Author's response to reviews

Title: Outcome Measures of a 6 Minute Walk Test: Relationships with Physiologic and Computed Tomography Findings in Patients with Sarcoidosis

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Author's response to reviews: see over
Re: MS: 1801645934294088

Outcome Measures of a 6 Minute Walk Test: Relationships with Physiologic and Computed Tomography Findings in Patients with Sarcoidosis

Dear Dr. Norton,

It is my pleasure to submit the revised version of our manuscript. Changes made in the revised text are highlighted in blue.

Per your reviewer request we performed a stepwise multiple regression analysis using backward elimination along with bootstrap method. It confirmed our previous findings that FEV₁ was more strongly related to DSP than for distance. This have resulted in generating additional Tables 1-7.

Performing regression coefficients of study variables based on 1000 bootstrapped samples and their 95%CI have been reported for all the study variables in relation to distance and DSP (Table 8, and Table 9). We believe this information does not add additional information to the manuscript, as such Table 8, and Table 9 can be viewed separately in the supplement section.

We thank the Dr Giorgio Bedogni for his valuable comments. We believe that we have adequately addressed his concerns in the revised manuscript and comments to the reviewer will be found below.

Should you or the reviewers have any questions, we will be happy to answer them.

Sincerely,

Esam Alhamad, MD
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Reviewer: Giorgio Bedogni

Dear Dr. Bedogni,

Thank you for reviewing our study, and we are delighted to respond to your comments.

Comment 1:

While I *fully* understand the difficulty of recruiting patients with a rare disease such as sarcoidosis even at highly specialized tertiary centers as yours, you must consider this limitation of your study.

Response:
Thank you for pointing this out. We have provided a statement indicating the limitations of our study highlighted in blue page 14, 15.

Comment 2:

My suggestion is to perform stepwise regression using backward elimination and bootstrap selection of predictors. Bootstrap will also allow to calculate 95% confidence intervals for the determination coefficient and for the root mean squared error of the estimate.

Response:
As requested, we performed the required analysis, and modified Tables 1-7 have been added to the manuscript. Performing regression coefficients of study variables based on 1000 bootstrapped samples and their 95% CI have been reported for all the study variables in relation to distance and DSP (Table 8, and Table 9). We believe this information does not add additional information to the manuscript, as such Table 8, and Table 9 can be viewed separately in the supplement section.

Comment 3:

You should clearly write that the low sample size you studied (relative to the number of modeled variables) makes it mandatory that your prediction models be validated in external populations (besides the obvious fact that external validation is the only gold-standard for any prediction system).

Response:
As requested, we have provided a statement indicating this limitation of our study highlighted in blue page 14, 15.
Comment 4:

Please, report regression models for ALL variables, even if they are not significant. The tables should report: regression coefficient, standard error of regression coefficient, true p-value (NOT just < 0.05 or > 0.05), determination coefficient and root mean square error of the estimate for both univariable and multivariable analysis. Using bootstrap will allow to calculate confidence intervals for these metrics.

Response:
As requested 9 tables have been added reporting all the required tests.

Comment 5:

The standard errors of the regression coefficients that you give in the text are *surprisingly* high. They are about 20-30 times higher than the regression coefficients. Of course, I suppose that with “beta” you mean “regression coefficient” and with “SE” you mean the standard error of the regression coefficient and there is no typing error. If this is the case, this estimate is very unstable. Please, comment on this very important point.

Response:
The standard error reported previously was related to unstandardized coefficient. However in the revised Tables we have included both standardized and unstandardized regression coefficients along with slandered error and their 95%CI.

Comment 6:

Please, consider that the effects that you attribute to treatment may be due to unknown confounders.

Response:
Thank you for pointing this out. We have clearly indicated in the manuscript that there are several potential confounding factors that might have a significant effect on the walking distance including, heterogeneity in disease progression, duration of corticosteroid use, effects associated with race and ethnicity, as well as extrapulmonary organ involvement, fatigue, or physical deconditioning.
Comment 7:

Please add page numbers.

Response:
As requested page numbers were added.