Reviewer feedback

Manuscript ID: ijerph-879461

Title: Metabolically Healthy Obesity: Presence of Arterial Stiffness in the Prepubescent Population

The authors are advised to submit a revised version of the paper and consider all comments to improve the paper.

Specific comments:
1. There appears to be an inconsistency between the title of the study (and introductory sentence of the abstract) and the conclusion (based on the actual focus of the study). The authors wrote: “Atherosclerotic cardiovascular disease, one of the world’s leading causes of death, first manifests itself at an early age.” This holds true; however, the focus of this study appears to be on pulse wave velocity (arteriosclerosis NOT atherosclerosis). Atherosclerosis = plaque formation in the carotid intima, coronaries, femoral arteries or popliteal arteries, while arteriosclerosis describes arterial stiffness, loss of arterial compliance and distensibility.

2. The conclusion in the abstract states: “PWV could potentially be a useful noninvasive technique to identify cardiovascular risk in childhood.”, yet, this was not the aim of the study – to identify PWV as a useful non-invasive technique to identify risk. This part of the conclusion should either be removed, or the authors need to perform separate analysis to determine the predictive value of PWV in identifying children at increased risk, by odds/hazard ratios.

3. The entire introduction is based on atherosclerotic CVD. The presence of plaque in the arteries will indeed manifest in increased stiffness, but arterial stiffness can also develop in the absence of atherosclerotic plaque. The authors should provide clarification of these different concepts and illustrate why reference to atherosclerosis is made throughout the manuscript instead of arteriosclerosis.

4. Similarly, the authors wrote in the introduction: “There is evidence that subclinical markers of atherosclerosis, such as endothelial dysfunction, intima-media thickness, and arterial stiffness (AS), are abnormal in children with obesity.” This is incorrect. Arterial stiffness is not a marker of atherosclerosis.

5. The authors should rewrite the section on: “Performing a cardiovascular risk stratification by measuring different vascular biomarkers could help to identify children at risk of developing ACVD.”, as this seems to be very similar to the review paper by: Cote AT, Harris KC, Panagiotopoulos C, Sandor GG, Devlin AM. Childhood obesity and cardiovascular dysfunction. J Am Coll Cardiol. 2013; 62:1309-19.

6. The part of the aim: “and Mediterranean Diet (MedDiet) adherence” is not well described in the introduction and seems odd to feature without prior introduction and its relevance.

7. The authors mentioned that their study population is a “prepubescent population aged 6–11 years”. This seems incorrect as some children, especially boys, will already...
start puberty at age 10 years, and for girls at age 8 or 9 years.
8. The authors use the terminology “metabolically healthy”, yet, the children are obese and +1 other metabolic risk factor. How is this definition metabolically “healthy”? The man-made syndrome (metabolic syndrome) is the inclusion of 3 or more risk factors for metabolic syndrome, but for children it is not “healthy” to be obese and have high blood pressure for example. This is contradicting the current advocating efforts of numerous pediatric bodies to improve child health.
9. Could the authors indicate in the methods section (recruitment), whether the measurements were performed at the schools (school-based setting) or at the hospital?
10. Please provide the manufacturer details of the body scale and the stadiometer used to measure body weight and height, respectively.
11. Blood pressure was “...measured using an automated electronic sphygmomanometer.” The authors should provide more detail. Is the device a pediatric validated device? Manufacturer details should be provided. Why did the authors use an average of the three blood pressure readings and not the average of reading 2 and 3 – giving the least variance? See: Moore MN, Schultz MG, Nelson MR, et al. identification of the optimal protocol for automated office blood pressure measurement among patients with treated hypertension. Am J Hypertens. 2017
12. The authors wrote: “In addition, information about each participant’s personal and family history was obtained.” What kind of personal and family history information was obtained?
13. Was the PWV adjusted for the 80% distance between the sites of applanation?
14. In the statistical analysis section, the Pearson correlations are mentioned after the multi-variate adjusted regression, but in the results section, it was shown before the regressions. Also, the authors listed several covariates for the multi-variate regression analysis with PWV as dependent variable, yet, mean arterial pressure or heart rate was not considered in the model. Can the authors explain why?
15. The authors wrote that: “Parameters of obesity showed a stronger positive correlation with carotid-femoral arterial stiffness in boys...”, yet, z-transformations were not performed to determine the strength of the correlation coefficients. Therefore, making the statement not true.
16. For the multiple regression, the authors should show all independent variables and their coefficients. Backward stepwise regression is also advised.
17. The first statement in the discussion seems flawed: “The main finding of our work is that insulin resistance and BMI are closely related to the presence of arterial stiffness in prepubescent children with obesity.” The authors stated that “in the presence of arterial stiffness”, yet the children did not show augmented PWV, hence no clinical arterial stiffness present. These associations are also without correction of mean arterial pressure and heart rate (known sympathetic activation in obesity or sympathovagal imbalance).
18. In the discussion, “We did not find any relationship between adherence to MedDiet and carotid-femoral arterial stiffness in our prepubescent MHO population.” The
authors should also test the regression analysis to correct for adherence when investigating the relationship between PWV and body composition variables. Again, the authors should show all output of the regression analysis.

**Technical comments:**
1. This “carotid-femoral arterial stiffness (cfAS)” is not a recognised abbreviation.
2. In the methods section the abbreviation “MedDiet” is used for the first time and need to be defined.
3. The authors are inconsistent with the terminology sex and gender. The preferred terminology is sex, since gender is a complex social construct of self-identification not studied in this analysis. This should be corrected throughout the manuscript.

4. The beta symbol seems strange in the results section.