Author’s response to reviews

Title: Prevalence of and risk factors for enlarged perivascular spaces in adult patients with moyamoya disease

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Author’s response to reviews:

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Professor Andreas Charidimou,
Editor, BMC Neurology

Dear Sir,

Thank you for your kind letter regarding our recently submitted manuscript. I have responded to the reviewers’ questions on a point-by-point basis, and the responses are presented below. I understand that final acceptance depends on satisfactory resolution of these issues.

Because analysis items were increased, we reassessed all the data and statistical analysis was examined again. Our results did not changed, though there were some numerical change. Moreover, our overall data were not normally distributed, and non-parametric analysis was used for statistical analysis. In accordance with reviewer’s comment, the data were expressed as median (interquartile range) values.
Editor

Please follow the STROBE checklist for structuring the manuscript, including methodological aspects. Finally, explain why other markers of small vessel disease, e.g. microbleeds, lacunas etc., where not assessed.

Response:

Thank you for your comment. In the revised version, we followed the STROBE checklist. To avoid confusion regarding statistical analysis, we selected the items that are considered to be related to high EPVS from the results of Table 3. As such, age, diabetes mellitus, hyperlipidemia, disease subtype, stroke lesions including lacuna, and microbleeds were not included in the multivariate analysis. This was mentioned in the statistical analysis section as follows:

“For tests that resulted in p values less than 0.10 in the Mann-Whitney U tests and Fisher’s exact probability tests, a simple logistic regression was used in the univariate analyses of the EPVS in the moyamoya group; female sex, hypertension, MRA score, flow voids in the basal ganglia, brain atrophy score, ivy sign, and white matter lesions were analyzed.”

Tackeun Kim, M.D. (Reviewer 2)

1) Although it is very interesting and novel topic in the field of MMD, clinical impact of EPVS and related risk factors seems to be weak. Are MMD patients with higher EPVS grade more prone to future stroke or neurological deterioration? Is perfusion status worse in higher EPVS patients?

Response:

Thank you for your insightful comment. This study is not a cohort study, but a case-control study. Thus, we could not evaluate future stroke or neurological deterioration. Instead, we examined clinical and radiological findings of stroke or ischemia at the time of the registration, and performed multivariate analysis.

In this study, we did not perform perfusion imaging analyses in all cases, though we evaluated ivy signs, which are thought to be correlated with perfusion. On these results, consideration about perfusion status was added in the discussion section.

2) The authors enrolled 50 subjects as control group against MMD group. Although they matched age and sex, the factors influencing EPVS should be presented for control group.
However, there were not any comment of risk factors related with EPVS among control group subjects. Medical history including TIA or previous stroke, hypertension, diabetes, dyslipidemia and presence of intracranial/extracranial atherosclerosis should be clarified and analyzed between MMD and control groups. (Does Table 3 include hemispheres from MMD/control group?)

Response:

In accordance with the reviewer’s comment, information about the control group (hypertension, diabetes, hyperlipidemia) was added, and compared with that of the moyamoya disease group. This was mentioned in the Table 1 and in the materials and methods section. The patients of the control group did not experience ischemic cerebrovascular disease. These patients were without TIA or previous ischemic stroke, and without intracranial/extracranial stenotic lesions. This was mentioned in the text. In the comparison between the moyamoya disease group and the control group, hypertension was significantly higher in the moyamoya disease group. Therefore, there is a possibility that hypertension might have a statistically strong influence on the comparison of clinical characteristics of high EPVS grades in moyamoya disease. This was also mentioned in the text.

In the moyamoya disease group, the characteristics of the patients in the high and low EPVS grade groups are presented in Table 3; therefore, Table 3 did not include the control group.

3) Although the authors used Mann-Whitney U test for continuous variables, data were expressed as mean and standard deviation. If continuous variables did not meet normal distribution, using median and interquartile range should be more helpful to understand the distributions.

Response:

Our overall data were not normally distributed, and non-parametric analysis was used for statistical analysis. Therefore, the data were expressed as median (interquartile range) values in the revised version.

We appreciate the reviewers’ thorough assessment of our paper. We would be grateful for a second review of our manuscript for possible publication in BMC neurology.

With best regards,

Takeshi Mikami, M.D.