

### Reply

# Sex-Related Differences in Cardiovascular Risk in Adolescents with Overweight or Obesity

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#### Dear Dr. Saleh,

Thank you for your letter to the Editor regarding our article titled "Sex-Related Differences in Cardiovascular Risk in Adolescents with Overweight or Obesity". We appreciate your interest in our work and welcome your stimulating comments that allowed us to better specify the protocol of carotid intima-media thickness (cIMT) measurement performed in our study.

First, we reply to the question on whether a singlesite measure of cIMT in the common carotid artery or a multiple-site assessment in different carotid sections (common carotid artery, bifurcation and internal carotid artery) should be performed. The choice to measure cIMT only in the common carotid artery is justified by the easier and much more accurate measurement on this segment compared to the bulb or the internal carotid artery. Ultrasonographic evidence of atherosclerotic plaques is frequent in adults with hypertension, diabetes or other cardiovascular risk factors, and in children with homozygous familial hypercholesterolemia; their presence worsen the cardiovascular risk. Differently from adults, carotid plaques are very uncommon in children with obesity or overweight and most of the authors who have published data on subclinical atherosclerosis in children limited the ultrasonographic exploration of the carotid tree to the common carotid artery [1–4]. However, the standardized examination protocol used in the present study included an initial quick transverse scan to identify focal thickenings of common carotid artery, bifurcation, and internal carotid artery. None of the subjects participating in this study had any plaque at these sites.

Regarding the question on whether cIMT should be measured only in the far wall or also in the near wall, we believe that measuring only the far wall (sometimes with a single scan angle) saves time and resources [5]. We are aware that this choice may often lead to misclassification of subjects, who sometimes have greater thickness on the near wall than on the far wall. Therefore, to reduce variability, three scanning angles were used in this study in each participant: anterior oblique, lateral and posterior oblique. According to a previous study published by our group in hypercholesterolemic children using the same ultrasonographic methodology reported in the present study, the average coefficients of variation for mean thickness were quite similar: near wall, 2.9%; far wall, 3.0%; and both walls, 2.4% [6]. Indeed, these coefficients of variation were by far less than 6%, the threshold recommended by the Association for European Paediatric Cardiology Working Group on Cardiovascular Prevention [7]. Therefore, the risk that manual cIMT measurements might have contributed to inaccuracy in cIMT estimation is largely attenuated. About this question, we also quote Ravani et al. [5] who stated that "cIMT measurements performed directly with the elec-

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tronic caliper of the ultrasonic device itself are accurate enough and allow to detect associations with vascular risk factors or, possibly, to perform individual cardiovascular (CV) risk stratification" [8].

Lastly, the influence of the cardiac cycle on cIMT measurement was also underscored in the letter. In our study, cIMT was measured in both systole and end-diastole, along with the carotid artery diameters. Values reported in our study refer to data in end-diastole.

Anyway, we recognize that some procedural techniques employed in our study, such as the use of manual measurements could represent a flaw in the accuracy in cIMT estimation. Therefore, in view of this debate, our results relative to cIMT need to be considered cautiously. However, despite the different procedures, our findings in adolescents with obesity are in agreement with previous research in normal pediatric populations, that presented higher cIMT in boys than in girls [9,10]. In these studies, measurements were performed only on the far wall with a semi-automated edge detection through a computer software package, with coefficients of variation similar to that reported by our group [6].

## **Author Contributions**

PDB, AI and GV wrote the first draft. PDB, ADS, MRL, DC, MW, EMDG, AM, CM, MFF, EM, VC, FF, GM, NM, AI and GV contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

# **Ethics Approval and Consent to Participate**

Not applicable.

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# **Conflict of Interest**

The authors declare no conflict of interest.

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