Author's response to reviews

Title: Association between smoking status and the parameters of vascular structure and function in adults. Results from the EVIDENT study.

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Author's response to reviews: see over
Dear Editor of the BMC Cardiovascular Disorders:

Thank you for your help in reviewing this manuscript for consideration of publication in the BMC Cardiovascular Disorders.

Following the suggestions of the editor, we enclose a new version of our manuscript entitled: “Association between smoking status and the parameters of vascular structure and function in adults. Results from the EVIDENT study.” MS: 1985126110103178, together with replies to all the issues raised.

GENERAL COMMENTS:

1. All the changes made in the manuscript (text, tables and figures) are underlined.

2. The current version of the manuscript has been fully checked by a native English speaker with expertise in scientific translations. A certificate of quality is enclosed.

We look forward to hearing from you. If you have any additional request or need any information, please contact us.

Sincerely:

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**Editor’s Comment:**

Requesting copyediting. After reading through your manuscript, we feel that the quality of written English needs to be improved before the manuscript can be considered further. We advise you to seek the assistance of a fluent English speaking colleague, or to have a professional editing service correct your language. Please ensure that particular attention is paid to the abstract.

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In relation to the multivariate models, Reviewer 2 indicates in its comments that “I leave it to the Editor to choose whether the data should be shown as a graph or as a table”. For this reason I present to you the two possibilities: The first one is the graphical representation. In the second one we present the multivariate analysis in a table.

We have used this type of graphical representation because it seems the most appropriate for the data presented, but if the editor prefers these data in a table, we have no objection to present the table in the main manuscript instead of the figure. Either way, we present the table as supplementary material (Table S2).
Table S2: Multivariate analysis of structure and function vascular parameters with smoking status (GLM)

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>Independent variable</th>
<th>Mean</th>
<th>Standard error.</th>
<th>CI 95%</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMT</td>
<td>Nonsmokers</td>
<td>0.66</td>
<td>0.01</td>
<td>0.65</td>
<td>0.68</td>
</tr>
<tr>
<td></td>
<td>Former smokers</td>
<td>0.69</td>
<td>0.01</td>
<td>0.67</td>
<td>0.70</td>
</tr>
<tr>
<td></td>
<td>Present smokers</td>
<td>0.70</td>
<td>0.01</td>
<td>0.68</td>
<td>0.72</td>
</tr>
<tr>
<td>PWV</td>
<td>Nonsmokers</td>
<td>7.61</td>
<td>0.13</td>
<td>7.35</td>
<td>7.86</td>
</tr>
<tr>
<td></td>
<td>Former smokers</td>
<td>7.58</td>
<td>0.14</td>
<td>7.30</td>
<td>7.87</td>
</tr>
<tr>
<td></td>
<td>Present smokers</td>
<td>7.71</td>
<td>0.19</td>
<td>7.33</td>
<td>8.09</td>
</tr>
<tr>
<td>PAIx75</td>
<td>Nonsmokers</td>
<td>96.97</td>
<td>2.12</td>
<td>92.80</td>
<td>101.15</td>
</tr>
<tr>
<td></td>
<td>Former smokers</td>
<td>90.89</td>
<td>2.38</td>
<td>86.21</td>
<td>95.57</td>
</tr>
<tr>
<td></td>
<td>Present smokers</td>
<td>91.98</td>
<td>3.18</td>
<td>85.72</td>
<td>98.24</td>
</tr>
<tr>
<td>ABI</td>
<td>Nonsmokers</td>
<td>1.20</td>
<td>0.01</td>
<td>1.18</td>
<td>1.22</td>
</tr>
<tr>
<td></td>
<td>Former smokers</td>
<td>1.20</td>
<td>0.01</td>
<td>1.18</td>
<td>1.22</td>
</tr>
<tr>
<td></td>
<td>Present smokers</td>
<td>1.18</td>
<td>0.01</td>
<td>1.15</td>
<td>1.21</td>
</tr>
</tbody>
</table>

Adjusted for age, sex, systolic blood pressure, body mass index, HDL cholesterol, diabetes and the presence of antihypertensive, antidiabetic and lipid-lowering drugs.
**Referee 2: Grzegorz Bilo**

*In the revised version of the paper the Authors have addressed and/or acknowledged most issues raised in the reviews of the original submission. I still have a few minor comments:*

**Major Compulsory Revisions: None**

**Minor Essential Revisions**

1) *For major clarity please include also the N (1553) for Alx and ABI in Tables 2 and 3.*

   We have added the N (1553) in the column headings of tables 2 and 3.

2) *The means in Figure 2 – please indicate if these are adjusted (least square) means (likely so, since unadjusted means go the other way, but this should be stated).*

   We have indicated in the figure legend of table 2 that the means are the adjusted means. Now, the figure legend reads as follows:

   **Figure 2**: Relationship of the smoking status with vascular structure and function parameters adjusted by age, sex, systolic blood pressure, heart rate, body mass index, HDL cholesterol, diabetes and the presence of antihypertensive, antidiabetic and lipid-lowering drugs. Figure represents the adjusted means and 95% CI. **Statistical significance**: IMT $p=0.011^*$, PWV $p=0.872$, PAI<sub>x75</sub> $p=0.150$, ABI $p=0.464$.

3) *Figure 2 legend. Replace “Statistical significant” with either “Statistically significant” or “Statistical significance”.*

   We have changed these words as suggested by the reviewer.
Discretionary Revisions

1) I would suggest the inclusion of additional Tables provided in the Authors’ response to reviewers in the published material (as supplementary material, if possible).

We have included the table with the Characteristics of patients by smoking status in the 265 subjects for whom the IMT and the PWV was assessed as table 1 of the supplementary material (Table S1).

In the results section, we have included a reference to view the table (pag. 7, Line 14): An analysis of the 265 individuals for whom the IMT and PWV were performed is shown in supplementary material, table S1.

In the same manner, we have included the table with more details about the multivariate analysis as table 2 of the supplementary material (Table S2).

In the results section, we have included a reference to view this table (pag. 8, Line 12): ... values in present smokers than in former smokers (Figure 2). More details of the multivariate analysis are shown in table 2 of the supplementary material (Table S2).

2) As far as Table 2 (multivariate models) is concerned, it would be useful to provide not just the information on primary variables of interest but also the information on the contribution of covariates to the models and the general statistics of each model.

I leave it to the Editor to choose whether the data should be shown as a graph or as a table (my feeling is that a table, expanded with the above information should be shown to give more complete information).

Following the suggestions of the reviewer, we have presented the multivariate analysis data to the editor to choose whether he prefers the graphical representation or the detailed table. In any case, the option not chosen will be presented as supplementary material.

3) Since the quantitative estimate of smoking burden is available (package-years), it would be of interest to verify if it correlates with vascular parameters (independently of age, of course).

We have analyzed the partial correlations, adjusted for the age, between package-years with each vascular parameter analyzed.

A paragraph was added in the results section (pag. 7, Line 18):
The mean package year in the present smokers was 16.78 ± 16.31, and the average smoking history was 30.39 ± 12.57 years. In an age-adjusted correlation, we found a positive correlation between the package years and the PAIx75 (r=0.332, p=0.015) and a negative correlation with the ABI (r= -289; p=0.036). The PWV and IMT showed no significant correlations.
We added a paragraph in the discussion section to explain the results in relation to the findings (pag. 9, Line 3). We found no correlation between the mean package years in present smokers with IMT. This result can be explained by the small number of present smokers for whom the IMT was analysed.

4) The contrasts in figure 2 – I feel that they could be shown directly on the graph for more clarity.

We have included the post hoc contrasts directly on the graph for more clarity and deleted from the figure legend.

Quality of written English: Needs some language corrections before being published

The current version of the manuscript has been fully checked by a native English speaker with expertise in scientific translations. A certificate of quality is enclosed.
EDITORIAL CERTIFICATE

This document certifies that the manuscript listed below was edited for proper English language, grammar, punctuation, spelling, and overall style by one or more of the highly qualified native English speaking editors at American Journal Experts.

Manuscript title:
Association of the smoking status with parameters of vascular structure and function in adults. Results from the EVIDENT study.

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Date Issued:
November 16, 2013

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