Reviewer's report

Title: Cognition after malignant media infarction and decompressive hemicraniectomy

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Reviewer: Eric Jüttler

Reviewer's report:

This describes neuropsychological deficits and the quality of life in a 20 patients with malignant MCA infarctions who were treated by hemicraniectomy.

Although the patient population is not representative for the usual patient population of malignant MCA infarcts, a control group of conservatively treated patients is lacking and there are bias and several confounders, this report is very valuable, because for the first time very detailed data on neuropsychological deficits in these patients are given. Although the results themselves must be interpreted with caution, especially due to the mentioned shortcomings and the very low number of patients, it may be used as methodological basis for larger future studies. However, several points must be addressed by the authors, before this manuscript can be considered for publication in BMC Neurology:

Major points:

1. The major drawback of this report is clearly its retrospective nature and highly selected patient population. The authors should explain why not even one third of patients with malignant MCA infarction were operated. This may explain or at least describe the selection bias. The fact that almost one third of patients fulfilling the inclusion criteria were lost is also a major confounder and should be addressed by the authors. This already points to the direction that these 20 patients may not be representative for the usual patients with malignant MCA infarction.

   This is also shown by the extreme poor results of their patients: 75% had a mRS score of 4 or 5 after one year or longer after the ictus. This is three times more than in DESTINY and DECIMAL, 2-times more than in the pooled analysis of the RCTs, and even 1.5 times higher than in HAMLET where patients were operated much later and were very soon treated on a stroke unit instead on an intensive care unit, i.e. less aggressively. The authors must clearly try to explain this difference and must very clearly state that these results are unexpectedly poor and that therefore their patient population is not at all representative compared with most other centres. They must also clearly interpret their results very carefully with respect to this.

2. The authors must clearly explain why they used these specific instruments for evaluation and not others. There are several other studies using different scales for QoL, and depression. In HAMLET and DECIMAL other instruments for QoL were used. Why did he authors not choose those instruments that have already
been used in this particular patient population and would have made their results comparable to those of others?

3. I would strongly recommend not to use a cut-off for age. The number of patients is much too low to do this or other subgroup analyses. It is no surprise that higher age is associated with poorer prognosis. This is true for almost every disease, especially for every neurological diseases, and here especially for stroke. It is completely unclear why the authors use a cut-off at 55 years. Later in the discussion they use a cut-off of 60 years, which is confusing. Most other authors also use 55 or 60, again others 65. Why not 54, 57, 61, 64? All cut-offs that have been used in the literature are nothing but arbitrary and not based on reasoning. Age should better be used as a continuous variable, which is much more reasonable than using a distinct cut-off. The authors should not get in this same row, speculate and, without proof, use these speculations in the evaluation and description of their data thereby diminishing rather than increasing the true value of their report.

4. I am not a statistician, but parameters such as the NIHSS score must be described as median, not as mean and non-parametric tests should be used. The fact that many others use means and t-testing does not justify this statistical sin. In addition, a number of 20 patients seems much too low to justify a multivariate analysis, not even reliable comparisons between subgroups such as older or younger than 60. I would strongly recommend to the authors to keep their data merely descriptive. There is already major bias due to the patient selection and the retrospective nature. This should not be increased by multiple testing. I clearly recommend that the authors should ask a statistician to do the analysis, who then should be named as co-author or in the acknowledgements.

5. The majority of patients suffered from depression. Were the results correctly interpreted with respect to the presence of depression, because this may influence neuropsychological testing and other tests, quality of life and the decision to retrospectively agree with treatment. Were these patients adequately treated for depression? There should be clear descriptions by the authors, because this may be a major confounder.

6. To me it is unclear what the comparison of these patient to healthy subjects should explain or demonstrate. The fact that patients missing most of one hemisphere do poorer than healthy controls is anything but unexpected. To me it is also unclear what this message should help in everyday clinical practice. It would be more useful if the authors would compare the results to other severely brain injured patients such as patients with SAH Hunt and Hess grade 4 or 5 (where our neurosurgeons are often much less reluctant to intervene or use intensive care treatment), patients after cardiac arrest (with true success rates of 1-6% (nevertheless nobody would not resuscitate) or at least average stroke patients.

7. The discussion is much too long and has no clear structure. It should be completely re-written, not so much focussing on aspects such as the influence of age (which is not the topic of this study and patient numbers are much too small
to find relevant differences or evaluate age as prognostic factor), but on comparing the results of this study with those of other studies on quality of life, retrospective agreement to the procedure, and depression as well as neuropsychological deficits in patients with malignant MCA infarction and maybe right hemispheric stroke in general. It would also be desirable that the authors should speculate why some of their patients did comparatively good and others did not.

To do this I would recommend the following literature:


Minor points:
1. The introduction is too long. Several aspects belong in the discussion section.
2. I am no native English speaker, but the manuscript suffers from several grammatical errors. For example „hardly“ is used in the meaning of „largely“. The manuscript would clearly profit from a revision by a professional translator.

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

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

**Statistical review**: Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests**: I declare that I have no competing interests.