Reviewer's report

Title: Cognitive profile in patients with a first-ever lacunar infarct with and without silent lacunes: a comparative study.

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Reviewer: Carme Junque

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In the paper “Cognitive profile in patients with a first-ever lacunar infarct with and without silent lacunes: A comparative study” by Blanco-Rojas et al. the authors compared the neuropsychological performance of 34 subjects with a single lacunar infarct (SI) with those with multiple lacunar infarcts (MLI). Groups did not differ in age, sex, education, MMSE, in vascular risk factors or in laterality of lesions. As expected, they found that patients with MLI had significantly poorer performance in some neuropsychological tests such as semantic verbal fluency and short term memory.

The strongpoints of this paper are:
1) The originality in comparing single versus multiple silent lacunar infarcts.
2) Large, matched sample.

1. The main problems with the manuscript are in the analysis and interpretation of the data. Since leukoaraiosis (LA) was more frequent in the MLI than in the SI group, neuropsychological differences might be due to its presence rather than to the greater amount of focal lacunae. Lacunae per se may partially impair specific cognitive functions, but LA is indicative of greater diffuse vascular damage which could better explain the cognitive impairment than the sum of dispersed focal lacunae, and could perhaps indicate concurrent Alzheimer’s disease.

The problem with this study is that the effect of LA is neither analyzed nor controlled for.

2. The authors should quantify the LA and analyze its effect on neuropsychological performance. All analyses should therefore be repeated using an analysis of variance, adding LA as a covariate.

Other minor issues:
- 1. In the neuropsychological assessment, only tests not subject to motor aspects should be included. A considerable percentage of patients have motor or sensory deficits which might interfere in the execution of some of the tests used.
- 2. The manuscript’s composition should be thoroughly revised. The second paragraph in the background session and the second paragraph in the discussion session are very difficult to understand.
- 3. The use of the verbs in the text should be revised. They are not adequate to scientific vocabulary.
- 4. In the tables, besides p values, test statistics should be included.
- 5. All paragraphs in the discussion should be linked to some of the study’s results.
- 6. Current literature on leukoaraiosis and cognition from the LADIS Study Group should be reviewed and included in the discussion.

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

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

**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