Author's response to reviews

Title: Subcortical White Matter Infarcts Predict of 1-year Outcome of Fatigue in Stroke

Authors:

WK Tang (tangwk@cuhk.edu.hk)
YK Chen (davis78@cuhk.edu.hk)
HJ Liang (hedy.huainliang@gmail.com)
WCW Chu (winnie@med.cuhk.edu.hk)
VCT Mok (vctmok@cuhk.edu.hk)
UG Ungvari (sungvari@e.cuhk.edu.hk)
KS Wong (ks-wong@cuhk.edu.hk)

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Author's response to reviews: see over
We sincerely thank the Reviewer for the careful reading of our manuscript and the valuable comments. We have revised the manuscript according to the recommendations as detailed below. All changes are clearly indicated in the revised manuscript with **BOLD** for easy inspection.

Reviewer #1: There are some concerns that the authors may need to address as follows:

1. Describe the stat methods about multivariate logistic analysis as shown on Table 3. What factors were put in the model? How? And, the odds ratios should be called adjusted odds ratio.

**Authors’ reply:**

The following footnote has been added into Table 3: “The presence of subcortical white matter infarcts, pain, insomnia, Geriatric Depression Scale score, age, sex and National Institute of Health Stroke Scale score were entered in the regression model”.

The phrase “odds ratio” has been changed to “adjusted odds ratio” (line 438 - 443).

2. The authors need to discuss how fatigue different from depression? Which is cause and effect? And, also the results of this study between fatigue vs depression.

**Authors’ reply:** A discussion on the possible overlap between poststroke fatigue and depression has been added to the revised text (line 254-263).
Reply to Reviewer #2

We sincerely thank the Reviewer for the thorough reading of our manuscript and the helpful comments. We have revised the manuscript according to the recommendations as detailed below. All changes are clearly indicated in the revised manuscript with **BOLD** for easy inspection.

Reviewer #2: post stroke fatigue (PSF). This is topic is important and little studied. I have some comments.

1. The main finding was an association between subcortical white matter infarcts (SWMI) and not remitting from PSF. The definition of SWMI in the methods is not clear to me. Patients with SWMI often suffer from acute infarctions of the gray matter as well. How did you deal with patients with infarction in both white and gray matter?

   **Authors’ reply:** If an infarct involved both subcortical white and grey matter, it was counted as both a SWMI infarct as well as a grey matter infarct (line 163-165).

2. In the multivariate analysis (table 3) I recommend that you include age, sex and severity of stroke (mRS or NIHSS) even if the p-value>.05. It could be that SWMIs are markers of large infarctions? Or higher age?

   **Authors’ reply:** Age, sex and NIHSS score have been added to Table 3. The Odds ratio was revised in the Abstract (line 43) and the Result sections (line 212) accordingly.
Minor comments

1. Line 73 and 76: infarcts and the risk of PSF. I think you mean infarct location and the risk of PSF.

Authors’ reply: The word “location” has been added after the word “infarct” (line 72 and 76).

2. In the method is should be stated clearly in the first paragraph that 3 months and 15 months follow-up were in person (if that is the case).

Authors’ reply: The following sentence has been added to the Method section: “All included patients attended both the 3-month and 15-month follow ups in person.” (line 82-83).

3. On line 108 and 110 you refer to age differences. It is confusing which groups you compare.

Authors’ reply: The comparison was made between patients who attended the follow-up and those who did not. This point has been clarified in the text (line 109).

4. On line 119 you refer to NIHSS score for stroke severity. Did you use NIHSS score on admission or the highest score within the first 2 days?

Authors’ reply: We used the NIHSS score on admission (line 120).

5. One line 196 you write about one-year follow-up. You should write 3 months and 15 months follow-up to avoid confusion.
Authors’ reply: We have changed “one-year follow-up” to “15-month follow-up” (line 198).

6. As you state in the discussion a limitation is the high loss of patients to follow-up. You started with 4,048 patients and ended up with 97 patients. It would be interesting to estimate the total number of participants in an ideal study with no loss of patients (except patients with exclusion criteria).

Authors’ reply: The ideal recruitment rate at 3-month follow up is 52% (435/824). If the total sample size is 4,048, the ideal number of patients attending 3-month follow-up would be 2,105 its 52%. Based on the frequency of PSF of 31% (139/435=31%), the ideal sample size would be 653 31% of 2,105. (line 268).