or ensure that such drop-out will not occur (minimalized) and clearly report the numbers, reasons and characteristics of suspected patients not undergoing CBA.

8. Methods page 10, about study flow, line 254

This study will not be based on a consecutive series, as inclusion may depend on availability of personal trained in CBA measurement. Careful document and describe all patients fulfilling the inclusion and exclusion criteria, but in whom no CBA measurement was performed and state reasons. This information will be crucial to judge the risk of bias and concerns about applicability.

9. Methods page 14, Index test section, type of measurement

Please describe what the (final) result of CBA measurement looks like with respect to its measurement scale like ordinal categories, percentage, continuous measurement.

10. Methods page 14, Index test section, use thresholds

Add information whether thresholds in case of a continuous measurement will be used and whether these thresholds are pre-defined (report thresholds) or will be determined.

11. Methods page 14, Index test reading

Explicitly state which patient characteristics and other test results will be available to the person(s) reading the index test.

12. Methods page 15, Reference standard test section

Remove the word comparator. In diagnostic accuracy research we aim to reserve the word comparator and comparative for studies comparing two or more index tests. Your study is a single test diagnostic accuracy study.

13. Methods page 15, Reference standard test section

This section might be more informatively labelled as "Target conditions" as the techniques how to establish these target conditions are described in the next section correctly labelled as "Reference standards"

14. Methods page 23, Blinding
Also clearly state which information was available to those performing and reading the CBA measurement

15. Methods page 25, Statistical analysis section

This section is now too generic and not directly linked to the different objectives of the study. So please describe the statistical analysis for each of the objectives. First: To determine the diagnostic accuracy of CBA measurement to identify complex stroke. If sens, spec and predictive values will be calculated, clearly stat which threshold will be used or selected. Explain how the ROC curve will be constructed and if the ROC is constructed from a logistic regression indicate whether other factors than CBA will be added to the model. Second, To determine the diagnostic accuracy of CBA measurement to identify LVO. See remarks above.

Third, To explore key clinical and radiological influences upon the diagnostic accuracy of CBA measurement for complex stroke and LVO. Clearly indicate which variables will be examined and in which way.

16. Methods page 25, Statistical analysis section

Please pre-specify in the protocol which subgroups will be analyzed and which factors will used in the multivariable modelling.

17. Methods page 25, Statistical analysis section

Good to see the clear description which patients will be excluded from the analysis. Can you provide the values for the pre-defined physiological range? Please add specifically that patients in whom the GBA reading failed will be reported but excluded from the analysis.

18. Methods page 26, Sample size consideration

I miss the rationale for focusing on specificity in the sample size section. Please provide this rationale. Also provide an indication what kind of precision can be expected around estimates of sensitivity.

19. Methods page 25, Statistical analysis section

STARD is general guideline to improve the reporting (complete and accurate) for diagnostic accuracy studies. It is useful reminder what type of information needs to be present However, it provides no guidance how to set-up the statistical analysis or how to design the study. Therefore, remove it from the statistical analysis section. Only have a general statement in the Methods that STARD will be used in the reporting of the study.

20. General remark

Check whether all the abbreviations are necessary as reading becomes more difficult especially for more general readers.
Level of interest
Please indicate how interesting you found the manuscript:

An article of importance in its field

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

Declaration of competing interests
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interest

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal