Author's response to reviews

Title: Thoracic gas compression during forced expiration in patients with emphysema, interstitial lung disease and obesity

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Version: 2
Date: 23 December 2013

Author's response to reviews: see over
Helsinki, December 23th, 2013

Dear Sir,

The manuscript Piirilä et al. entitled “Thoracic gas compression during forced expiration in patients with emphysema, interstitial lung disease and obesity” has now been revised according to the referees of the BMC Pulmonary medicine. The corrections point by point are indicated on the next pages. The English language has been edited by a native English speaker (Ms Carol Pelli). The corrections made in the manuscript point by point are presented in the next pages.

We hope that the manuscript now is suitable for publication in the BMC Pulmonary medicine.

Sincerely yours,

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Reviewer's report, REVIEVER 1
Title: Thoracic gas compression during forced expiration in patients with emphysema, interstitial lung disease and obesity
Version: 1 Date: 3 August 2013
Reviewer: christina alexopoulou
Reviewer's report:
This is an interesting and well presented study about thoracic gas compression during forced expiration in different groups of patients.

Discretionary Revision
Data in Table 4 are already shown in Table 3. You can skip Table 4

ANSWER: Table 4 has been deleted.

It would be interesting if you have data about MIP and MEP of your patients
ANSWER: Unfortunately the MIP and MEP values were not available.

Minor Essential Revisions
page 1: Department of Clinical Physiology and Nuclear Medicine – this has been corrected
page 3: results line 3: (p=0.012, p=0.001) – this has been corrected
page 4 line4:....and was higher in obesity comparing to emphysema – this has been corrected
page 5 second paragraph line 2: artifact - this has been corrected
page 13 line 3 and line 16: the word why doesn't make sense - this has been corrected
page 14 second paragraph line 1: As a conclusion, patients....... – this has been corrected

Reviewer's report  REVIEVER 2
Title: Thoracic gas compression during forced expiration in patients with emphysema, interstitial lung disease and obesity
Version: 1 Date: 5 November 2013
Reviewer:Tomasz Golczewski
Reviewer's report:
The manuscript presents interesting experimental results which seem to confirm results that could be derived theoretically by biomedical physicists or engineers.
Thus, the work could be valuable for such scientists as experimental proof of the theoretical knowledge. On the other hand, the work could be valuable as a 'direct experimental knowledge' for physicians who are not familiar with mathematics and physics, which is more important here as the Journal is a medical journal.
Unfortunately, interpretation and discussion of results are not perfect and, in consequence, they can mislead those readers who cannot interpret results by themselves.
Major Compulsory Revisions
1. The 1st sentence (Introduction) might suggest that compression is a result of forces developed by respiratory muscles and elastic properties of the lungs and
thorax; but it is not the whole true because the compression is caused mainly by the forces and existence of airway resistances. For example, if there was no airway resistance i.e. if the airway resistance was equal to zero (air was superfluid), no compression would exist; only some compression-decompression oscillation related to the resonance system composed from air inertance and compliance (=compressibility) could appear. 

**ANSWER to point 1:** *The sentence has now been changed into:* “During forced expiration alveolar gas is compressed due to muscular force and the combined effect of elastic pressures of the thorax and lungs acting against airway resistances [1].” In addition, in the second paragraph of the introduction chapter, the presence of airways resistance has more pointed out: “Several reports exist on increased thoracic gas compression in asthma, the compression increasing with increasing airways resistance [4 - 6].”

2.

It is not clear whether the term ‘gas compression’ means here the effect (increased pressure, compressed gas) or act (pressure alteration) of compressing. However, the discussion of results seems to suggest the first possibility, i.e. that the ‘compression’ means here the effect. If it is not true, the text should be reedited to eliminate this doubt. If it is true, treating the difference between the thoracic and mouth flows as a quantification of compression (=effect of compressing) is a mistake because this difference reflects rather changes of the compression than the compression per se. For example, if the airway resistance was infinite (airways closure), the whole thoracic flow would result in compression change; and if significantly increased alveolar pressure balanced the forces, a significant constant gas compression would still exists despite that the difference between thoracic and mouth flows would be equal to zero (since both flows would be equal to zero).

These two fundamental aspects, i.e. (a) compression as a result of the airways resistance existence and (b) the difference between the flows as a quantification of compression alteration, are not taken into account in the discussion. Instead of that, the discussion contain several not justified statements and general ones related to well-known facts but having no direct relation to the discussed results. For example, there are description of tobacco smoking influence on the respiratory system (well-known facts not connected by the authors with their results) and the statement that ‘gas compression must be low when MEF25 is low in patients with emphysema’ (neither justified nor explained statement; moreover, usually the lower the mouth flow is because of elevated airway resistances, the greater the compression, whether it is treated as the effect or act of compressing).

**ANSWERS to point 2:**

2. 1) The whole paragraph beginning : “In emphysematic COPD, tobacco smoking causes inflammation of bronchi and alveoli, which leads to bronchial obstruction…” has been deleted.

2. 2) On page 11, last paragraph (beginning with: In normal subjects) has been edited followingly: “In bronchial obstruction, the intrabronchial gas compression in forced expiration has been reported to be increased [4, 5, 9], explained by the elevated airways resistance. Since in asthma the airways
obstruction may vary, only patients with stable pulmonary diseases, without a significant bronchodilator response measured with spirometry, were included in the study.

2.3) On page 12, the discussion on MEF25 has been changed into following: “In emphysematic COPD, the peripheral obstructions typically affect the MEF50 and MEF25 values. In this study, MEF25 in patients with emphysema was very low because of elevated airway resistance. Gas compression at this flow level was also elevated.”

3. Presentation of "uncomfortable negative compression" proofs authors’ honesty. Unfortunately, the proposed explanation of such a compression with some imperfections in measurement procedures seems to be not very correct. On the one hand, "negative compression" exists only in the case of ILD patients (and one? healthy subject) whereas measurement procedures are the same for the all subjects (I suppose). On the other hand, such a ‘negative compression’, i.e. mouth flow bigger than thoracic flow, has to appear in some ILD patients soon after the beginning of the forced expiration (MEF75 or MEF82 or ... etc.) because of reasons mentioned above.

ANSWER: Actually I am now sure if I have understood the referee right. We think that the negative flow is depending on measurement accuracy in very small differences. There were in all groups single measurements with negative difference, especially at MEF25 level.

Minor Essential Revisions
1. The 2nd paragraph: there are 7-8 and 10-11 in references; what is it?
   ANSWER: You are quite right, this is silly. This has been corrected.

2. Usually, 25<BMI<30 is treated as overweight; why here ‘lean’ means BMI<30?
   ANSWER: The word lean has deleted there. The groups are called now simply as group obese (subjects) BMI >30 and controls with BMI <30.

3. Why is COPD sometime used for the emphysema group? - e.g. in figs. 2 and 5 is COPD; the same is in the text. COPD and emphysema are not the same: COPD can be related to either bronchial obstruction or emphysema (or often to coexistence of both). Thus, emphysema is COPD but COPD is not emphysema.
   ANSWER: The figures have been corrected. In the original version we had problems to manage between different programs and file types. Old versions of the figures 2 and 5 were therefore there.

4. Although the fig.1 presents results in a schematic, approximate form, it should not suggests that the ‘distance’ between PEF and MEF75 is the same as between MEF75 and MEF50 or MEF50 and MEF25, i.e. it is equal to 25% of FVC; in fact, PEF is usually close to MEF75.

   ANSWER: figure 1 has been renewed, and the MEF75, MEF50 and MEF25 are now in right situations. The 0 flow at the beginning and end of the curve have been approximated to simulate a spirometric curve. If the 0 flows are not desired, they can be deleted.
Discretionary Revisions
In general, tables and figures well present the results. However: (a) why MEF75 is not presented in the table 2?
ANSWER to point 4 a: The Table 2 presents the results of conventional spirometry, as indicated in the header of the table. Our spirometric results do not include MEF75, and therefore it is lacking in the table 2. In our laboratory, MEF75 is only measured with transmural plethysmography. It is not possible to get the spirometric MEF75 values afterwards.

(b) there is TLCb in this table while its caption contains TGVb;
ANSWER: There was a mistake in the caption of TLC, this has been corrected.

(c) table 3 - since the paired t-test was used, the mean, SD, and range of differences between flows could be (also) presented;
ANSWER: The ranges of differences have been added in Table 3.

Presentation of all investigated groups and then description of methods used to determine these groups may be a little confusing. For example, the emphysema group is presented as patients with FEV1/FVC<0.7, which is not precise since FEV1/FVC<0.7 can be caused only by bronchial obstruction. Detailed presentation of methods used to created the emphysema group is three paragraphs below. Perhaps it would be better to present each group and corresponding methods in a separate paragraph for this group.
ANSWER: The description of the emphysema group has been changed and the description begins now with the diffusing capacity results. The recruited patients had both emphysema and obstruction.

Level of interest: An article of importance in its field
Quality of written English: Not suitable for publication unless extensively edited
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests: I declare that I have no competing interests