Author’s response to reviews

Title: Impact of diabetes mellitus on functional exercise capacity and pulmonary functions in patients with diabetes and healthy persons

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Author’s response to reviews:

Title: The six-minute walk test in the assessment of daily physical capacity in patients with diabetes

BMC Endocrine Disorders

Thanks to the dialogue between BMC Endocrine Disorders, reviewer and the author, the publication will be able to shed new light on little-known and little-appreciated problem of lung damage in diabetes.

The authors of the publication would like to thank the reviewers for their effort they put into the factual insight into this problem. According to your suggestion the following changes in the paper have been made.

All changes in the main text are marked in red color.

(Reviewer 1):

6MWT is a exercise test of functional/physical capacity All of the physical activity in the methods must be changed with physical capacity in the paper.

YES all phrases have been converted into physical capacity abstract line 55, keywords line 56, Background p.5 line 49, 50, p.6, line 32, heading p.8 line 6 “Assessment of physical capacity”,
Although they didn't do any correlation or regression, in the conclusion and discussion the authors say 'particularly impaired breathing mechanics influence indirectly the reduction of distance walked'. We can not say this conclusion It must be changed.

Yes, this is a very important remark. This point of view in “conclusions” was changed p. 4 line 47-52 and p. 15, line 31-36 and 46-51.

The research aimed to assess the 6MWT test for the estimation of daily physical capacity in patients with diabetes, particularly in patients with pulmonary complications of diabetes' they say in the aim of study but the patients don't have a pulmonary pathology or disorder. This must be corrected.

Yes 'The research aimed was changed to be correct: “The research aimed to compare functional exercise capacity and pulmonary functions in persons with diabetes and healthy persons”

- Before the abbreviations were done, the full name must be written there are some mistakes.

Yes appropriate changes have been added: Background p.5 line 18, line 58, p. 7 line 12, p. 7 “Experimental design” line 44 and 45.

- The weight BMI age results of two groups are statistically different. Can the authors do a new analysis after the removing the extreme values in the control group? Because they affect the pulmonary function and 6MWT results.

The assumption of the work was the examination of all consecutive patients with real body mass therefore no results were discarded. Any degree of overweight or obesity can affect the result 6MWT and so on 6MWD. The table 1. shows the weight value (kg) as p=0,062. More information is given in the limitations of the study p. 12 line 49 – 61 and p. 15 line 1 -24. In this situations, the authors didn’t decide recalculate data of this patients.

In the first paragraph of discussion, main results must be included.
Yes, main results were included in the first paragraph of discussion heading “Discussion” p. 10 line 48-53.

(Reviewer 2):

There are two main concerns related to your manuscript. First, throughout the manuscript, I realize that you confused about the aim of 6MWT. 6MWT is located under "activity" domain of International Classification of Functioning, Disability and Health (ICF). However, it does not mean it assess the daily physical activity, yet, 6MWT and daily physical activity are correlated. Actually, the 6MWT is an alternative to maximal exercise test. Therefore, you should be aware that the 6MWT represents functional exercise capacity or walking capacity.

Yes, this is a very valuable observation. Information that 6MWT is an alternative to maximal exercise test was included in heading “Background” p.6, line 24-29.

YES all unfortunate phrases have been converted into physical capacity (abstract line 55, Keywords line 56, Background p.5 line 49, 50, p.6, line 32, heading p.8 line 6 “Assessment of physical capacity”, heading p.10 “Assessment of physical capacity and pulmonary function tests”, p.11 line 7, p.12 line 7 and 24.

Second, in current methodology, you cannot properly evaluate the usability of 6MWT. Although you checked the adverse event during the test, it is not enough. You have to examine its psychometric properties such as test-retest reliability, inter-rater reliability, validity (correlates to a validated exercise capacity test in persons with diabetes). Therefore, I believe you should change the aim of your study to compare functional exercise capacity and pulmonary functions in persons with diabetes and healthy persons. According to the main concerns, I believe you have to re-write your introduction and discussion.

Yes is a very valuable observation. According to suggestions the aim of work has been changed to the more appropriate one: “The research aimed to compare functional exercise capacity and pulmonary functions in persons with diabetes and healthy persons” (heading Abstract p.4 line 13-14 and “Background” p.6, line 32-34.

According to suggestions the reviewer the introduction and discussion have been changed. In addition, the introduction and discussion were redefined. Appropriate changes in the introduction and discussion of contents, they are:

a) Background p. 5 line 45-52 and 58-59, p. 6 line 2-10, 19 and 24-29.
b) Heading “Assessment of physical capacity” p.8, line 9-14

c) Discussion p.10 line 48-61 and p.11, line 1-2 and line 24-61 and p.12, line 1-6 and heading “Pulmonary function tests and diabetes mellitus” p.13, line 24-38. The new paragraph “study limitation” p. 14, line 49- 61 and p. 15, line 1- 24 was added.

The conclusions were also clarified according to the reviewer's suggestion p.15, line 30-36 and 45-51.

Report full p values, do not just write as "ns".

Statistical data were calculated and added in tables, the value "ns" has been removed; Table 1. p. 22, line 10-13, line 25-28 and Table 2. p23, line 3-28 and Table 3. p.24 line 3.

Report the disease duration.

This information is on page 9, line 17-18 “The mean (SD) duration of diabetes was 13.2 (8.8) year”- not repeated in the text of the information contained in the tables

There is a significant difference in age, height and BMI between the persons with diabetes and healthy participants. It is well known that they are closely related factors with 6MWT distance. Therefore, you have to perform ANCOVA adjusted to age, height and BMI. Please report how you checked the normal distribution of the data. Did you perform a sample size calculation? Please report it.

At this level of the study was not performed a sample size calculation

Appropriate changes have been added p.8, line 58-60 “The normal distribution of the data was confirmed using Kolmogorov–Smirnov test”.

Please state the limitations of the study.

Appropriate paragraph “study limitation” p. 14, line 49- 61 and p. 15, line 1- 24 was added.
Reviewer 2 (Reviewer 3)

REQUESTED REVISIONS:

Abstract: I suggest you remove the SDs from abstract. There is a missing 'the' in the first sentence of abstract.

Yes the SDs from abstract were removed p 4, line 32-41 and the missing “the” was added p.4, line 3

Introduction: the references used are old and out of date, especially references 1-3. These need replacing. The statement on line 20 requires a reference.

Yes, the new data on the prevalence of diabetes have been added. Three new references have been added

a) background p.5, line 3-35, line 44-47,

b) the new references are below (Heading “References” p. 17, line 33-44)

1. http://www.who.int/news-room/fact-sheets/detail/diabetes [accessed 22.08.18]


There is no discussion or references to other studies who have completed this test on those with diabetes. The reader is not told how this study is unique or what gap it filled. This would be a useful addition. The last line of the introduction does not make sense.

In our discussion are references to the literature ie. p 11 line 7 and next lines. The last line of the introduction was deleted and crossed out and converted into new one p.6 line 32-35.

Did you recruit those with or without pulmonary complications? In the methods it says the opposite that no patients had pulmonary disorders. The recruitment strategy of this study is unclear. Those with dm and those without should be recruited from the same broader population
or selection bias creeps in. As it stands, you have a very select group of individuals. Among those with diabetes, the level of control is poor which tells us that they are uncontrolled diabetes. If you compare these people to healthy, of course there walk test will be different. Further you have a high proportion of individuals on insulin again suggesting your population is on the severe end. This means your findings are only generalizable to this group of people with diabetes. This is not discussed as a limitation. There are not limitations discussed.

Yes, it's very valuable remark. It was mentioned on p. 6 “Group demographics” line 59-60 “None of the participants had acute or chronic pulmonary or connective tissue disorders”. The assumption of the work was the examination of all consecutive patients with real body mass. Patients were not selectively matched. The description of the recruitment strategy of this study was rewritten p. 7 “Methods”, line 1-19 and 59 and p.8, line 9-14.

In order to better understand the work, the appropriate paragraph for limiting the study have been added “study limitation” p. 14, line 49- 61 and p. 15, line 1- 24 was added.

I think you should have restricted the study to type 2 patients only. Mixing type 1 and type 2 just gives you results which are tricky to interpret.

Such a selective approach would narrow the group included in the study. Therefore, the authors were decided to evaluate both patients with type 1 and 2 diabetes. In order to better understand the work, the appropriate paragraph for limiting the study have been added “study limitation” p. 14, line 49- 61 and p. 15, line 1- 24 was added.

The word 'anamnesis' is poorly used in the methods and should be replaced or the sentence should be rewritten. What is a proprietary questionnaire? This should be explained and a reference should be given.

Yes, it's very valuable remark appropriate paragraph have been added heading “Group demographics” p.7, line 1-9 and word “proprietary questionnaire” was explained p.7, line 5-7 “Physical examination was performed according to the protocol routinely applied in the Department of Allergology and Pneumonology”.

The methods used to measure BMI etc should be described rather than saying special attention was paid to this. The reader does not know what this means. The text in the results does not mention whether any differences you observe are statistically significant. There is some
discussion in the results. This should be removed (line 50 onwards). It is not clear how the diabetes complications were measured. This is not mentioned in the methods.

In the paragraph METHODS appropriate information have been added p. 7 line 1-20. Information on diabetic complications came from available medical history and referring doctors p. 7 line 1-20. BMI was given as body mass index (BMI, kg/m2).

Statistical data were calculated and added in tables, the value "ns" has been removed; Table 1. p. 22, line 10-13, line 25-28 and Table 2. p23, line 3-28 and Table 3. p.24 line 3.

For table 1, if you have not measured the same factors in the dm vs no dm, you should not report them. ie: glucose, microalbuminuria.

The inclusion of such data (glucose, microalbuminuria etc.) in Table 1 better characterizes conditions patients with diabetes mellitus. In our opinion it should stay in Table 1.

Fibrinogen is missing units.

Yes the unit of fibrinogen was added (g/l) Table 1 p. 22, line 37-38.

The discussion needs rewriting. For example: first paragraph of the discussion should be about your results and it is currently a statement about pulmonary disease in diabetes. Your main hypothesis is to test the walk test and this is what your discussion should be about. There are many statements in the discussion that are not really true. You have shown no evidence that bodyweight and complications explain the differences in walking time. You need to do regression to find this out. You have shown no real evidence that diabetes decrease the strength and resistance of respiratory muscles. You should not make that statement. It is speculation. On page 11, the lines 10-11 are just not really true. All your discussion restructuring and the language needs toning down.

Yes, it's very valuable remark. The language of the discussion was toned down. But in medical literature there is a lot of data on the complications of diabetes mellitus. One of the complications of diabetes is diabetic neuropathy. It can affect the efficiency of the respiratory muscles. Appropriate data and references to literature have been added in the text: p.11, line 56-61 and p.12 line 1-5.


According to suggestions the reviewer the introduction and discussion have been changed.

“Discussion” p.10 line 48-61 and p.11, line 1-2 and line 24-61 and p.12, line 1-6 and heading “Pulmonary function tests and diabetes mellitus” p.13, line 24-38. The new paragraph “study limitation” p. 14, line 49- 61 and p. 15, line 1- 24 was added.

The new references have been added in references number 19 and 20


The conclusions were also clarified according to the reviewer's suggestion p.15, line 30-36 and 45-51.