Reviewer’s report

Title: Acupressure Therapy and Liu-Zi-Jue Qigong for Pulmonary Function and Quality of Life in Patients with Severe Novel Coronavirus Pneumonia (COVID-19): study protocol for a randomized controlled trial

Version: 0 Date: 04 May 2020

Reviewer: Christina Easter

Reviewer's report:

Thank you for inviting me to review this particular study protocol. As this is quite a topical area with great focus from around the world then such coronavirus related papers need to be clear for the target audience, which in this case may reach a more lay population as well as those with medical/epidemiological training. There are some aspects in this protocol that I would like the authors to address in the first instance.

*I found the protocol paper difficult to read due to the spelling mistakes and also the language that was used. Many sentences did not make sense and also were not formed correctly. There were too many incidences of this occurrence and so I cannot mention them all. Therefore I would advise that the authors would benefit from someone whom English is their first language to read over this manuscript to greatly improve the readability.

*On page 3, line 49-50, the authors state that only one rapid advice guideline has been used, I find this hard to believe so I think this needs to be time stamped to highlight the time of when the research into the background was completed whereby this was correct. Especially as this area is rapidly evolving and updates are being made to such guidelines.

*As part of the background and discussion sections the authors make reference to how the intervention has been used previously. However this is not clear enough, this needs to be expanded on greatly to persuade the reader that using this intervention could be applied to the proposed type of patients in the study the authors are wanting to complete. I think that the authors need to address such things as: How relatable is the previous research on this intervention to this study, also the similarities/differences in these types of patients that would indicate that there is sufficient logic to assess if such an intervention could be appropriate. It also occurred to me what the current practise is for those with pneumonia and if indeed this is something that had been thought about.

*The protocol for this study could be greatly improved if there was a diagram of what the intervention was and how it would be implemented, i.e. an instruction diagram. This can give the reader a greater understanding of what the intervention is.

*Under the section "Drop out and suspension criteria" the authors state in point (5) 'Researchers do not consider the participants appropriate to continue participating in this research'. This is not an adequate form of stopping criteria for a patient in such a trial, there needs to be specific criteria in
which a patient would need to meet, not on the decision of the researchers, this could lead to bias being induced into the study.

*Some of the subheadings under primary and secondary outcome measures are acronyms please can these be written out in full.

*Under the sample size calculations section the author's state that the primary outcome is MDS. However this is not reflected in the rest of the protocol. The authors state that there are two primary outcomes in the rest of the protocol. The authors either need to choose which one is there primary outcome and mover the other to the secondary outcomes or state that the two primary outcomes as currently documented are co-primary outcomes and this needs to be reflected in the sample size calculations.

*Additionally in the sample size calculations section, there is not enough information to replicate the calculation and arrive at a sample size of 120 participants. Please could the authors provided further clarification on the information that they used and how they arrived at a sample size of 120 participants.

*Under the randomisation section, I wondered if the authors had thought about a more sophisticated way of completing the randomisation apart from using a simple random number generator. For example, minimisation, block randomisation etc. Additionally in this section, the phrasing of how the participants will be allocated to each arm gets quite confusing, this needs to be looked at further and ensure that it is clear to the reader how the allocation of treatments to the participant is completed.

*Under the section 'Blinding', it does not state if those that are recruiting the participants know of the treatment and the objectives of the study. This needs to be detailed, as if those recruiting the participants know of the interventions and objectives of the study, they may be able to induce bias in terms of if such a patient should be included into the study.

*Under the 'Data collecting and monitoring' section, the authors state that they will 'exclude the data if very few data are lost'. I am unsure as to what this means and therefore needs to be made clearer. I would like to know if the authors had considered using multiple imputation to impute on the missing data values. Currently the statistical analysis is inferred that complete case analysis would be completed however this needs to be explicitly stated.

*Under ' Statistical analysis' section, the authors state that mean and standard deviations will be used (line 334), however the authors should also state that the median and interquartile range will be reported if the continuous variable is not normally distributed i.e. skewed.

*Additionally in the statistical analysis section, for the demographic baseline information the authors will test to see if there is a difference between the groups, however, as this is a RCT then the randomisation should be sufficient enough to ensure that the baseline characteristics are balanced. Current literature is of the opinion that testing between groups for baseline characteristics in an RCT is not required due to the nature of the study. If by looking across the groups for each of the baseline characteristics and there seems to be imbalance then this is due to
the randomisation. This would then imply adjustment in the main statistical analysis. However imbalanced across the two treatments should not be tested.

*Again within this section it is unclear as to how the analysis for each of the primary and secondary outcomes will be performed. Additionally, it would be advised to pick one of the follow up times to be the main primary outcome assessment and the other to be assessed as a secondary outcome. Therefore a linear regression model could be used to assess the outcome whilst adjusting for the baseline measurement. As it stands the statistical analysis section needs to be made clearer to the reader on what exactly is going to be assessed and how with relation to the primary and secondary outcome.

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