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 yellow.

Regarding informed consent documentation: given the retrospective nature of our study, written informed consent specific to the present study was not obtained. However, the study protocol was approved by the Ethics Committee of each hospital, as indicated in the manuscript.

In regard to the concerns raised about similarities between the present study and two studies previously published by our group, I would stress that there is no duplication of information among these three papers, even though the studies may appear similar because the patients share the same diagnosis and some of the participants involved in the current investigation were also included in the previous studies (as stated in the Methods section, page 5).

Several significant differences exist among the studies. These include:

1) The objective of the present study was primarily to determine the relationship between outcome measures of the 6MWT (i.e., distance and the DSP), physiologic parameters and computed tomography (CT) patterns.
2) The study published in Ann Thorac Med. 2009 Apr;4(2):60-4 was primarily performed in one center and limited to a small number of patients. More importantly, the objective of the study was to assess the functional capacity during various radiographic stages of pulmonary sarcoidosis, identify variables that correlate with a reduction in walking distance, and to develop a scoring system to assess functional status. Pulmonary hypertension and CT findings were not examined, and a logistic regression model was not used.
3) In the study published in Ann Saudi Med. 2009 Nov-Dec;29(6):454-9, the primary objective was to explore the clinical, physiological and radiological characteristics of pulmonary sarcoidosis in a large sample of patients from three hospitals. The study compared age, gender, extrapulmonary involvement, physiologic tests, and radiographic stages along with CT findings of Saudi patients with those of other ethnic groups. The 6MWT was not examined and correlations with physiologic tests or radiological imaging were not analyzed.

We thank the reviewers for their valuable comments. We believe that we have adequately addressed their concerns in the revised manuscript. Point-by-point responses to the comments of each reviewer can be found below.

We thank you for your consideration of our manuscript.
Sincerely,

Esam Alhamad, MD

Assistant Professor of Medicine

Pulmonary Critical Care Medicine

King Khalid University Hospital

King Saud University

Email: esamalhamad@yahoo.com
Reviewer: Alfredo Chetta

Dear Dr. Chetta,

Thank you for reviewing our study. We are delighted to respond to your comments.

Comment 1:
The authors did not use the best way in the statistical analysis of the data.

Response:
The objective of our study was primarily to determine the relationship between outcome measures of the 6MWT (i.e., distance and the DSP), physiologic parameters and computed tomography (CT) patterns. As such we believe that the current statistical method was appropriate. However, if the objective were to predict the presence of pulmonary fibrosis or pulmonary hypertension, then we agree that constructing ROC curves using DSP or WD would be the appropriate test, as stated in the Discussion (page 11).

Comment 2:
I do not think that a cross sectional retrospective study could provide information of prognostic value.

Response:
We agree with your statement and further studies are needed to address this issue. We have modified the statement in the last paragraph of the Introduction section.

Comment 3:
The authors should provide the reference of the predicted values of the spirometry.

Response:
Thank you for pointing this out; we have provided the relevant references.

Comment 4:
The authors should also provide some characteristics (name, make, country of manufacture) of the equipments they used.

Response:
Manufacturer details have been added to the Methods section.

Comment 5:
The authors used only parametric tests in their statistical analysis. Did the authors assess the distribution of the variables before their processing?

Response:
Both parametric and nonparametric tests were performed, and yielded similar results. Hence, we decided to report only the parametric results.

Comment 6:
There are no figure in the manuscript. Some figures illustrating the main results could ameliorate the readability of the text.

Response:
We agree that, in general, figures aid in understanding the objective of a study; however we felt that Table 2 adequately addressed the comparison between the two independent variables and that adding figures would not provide additional information.
Dear Dr. Holland,

Thank you for your review. We are pleased to respond to your comments.

Comment 1:

Response:
Thank you for your query. In regard to the similarities between the present study and the two studies previously published by our group, we would stress that there is no duplication of information among these three papers, even though the studies may appear similar because the patients share the same diagnosis and some of the participants involved in the current investigation were also included in the previous studies (as stated in the Methods section, page 5).

Several significant differences exist among the studies. These include:

1) The objective of the present study was primarily to determine the relationship between outcome measures of the 6MWT (i.e., distance and the DSP), physiologic parameters and computed tomography (CT) patterns.
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Comment 2:
The manuscript would benefit from increased use of paragraphs – currently several of the paragraphs are a page and a half in length.

Response:
As requested, we have increased the use of paragraphs.

Comment 3:
The abstract would benefit from demographic information regarding disease severity (eg lung function data)

Response:
Pulmonary function parameters have been added to the Abstract.
Comment 4:
The introduction does not make it clear how this study might add to previous literature evaluating the 6-minute walk distance in sarcoidosis.

Response:
We have modified the Introduction to include a statement that no previous study has sought to correlate CT findings with 6MWT results. In addition, we have added a comment that, compared to 6MWD, DSP may be a better indicator of the functional status of sarcoidosis patients.

Comment 5:
Were the blood gases taken on the same day as the 6-minute walk tests?

Response:
Yes, they were taken on the same day. A statement was added to the Methods section.

Comment 6:
Was the 6-minute walk test performed once or twice? There is a documented learning effect for this test and two tests are required to account for this. Given the low distances that are reported (which seem overly low for such a relatively young and well population) I am concerned that the 6-minute walk distance may be underestimated.

Response:
The 6MWT was performed once. Although a learning effect has been reported, our experience has been that repeating the test has little impact on the walking distances achieved by Arab patients. We share your concern that walking distance may be underestimated; however, to quantify the degree of this underestimation, one would need to consider the effect of race and ethnicity on the normal predicted distance. Recently Alameri and colleagues (Respir Med. 2009 Jul;103(7):1041-6) noted that healthy Saudi individuals have significantly shorter 6MWDs compared to other ethnic groups, with mean 6MWDs of 429± 47 m for males and 386± 45 m for females.

Comment 7:
Statistical analysis – terminology requires attention. All data are quantitative. The term ‘qualitative’ does not appear to be appropriate here – I think that you are referring to categorical data. The term ‘quantitative’ is not used correctly here – I think that you are referring to continuous data.

Response:
Thank you for pointing this out. The statistical terminology has been changed to continuous and categorical data.

Comment 8:
The regression analyses should be presented in tables with betas and standard errors. The utility of the predictive models cannot be adequately assessed without this information.

Response:
Thank you for your valid point. We have added the beta and standard error in the Results section as well the Abstract.

Comment 9:
Discussion – can the authors suggest why FEV1, a measure of obstruction, might be the sole predictive factor?

Response:
The reviewer raises an interesting point. Given the retrospective nature of our study, it is difficult to explain why FEV1 was the sole predictive factor. One possible explanation is that our patients had exercise-induced expiratory flow limitation secondary to endobronchial involvement. A prospective study is needed to validate this speculation.