Author's response to reviews

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

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Version: 4  Date: 21 October 2013

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 of the smoking status with 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. Following the suggestions of the reviewers, we think that the manuscript has improved in terms of understanding and clarity. We therefore think that its interest has increased considerably.

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

Sincerely:

José Ignacio Recio Rodríguez,

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Editor's Comment:

"You will see that both expert reviewers found your work interesting but identified a number of issues that need to be addressed before a decision on acceptance of your paper for publication can be reached. I would like to point out to you that both reviewers would like you to emphasise more strongly that a full set of data is only available in a small subset of the EVIDENT study. Both reviewers also wanted to know more about the definition of smoking status and possible objective and/or quantitative measures of smoking status. I agree with their assessment and invite you to address these and other issues detailed in their reports thoroughly. I look forward to receiving a revised version of your manuscript."

"both reviewers would like you to emphasise more strongly that a full set of data as only available in a small subset of the EVIDENT study".

We repeated the analysis of the table 1 (Characteristics of patients by smoking status) with the 265 subjects in whom IMT and PWV were evaluated. The table is presented as annex (table 1) of this document.

As shown in the table, characteristics, according to their smoking status, of the 265 subjects in whom the IMT and PWV were assessed, are similar to those found in the main population analyzed (1553 Individuals). We have not found other variables that have to be taking into account for the multivariate analyzes.

We modified the methods section of the abstract including the number of participants in which the IMT and PWV were evaluated. Now, reads as follows (pag 3, line 5):
Methods: Cross-sectional and multi-center study. Random sample of 1553 participants from the EVIDENT study. Measurements: In all the participants the peripheral augmentation index and the ankle-brachial index were measured. In a small subset of the main population (265 participants) were measured, also, the IMT and PWV.

We have included the following paragraph in the results section (pag 7, line 13):
An analysis of the 265 individuals in whom the IMT and PWV were performed. The results showed that the demographic and biological characteristics, according to the smoking status, were similar to the overall sample analyzed.

We have included in the column headings of table 2 and 3 the number of subjects in whom PWV and IMT were performed.

Lastly, we added this point as a limitation of the study in the discussion section (pag 10, line 18):
Lastly, a full set of data (IMT and PWV) are only available in a small subset of the EVIDENT study. However, this sample has similar demographic and biological characteristics, according to the smoking status, than the overall sample analyzed.
“Both reviewers also wanted to know more about the definition of smoking status and possible objective and/or quantitative measures of smoking status”.

The results of this manuscript are a subanalysis of the EVIDENT Study. The main results of the EVIDENT study were published recently [1]. The main objective of the EVIDENT study was to analyze the relationship between the regular physical exercise with the circadian pattern of blood pressure and arterial aging.

We added the following paragraph in the methods section (study design and population) (pag 5, line 8):

The findings presented in this manuscript are a subanalysis of the EVIDENT study. The main results of which were published recently [1].

Because the purpose of this manuscript was not the primary endpoint, it has not been possible to collect objective data of current smoking (eg by CO analysis in the expired air) or information on passive smoking exposure. However, we include the results of the variable package-years and the average time of smoking in the results section (pag 7, line 16).

The mean packages / year in present smokers was 16.78 ± 16.31 and the average time of smoking was 30.39 ± 12.57 years.

Furthermore, as suggested by the reviewers, we have included a paragraph in the discussion section stating this limitation (pag 10, line 15):

Another limitation of this study is that smoking status was collected through questions and were not used objective measures such as CO in the expired air analysis, although such questionnaires have been used previously in other studies to explore the relationship between arterial stiffness and smoking [2].
Referee 1: Christian Ott

The study examined the association of smoking status with parameters of vascular structure and function. The study question is well-defined and statistics appropriate. Mostly, the data appear sound, the discussion focussed and limitations reported.

Major compulsory revisions:

- It should be clearly noted that this is a subanalysis of the EVIDENT study (NCT01083082), which was previously accepted for publication (Garcia-Ortiz et al Am J Hypertens. 2013 Aug 24. [Epub ahead of print]).
As noted by the reviewer, the results of this manuscript are a subanalysis of the EVIDENT Study. The main results of the EVIDENT study were published recently [1].

We added the following paragraph in the methods section (study design and population) (pag 5, line 8):
The findings presented in this manuscript are a subanalysis of the EVIDENT study. The main results of which were published recently [1].

- Only in about 1/6 (265 out of 1553 individuals) IMT and PWV was assessed. In this limited number of individuals, are there differences in clinical characteristics according to their smoking status? Hence, should additional/other parameters be taking into account for multivariate analyses.
The limited number should be given in the abstract as well as limitation.
We repeated the analysis of the table 1 (Characteristics of patients by smoking status) with the 265 subjects in whom IMT and PWV were evaluated. The table is presented as annex (table 1) of this document.
As shown in the table, characteristics, according to their smoking status, of the 265 subjects in whom the IMT and PWV were assessed, are similar to those found in the main population analyzed (1553 individuals). We have not found other variables that have to be taking into account for the multivariate analyzes.

We modified the methods section of the abstract including the number of participants in which the IMT and PWV were evaluated. Now, reads as follows (pag 3, line 5):
Methods: Cross-sectional and multi-center study. Random sample of 1553 participants from the EVIDENT study. Measurements: In all the participants the peripheral augmentation index and the ankle-brachial index were measured. In a small subset of the main population (265 participants) were measured, also, the IMT and PWV.

We have included the following paragraph in the results section (pag 7, line 13):
An analysis of the 265 individuals in whom the IMT and PWV were performed. The results showed that the demographic and biological characteristics, according to the smoking status, were similar to the overall sample analyzed.

We have included in the column headings of table 2 and 3 the number of subjects in whom PWV and IMT were performed.
Lastly, we added this point as a limitation of the study in the discussion section (pag 10, line 18):

Lastly, a full set of data (IMT and PWV) are only available in a small subset of the EVIDENT study. However, this sample has similar demographic and biological characteristics, according to the smoking status, than the overall sample analyzed.

- **In contrast to radial Alx, central Alx is established and acknowledged as marker of pulse wave reflection. Radial and central Alx are not interchangeable. This should be addressed in the manuscript.**

Central Alx is established and acknowledged as marker of pulse wave reflection. However, some authors have found that there is a close relationship between CAIx and PAIx [3, 4]. In a subsample of subjects in the EVIDENT study we found a correlation between the two measures (CAIx and PAIx), both estimated with Sphygmocor, of 0.871 (p <0.01) [5].

In our study we analyzed the peripheral or radial augmentation index, which is a marker of vascular aging [6].

As noted by the reviewer, Radial and central Alx are not interchangeable in the clinical practice. For this reason, we have added the following paragraph in the discussion section (pag 9, line 21):

Furthermore, Janner JH et al. and Minami J et al. [7, 8] analyzed the relationship of smoking with CAIx, while in our work we use the radial or peripheral augmentation index. Radial and central Alx are not interchangeable in the clinical practice, although the radial augmentation index has been established as a marker of vascular aging [6].

- **It is stated in the results “PWV behaves likewise although it does not reach statistical significance”. Moreover, it is given in the discussion “After controlling for confounders, we found no association between the presence of smoking and increased arterial stiffness, although the trend is similar to that found in relation to IMT.”**

However, according to multivariate analysis p-value for PWV was 0.621 (Figure legend). Explanation?

Before adjustment, we found a difference in the PWV with lower values in present smokers (6.65 m / sec) than in non-smokers and former smokers (7.10 and 7.30 m/sec). After adjusting for the confounding variables, the lowest value of PWV is for the non-smokers and highest for smokers. Among the major determinants of PWV we found the age and SBP [9]. In our study, the group of smokers is the youngest and the one that has lower values of SBP. Although these variables were included in the multivariate analysis model may not be sufficient to control the effect they may have on the results of this study.

We have included the following paragraph in the discussion section (pag 9, line 9):

Among the major determinants of PWV are found the age and SBP [9]. In our study, the group of smokers is the youngest and the one that has lower values of SBP. Although these variables were included in the multivariate analysis model, it may not be enough to control the effect they may have on the results of this study.
In order to improve the understanding of the manuscript we have decided to delete the following sentence in the discussion: “...although the trend is similar to that found in relation to IMT”.

- The given conclusion is too strong!
  We have changed the conclusion, and now reads as follows (pag 3, line 13), (pag 10, line 23):
  **Among the parameters of vascular structure and function analyzed, only the IMT shows association with the smoking status, after adjusting for confounders.**

**Minor essential revisions:**

- In the methods section, it should be clearly outlined that smoking was not allowed within 3 h prior to measurement (i.e. not only for PWV, but also for central BP and PAIx).
  We have included the following in the methods section (pag 6, line 9):
  **All measurements (IMT, PWV, PAIx75 and ABI) were performed in the morning. Smoking was not allowed within 3 h prior to measurements.**

- PAIx is higher in non-smokers compared to former smokers as well as smokers.
  Any explanation?
  Among the major determinants of PAIx is found the age, SBP and the BMI. In our results, the group of smokers is the youngest and which has lower values of SBP and BMI. Although these variables were included in the multivariate analysis model, it may not be enough to control the effect they may have on the results of this study.

  We have included the following paragraph in the discussion section (pag 9, line 17):
  **Among the major determinants of PAIx75 are found the age, SBP and the BMI. In our study, the group of smokers is the youngest and the one that has lower values of SBP and BMI. Although these variables were included in the multivariate analysis model, it may not be enough to control the effect they may have on the results of this study.**

- No data about maximum IMT are given, as outlined in “variables and measurement instruments”.
  We added the average maximum IMT in the table 1 (General characteristics of the sample), but the results are similar to those found with the average mean IMT. Because the average mean IMT is the measure that best predicts cardiovascular risk and due to its greater clinical utility [10], we think is better to use it in the regression analysis.

**Discretionary revisions:**

- Table 1:
  - Please provide units for all parameters.
  - Waist circumference for men and women is interchanged.
  We have provided units for all parameters in table 1 and the mistake in the waist circumference has been corrected.
- **Table 3: Please add p-values.**
  We have added the p-values in table 3. *p<0.05, **p<0.01

- **Figure 1: Please add correlation coefficient and p-value.**
  We have added the correlation coefficient and p-values in the figure legend of figure 1, and now, reads as follows:

  **Figure 1:** Scatterplots that represents the relation between age and each vascular structure and functional parameter analyzed (PWV r=0.558; p<0.01, IMT r=0.687; p<0.01, PAIx75 r=0.222; p<0.01 and ABI r=0.045; p>0.05).

**Level of interest: An article whose findings are important to those with closely related research interests**

Following the suggestions of the editor and the reviewers, we think that the manuscript has improved in terms of understanding and clarity. We therefore think that its interest has increased considerably.
Referee 2: Grzegorz Bilo

The paper summarizes the results of an analysis of data from EVIDENT population study aimed at assessing the relationship between smoking status and vascular alterations (cIMT, PWV, AIX, ABI). The main conclusion of this analysis is that cIMT is the variable which best correlates with smoking status.

Major Compulsory Revisions

1) As correctly reported by the Authors in the discussion the associations between smoking and vascular alterations have been quite extensively studied in the past. Please explain more clearly what is the new information that this study adds.

In this paper we present data about the relationship of smoking status with a large variety of parameters that assess vascular structure and function in a general population sample of primary care clinics. Studies with similar objectives to our, analyzed only one of these parameters in an isolated manner or in a selected population [7, 11].

Nevertheless, when evaluating vascular structure and function, every test has different ease of access and cost [12]. The results of this work show that IMT is the parameter that best relates with smoking status in a representative sample of adult population.

We added the following paragraph to the first paragraph of the discussion (pag 8, line 10).

In this paper we present data about the relationship of smoking status with a large variety of parameters that assess vascular structure and function in a general population sample of primary care clinics.

2) Sample size. Although the sample size reported (e.g. in the abstract) is of 1553 subjects, only in 265 of them complete assessment, including cIMT and PWV, was performed. Since the main conclusion regards cIMT, such presentation of the data is misleading. It is also confusing when looking at Table 1 where part of the data are shown for 1553 and part of them for 265 subjects. A demonstration is needed that the subgroup of 265 subjects is representative of the main population. If this is not the case only the data for 265 subjects may be used, in my view. Also, indicate N for each variable in Tables 2 and 3.

We repeated the analysis of the table 1 (Characteristics of patients by smoking status) with the 265 subjects in whom IMT and PWV were evaluated. The table is presented as annex (table 1) of this document.

As shown in the table, characteristics, according to their smoking status, of the 265 subjects in whom the IMT and PWV were assessed, are similar to those found in the main population analyzed (1553 individuals). We have not found other variables that have to be taking into account for the multivariate analyzes.

We modified the methods section of the abstract including the number of participants in which the IMT and PWV were evaluated. Now, reads as follows (pag 3, line 5):
Methods: Cross-sectional and multi-center study. Random sample of 1553 participants from the EVIDENT study. Measurements: In all the participants, the peripheral augmentation index and the ankle-brachial index were measured. In a small subset of the main population (265 participants) were measured, also, the IMT and PWV.

We have included the following paragraph in the results section (pag 7, line 13):
An analysis of the 265 individuals in whom the IMT and PWV were performed. The results showed that the demographic and biological characteristics, according to the smoking status, were similar to the overall sample analyzed.

We have included in the column headings of table 2 and 3 the number of subjects in whom PWV and IMT were performed.

Lastly, we added this point as a limitation of the study in the discussion section (pag 10, line 18):
Lastly, a full set of data (IMT and PWV) are only available in a small subset of the EVIDENT study. However, this sample has similar demographic and biological characteristics, according to the smoking status, than the overall sample analyzed.

3) Smoking status was only ascertained on a current/ex/never smoker basis, as reported by the patients. This surely is a limitation of the study – objective assessment of actual smoking (e.g. by CO analysis in the expired air) would be useful, although not easy to achieve. However, a more complete quantitative information of smoking exposure should have been obtained (package-years). Also information on passive smoking exposure would be useful. Please acknowledge the above as study limitations.

The results of this manuscript are a subanalysis of the EVIDENT Study. The main results of the EVIDENT study were published recently [1]. The main objective of the EVIDENT study was to analyze the relationship between the regular physical exercise with the circadian pattern of blood pressure and arterial aging.

We added the following paragraph in the methods section (study design and population) (pag 5, line 8):
The findings presented in this manuscript are a subanalysis of the EVIDENT study. The main results of which were published recently [1].

Because the purpose of this manuscript was not the primary endpoint, it has not been possible to collect objective data of current smoking (eg by CO analysis in the expired air) or information on passive smoking exposure. However, we include the results of the variable package-years and the average time of smoking in the results section (pag 7, line 16).
The mean packages/year in present smokers was 16.78 ± 16.31 and the average time of smoking was 30.39 ± 12.57.

Furthermore, as suggested by the reviewer, we have included a paragraph in the discussion section stating this limitation (pag 10, line 15):
Another limitation of this study is that smoking status was collected through questions and were not used objective measures such as CO in the expired air analysis, although
such questionnaires have been used previously in other studies to explore the relationship between arterial stiffness and smoking [2].

4) **Data presentation** – since the main conclusion is based on multivariate analysis, a more detailed presentation of multivariate models (as tables) is essential. In my view the data in Table 3 and Figure 1 provide the same message, which is helpful as a background for the other data, but if more space is needed one of them could be removed.

As noted by the reviewer, correlations between age and the different parameters analyzed vascular structure and function were repeated in Table 3 and Figure 1. We have added the correlation coefficient and p-values in the figure legend of figure 1. On the other hand correlation coefficients between age and parameters of vascular structure and function has been deleted from table 3.

The figure legend of figure 1 reads as follows:

**Figure 1:** Scatterplots that represents the relation between age and each vascular structure and functional parameter analyzed (PWV r=0.558; p<0.01, IMT r=0.687; p<0.01, PAIx75 r=0.222; p<0.01 and ABI r=0.045; p>0.05).

Data of multivariate analysis are presented in Figure 2 and in the section of statistical analysis. We have used this type of graphical representation because it seems the most appropriate for the data presented, but if the reviewer or the editor prefers these data in a table, we have no objection to doing so. Nevertheless, we present the multivariate analysis in a table, as supplementary material of this response (See annex, table 2).

**Minor Essential Revisions**

5) **The authors should specify more clearly how the smoking status was used in the multivariate analysis** – was it used to create categories (so the analysis could be basically an analysis of covariance) or was it used as an ordinal variable. If the former is true I would expect post-hoc contrasts to be show between the three categories (I understand that p=0.009 refers to overall comparison between the three groups so it does not directly imply which of the groups differed from the others meaningfully) – these contrasts should be also shown in Figure 2.

The smoking status was used as a categorical variable in the multivariate analysis. We have added the following in the statistical analysis section (pag 7, line 1):

To analyze the relationship of the vascular structure and function (IMT, PAIx75, PWV or ABI) with the smoking status (Nonsmoker = 0, Present smoker = 1, Former smoker =2), a General linear model (GLM) analysis was performed including age, sex, systolic blood pressure, heart rate, body mass index, HDL cholesterol, diabetes and the presence of antihypertensive, antidiabetic and lipid-lowering drugs as adjustment variables.

Furthermore, we performed post-hoc contrasts and the results are showed in the figure legend of figure 2:
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 means and 95% CI. Statistical significant: IMT p=0.011*, PWV p=0.872, PAIx75 p=0.150, ABI p=0.464. * Post-hoc contrasts: p<0.01 between present smokers and nonsmokers; p=0.05 between nonsmokers and former smokers; p=0.17 between former smokers and present smokers.

6) **Statistical analysis.** HDL-C was significantly lower in smokers. Unless there is any specific reason it should be included in multivariate analyses.

We have included the HDL cholesterol in the multivariate analysis but the main results are unchanged.

Figure 2 of the new version of the manuscript includes a new adjustment variable: HDL cholesterol.

7) **Please provide a better explanation for Figure 2 – do the points represent LS means? The bars SE or CI?**

Figure 2 represents means and CI 95%. We have explained this in the figure legend of figure 2:

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 means and 95% CI. Statistical significant: IMT p=0.011*, PWV p=0.872, PAIx75 p=0.150, ABI p=0.464. * Post-hoc contrasts: p<0.01 between present smokers and nonsmokers; p=0.05 between nonsmokers and former smokers; p=0.17 between former smokers and present smokers.

**Discretionary Revisions**

8) **Statistical analysis.** I am always concerned whenever multivariate analyses show results which are not consistent with univariate data and this is the case in this study: in Table 1 current smokers have the lowest mean IMT among the three groups. The authors suggest that the opposite finding in the multivariate analysis is due to the fact that smokers are younger and have lower BP - thus the expected cIMT values should be even lower. However, as they are, the results do not seem very convincing. Possibly these findings could be supported by e.g. comparing the cIMT values between smokers and nonsmokers of comparable age (e.g. within 5 years wide age strata) although sample size may be inadequate for such an analysis.

The results of this manuscript are a subanalysis of the EVIDENT study whose main objective was to analyze the relationship of regular physical activity with the circadian pattern of blood pressure and arterial aging. This limitation prevents us to establish comparable groups in their clinical characteristics, according to the smoking status. However, this limitation is, in part, addressed in the multivariate analysis. Among the main determinants of vascular structure and function measures, we found the smoking and other factors such as age, sex, SBP, BMI, diseases such as diabetes and the presence of lipid-lowering drugs, antidiabetic and antihypertensive. These variables
have been included in the multivariate analysis and the data changes to a more reasonable direction from a clinical viewpoint. As noted by the reviewer, age-stratified analysis comparing subjects of the same rank (smokers vs. nonsmokers) can not be performed due to the small number of smokers and the fact that there are tests such as PWV and IMT that were performed in only 265 subjects. However, we believe it is necessary to include a paragraph in the discussion about the need to conduct studies aimed at clarifying the chronic effects of smoking on vascular structure and function (pag 10, line 24).

Further focused studies on the smoking status are necessary to clarify the role of the chronic effects of smoking on the parameters of vascular structure and function and effects of passive smoking exposure.

**Level of interest: An article of limited interest**

Following the suggestions of the editor and the reviewers, we think that the manuscript has improved in terms of understanding and clarity. We therefore think that its interest has increased considerably.


Table 1: Characteristics of patients by smoking status in the 265 subjects in whom the IMT and the PWV was assessed.

<table>
<thead>
<tr>
<th></th>
<th>Nonsmokers (n=120)</th>
<th>Former smokers (n=91)</th>
<th>Present smokers (n=54)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.67±12.14</td>
<td>54.86±11.42</td>
<td>46.11±10.24</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Males (%)</td>
<td>33 (27.5)</td>
<td>52 (57.1)</td>
<td>23 (42.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>39 (32.5)</td>
<td>31 (34.1)</td>
<td>6 (11.1)</td>
<td>0.006</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>4 (3.3)</td>
<td>10 (11.0)</td>
<td>3 (5.6)</td>
<td>0.077</td>
</tr>
<tr>
<td>Dyslipidemia (%)</td>
<td>38 (31.7)</td>
<td>27 (29.7)</td>
<td>9 (16.7)</td>
<td>0.112</td>
</tr>
<tr>
<td>Obesity (%)</td>
<td>26 (21.7)</td>
<td>24 (26.4)</td>
<td>6 (11.1)</td>
<td>0.092</td>
</tr>
<tr>
<td>Antihypertensive Drugs (%)</td>
<td>38 (31.7)</td>
<td>33 (36.3)</td>
<td>6 (11.1)</td>
<td>0.004</td>
</tr>
<tr>
<td>Lipid-lowering Drugs (%)</td>
<td>23 (19.2)</td>
<td>19 (20.9)</td>
<td>5 (9.3)</td>
<td>0.179</td>
</tr>
<tr>
<td>Antidiabetic Drugs (%)</td>
<td>4 (3.3)</td>
<td>6 (6.6)</td>
<td>2 (3.7)</td>
<td>0.502</td>
</tr>
<tr>
<td>Office SBP (mmHg)</td>
<td>122.83±16.45</td>
<td>124.11±18.19</td>
<td>118.11±19.67</td>
<td>0.133</td>
</tr>
<tr>
<td>Office DBP (mmHg)</td>
<td>77.70±9.93</td>
<td>78.35±11.31</td>
<td>76.09±11.85</td>
<td>0.476</td>
</tr>
<tr>
<td>Office heart rate (bpm)</td>
<td>69.49±11.24</td>
<td>66.96±10.51</td>
<td>69.89±9.60</td>
<td>0.157</td>
</tr>
<tr>
<td>Central SBP (mmHg)</td>
<td>115.18±15.34</td>
<td>115.61±18.25</td>
<td>111.39±16.60</td>
<td>0.291</td>
</tr>
<tr>
<td>Central DBP (mmHg)</td>
<td>76.92±10.81</td>
<td>77.22±15.60</td>
<td>74.28±12.58</td>
<td>0.371</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.37±4.33</td>
<td>28.19±3.93</td>
<td>26.15±5.50</td>
<td>0.031</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>92.58±9.75</td>
<td>96.58±11.69</td>
<td>91.37±14.15</td>
<td>0.011</td>
</tr>
<tr>
<td>Total cholesterol (mg/dL)</td>
<td>219.81±38.97</td>
<td>209.25±39.15</td>
<td>200.15±30.90</td>
<td>0.004</td>
</tr>
<tr>
<td>Triglycerides (mg/dL)</td>
<td>103.65±47.99</td>
<td>114.55±62.83</td>
<td>117.09±109.65</td>
<td>0.378</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dL)</td>
<td>136.95±32.12</td>
<td>130.68±36.65</td>
<td>122.88±29.04</td>
<td>0.038</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dL)</td>
<td>62.60±16.43</td>
<td>55.71±15.00</td>
<td>54.11±12.91</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean IMT (mm)</td>
<td>0.68±0.10</td>
<td>0.70±0.11</td>
<td>0.65±0.11</td>
<td>0.045</td>
</tr>
<tr>
<td>PWV (m/sec)</td>
<td>7.69±1.91</td>
<td>7.83±2.22</td>
<td>7.02±1.73</td>
<td>0.053</td>
</tr>
<tr>
<td>PAIx75 (%)</td>
<td>99.76±25.97</td>
<td>88.75±23.66</td>
<td>88.18±16.31</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ABI</td>
<td>1.20±0.10</td>
<td>1.21±0.08</td>
<td>1.18±0.11</td>
<td>0.173</td>
</tr>
</tbody>
</table>

Normally distributed continuous variables are expressed as mean ± standard deviation, while non-normally distributed variables are presented as median and 75–25th percentile. Frequency distribution was used in categorical variables.

Obesity: BMI ≥ 30 Kg/m² or Waist circumference ≥ 88 cm in women and ≥ 102 cm in men. SBP: Systolic blood pressure; DBP: Diastolic blood pressure; BMI: Body mass index; HDL: high density lipoprotein; LDL: low density lipoprotein; IMT: Intima Media Thickness; PWV: pulse wave velocity; PAIx75: Peripheral or radial augmentation index adjusted for heart rate at 75 bpm, ABI: ankle brachial index.
Table 2: 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.