Reviewer’s report

Title: The presence of cerebral and/or systemic endothelial dysfunction in patients with leukoaraiosis - a case control study

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Reviewer: Toshiki Mizuno

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Major Compulsory Revisions

The authors showed a marked and significant decrease of both CVR and FMD in patients with LA compared to the control group. In addition, both CVR and FMD were significantly decreased in LA subgroup Fazekas 3-2 compared to subgroup Fazekas 1. Also, the authors found the positive correlation between CVR and FMD, suggesting that endothelial dysfunction increases in parallel with LA severity and correlates between cerebral and systemic arterial territory. Their clear results are important, but the authors should clarify some issues.

1. The authors stated the significant positive correlation between CVR and FMD in patients with LA group, but the authors should show this correlation by the graph. In addition, the authors should show whether the correlation is positive in all participants.

2. The authors stated that patients with lacunar infarction did not show impairment of cerebral endothelial function in the previous reports. However, both lacunar infarction and leukoaraiosis are considered as small vessel disease. Therefore, authors should discuss the difference of cerebral endothelial function between lacunar infarction and leukoaraiosis.

3. The authors used the aberration, LA1 and LA0 in the line 212, but definition of LA1 and LA0 were only defined in the figure legend. LA1 can be easily misunderstood as FAZEKAS1 group. Therefore, LA1 and LA0 should be replaced by LA group and control group, respectively.

4. The mean arterial velocity using TCD software could change easily. The authors should state the reproducibility of cerebrovascular reactivity to L-arginine using TCD software.

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.