Author’s response to reviews

Title: The association of sleep disordered breathing with left ventricular remodeling in CAD patients: a cross-sectional study

Authors:
Audrius Alonderis (audrius.alonderis@lsmuni.lt; audriusa@ktl.mii.lt)
Nijole Raskauskiene (nijole.raskauskiene@lsmuni.lt)
Vaidute Gelziniene (vaidute.gelziniene@lsmuni.lt)
Narseta Mickuviene (narseta.mickuviene@lsmuni.lt)
Julija Brozaitiene (julija.brozaitiene@lsmuni.lt)

Version: 3 Date: 21 Jul 2017

Author’s response to reviews:

Author's response to reviewers 3 and 4

Title: The association of sleep disordered breathing with left ventricular remodeling in CAD patients: a cross-sectional study

Authors:
Audrius Alonderis
Nijole Raskauskiene
Vaidute Gelziniene
Narseta Mickuviene
Julija Brozaitiene

Version: 3 Date: 21 July 2017
Dear Editor and Reviewers

Thank you for your letter and for the reviewer’s comments concerning our manuscript entitled “The association of sleep disordered breathing with left ventricular remodeling in CAD patients: a cross-sectional study” (ID: BCAR-D-16-00535) by Audrius Alonderis et al.

We have now made all corrections to the manuscript according to suggestions of the reviewers point by point (see below for details).

After performed improvements to the manuscript text, we hope that the manuscript would be suitable for publication in your journal.

A supplemental manuscript with all changes in response to reviewers 3 and 4 marked in yellow has been uploaded as a supplemental file.

Yours sincerely

Audrius Alonderis

Email audrius.alonderis@lsmuni.lt

Editor Comments:

BMC Cardiovascular Disorders operates a policy of open peer review, which means that you will be able to see the names of the reviewers who provided the reports via the online peer review system. We encourage you to also view the reports there, via the action links on the left-hand side of the page, to see the names of the reviewers.

Reviewer reports:

Phyllis K Stein (Reviewer 3): Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.

Please overwrite this text when adding your comments to the authors.

I have attempted to communicate my reservations via email to the editor but I guess I need to do it here. This is what I wrote.
Please advise the authors to have this paper translated into standard English syntax. After that is done, I will undertake the level of effort that if will require to review it, but right now it will be too frustrating. Also, it is not clear why some of the changes are in yellow highlight (and readable) and others are in blue highlighting and not readable. If they are meant to be read in the printed version, please change the color to something feasible.

We have made a lot of progress with this paper but until it is made easier to read, which means finding someone to translate it into clear English, I am not willing to undertake the unnecessary effort that will be needed to help the authors create an important research paper.

Response: Thank You for helpful comments about our manuscript. At first, we are very sorry that Reviewer 3 was not able to see the corrections marked by blue highlight in printed version. In response to Reviewer 3, we used a blue highlight for performed corrections marking. Yellow highlighting was used mark responses to Reviewers 1 and 2 suggestions. In the future we will try avoid such misunderstandings. Also all the text was reviewed by fluent in English person, and we hope, it improved our manuscripts English too.

Miguel Goncalves (Reviewer 4): Major Compulsory Revisions

1. Bonferroni correction: I welcome the mention and the inclusion of this. However, I am unclear what the actual implementation of the correction is. When applied this should be highlighted and show the impact on the decision on whether a difference is statistical significant or not.

Response: As mentioned in statistical section three or four groups comparisons were performed by commonly used statistical method one-way ANOVA. Analysis of variance (ANOVA) is used to determine whether there are any statistically significant differences between the means of three or more independent (unrelated) groups. We applied the Bonferroni to post hoc multiple pairwise comparisons. This correction reduces the Type I Error rate when testing multiple hypotheses.

2. Lines 265-267: Could the ESS figures be added to the table if we are going to refer to them. Also, the 'fact' that 2 figures are not statistically significant does not mean that they are similar.

Response: This is now clarified:

„No statistically significant between-group differences were found for frequency of excessive daytime sleepiness (ESS≥10) (respectively 16% and 19%; p=0.14 (Table 1).”
The ESS figures were added to the Table 1 (median (IQR), and Table 3 (mean, SD)

3. Table 2 and 3: what is the p value for trend? This should be clarified in the methodology section in terms of what hypothesis is being tested. In my head, this is simply an omnibus test to check whether all the differences between the 3 groups are all different from zero. Also, can we keep the number of decimal places constant. The 123 footnote (I guess only for the BMI) makes no sense.

Response:

p value for trend – In analysis of variance (ANOVA) for linear trends the most important things to note are the value of the F-ratio and the corresponding significance value. Analysis of variance gives a single overall test of whether there are differences between SA severity groups. Analysis of variance for linear trends, the P value of <0.05 indicates that at least two of the groups are different.

H0: All the SA SEVERITY groups have equal echocardiographic results on the average

1. In statistical section we clarified:

„To compare basic characteristics between non-SA and SA (AHI≥5) groups the significance of differences was assessed using Mann-Whitney tests (or t tests, if data were normally distributed) or chi-squared tests, respectively. Analysis of variance (ANOVA) was used to determine whether there are any statistically significant differences between the means of three (excluded non-SA group) or four independent SA severity (coded as 1=non-SA, 2=mild, 3=moderate, 4=severe) groups. For the linear trend the p value for F-ratio was presented. A Bonferroni correction was applied to post hoc pairwise comparisons of means.“

In Table 2 we replaced p value 0.1 to 0.087

2. Table 2: we clarified footnote b:

b p<0.002 severe SA vs. mild SA, and p=0.025 severe SA vs. moderate SA

4. Table 3, footnote 123: There is a „with“ there.

Response: We corrected this mistake
5. Table 3, footnote c: Where were the non-SA group excluded from this analysis? And if so, how do footnotes a and b come about - what is the test?

Response:

Footnote c: It was important for us to determine whether the polysomnography variables between three SA severity groups (mild to severe) are different or not: F statistic, p for trend, post hoc analysis (Bonferroni correction).

Footnote a: In results of analysis we presented only p value of the pairwise comparison non-SA vs. other SA severity group. As expected, the linear term was found to be highly significant (not shown)

This is now clarified in Table 3:

a p<0.01 between non-SA and each SA groups; b p<0.05 between non-SA and Severe SA (ANOVA for four group, post hoc with Bonferroni correction)

123 number in the superscript indicates SA severity groups, with significant differences p<0.05 (ANOVA for three SA severity group, post hoc with Bonferroni correction)

In statistical section we clarified: please read earlier our comments (2) for Table 2 and 3

6. Table 4: I don't understand the role of the Mann-Whitney and the ANOVA testing.

Response: It was important for us to determine whether the echocardiographic variables between three SA severity groups are different or not.

ANOVA. We tested whether differences between different three SA severity groups (mild to severe) are real. All p values for trend are >0.05 and Table 4 shows only non-SA and SA group (AHI≥5) comparisons. It’s suggests that SA severity according to AHI categories was not inducing changes in their LV thickness and mass (ANOVA for SA severity groups all p for trend >0.05, Table 4).

Mann-Whitney. This has now been stated in the statistics section and in fourth column of the Table 4 header:

“To compare basic characteristics between non-SA and SA (AHI≥5) groups the significance of differences was assessed using Mann-Whitney tests (or t tests, if data were normally distributed) or chi-squared tests, respectively. “

In Table 4, fourth column:
Variable     Non-SA
AHI: <5       n=472  SA
AHI: ≥5       n=300  t test,
Mann-Whitney or 2 test
p for trenda

Thickness and diameters
Left atrium, cm 3.8±0.5 4.1±2.2 <0.001 0.110

7. Multiple logistic regressions: I would really like to see some sort of model assessment to support the conclusions. For example, what is the goodness of fit for these models? Are they any good at explaining the dependent variables? Also, why were continuous variables dichotomized for the models (e.g. Age)? Isn't using continuous variables more robust?

However, we can expand the explanation of analysis:

Hosmer-Lemeshow is a commonly used measure of goodness of fit based on the Chi-square test (which makes sense given that logistic regression is related to crosstabulation). For the Hosmer & Lemeshow test, higher p-values are better. So 0.349 or 0.746 indicates that the model fits well. A large P value cannot reassure readers that the model presented is correct.

This has now been stated in the notes of Figures 3 and 4.

Figure 3:
Model: Hosmer & Lemeshow test $x^2 = 8.9$ df=8 p=0.349; Nagelkerke R2 = 0.213

Figure 4:
Model: Hosmer & Lemeshow test $x^2 = 5.1$ df=8 p=0.746; Nagelkerke R2 = 0.132

In statistical section we added:
“The goodness of fit and Nagelkerke R2 for these models presented”.

------------------------------------

In Statistical section we clarified description of dependent variables:

“To further substantiate the notion that mild-severe SA was an independent determinant of LVH by wall thickness criteria or concentric LV geometry (dependent variable coded 0=absent/1=present), bivariate analysis and multiple logistic regression analyses were performed.”

Minor Essential Revisions

--------------------------

8. It would be good to have more information (e.g., a table) on the statement that "Although the inclusion rate for eligible patients for study analysis was 772 (75%), the inclusion design was consecutive, and there were no significant differences in baseline characteristics with regard to comorbidities." This is quite a substantial drop rate and it would be good to reassure the reader that the excluded have the same characteristics as the included.

Response: This is now clarified in Methods, Design and Setting section

“Anthropometric and clinical profile of the patients not involved into the study did not differ significantly compared with the studied group. There were more cases of diabetes mellitus (23.5% vs. 13.7%, p<0.001) in studied patients than those in non-studied patients. The ratio of male patients was higher in not studied group (81.2% vs. 73.6%, p=0.001).“

9. Line 225: Instead of "multivariate logistic regression" it should be "multiple logistic regression" or just simple "logistic regression". Multivariate means multiple Y variables. In page 16, this is correct.

Response: We agree with Your comment and replaced term „multivariate logistic regression “to „multiple logistic regression”.

------------------------------------