Reviewer's report

Title: Selected risk factors for atherosclerosis in children and their parents with positive family history of premature cardiovascular diseases: a prospective study

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Reviewer: Seda Tierney

Reviewer's report:

This is a well written manuscript on an important topic - risk of premature atherosclerosis in childhood and associated risk factors - that evaluates serum parameters of lipid metabolism, homocysteine, soluble adhesion molecules and common carotid artery wall thickness in children from families with early symptoms of atherosclerosis. The study has two phases. In the first phase they study 137 pairs of mothers and newborns. And in the second phase they study 18 pairs from the initial group of 137.

In the initial large group, the authors report inverse correlations between birthweight, cord blood concentrations of triglycerides (TG), VLDL cholesterol and apolipoprotein B (Apo B). Also, serum concentrations of total cholesterol (TC), apolipoprotein A1 (Apo A1), LDL and HDL cholesterol and were significantly higher in female than in male newborns.

In the second small group, children from families with a history for premature CAD were shown to present with significantly higher serum concentrations of TG, VLDL cholesterol and lipoprotein A (Lp(a)) than the controls. Furthermore, their TC correlated positively with vascular cell adhesion molecule-1 (Rs=0.717, p<0.05) and intracellular adhesion molecule-1 (sICAM-1) levels (Rs=0.833, p<0.05). Moreover, positive correlations were found between maternal carotid intima media thickness (IMT) and TC (Rs=0.831, p<0.01), as well as between paternal IMT and Apo B (Rs=0.692, p<0.05), TG and sICAM-1 (Rs=0.912, p<0.01), TG and sE-selectin (Rs=0.678, p<0.05).
Based on these, authors concluded that serum Lp(a) may serve as a maker of cardiovascular risk in children and adolescents, whereas IMT is not a reliable measure of atherosclerosis in the youngest children.

A few comments:
I would recommend more details of carotid IMT measurements - how many measurements on each side, what is the timing of the measurements, what is the inter-observvariability, etc... I also think that carotid measurements in toddlers are almost impossible. How did the authors achieve this?

Some more details why there were only 18 patients left out of 137. Do the others live far away?

What was the power to detect difference with the 18 patients in the second cohort when so many variables are being tested?

Also it is not clear to me how the authors jumped from the 3 significant differences they observed in Table 5 to LpA being the most useful marker?

Another comment is while describing Table 5, I would refrain from comments such as "the concentrations of XX was greater but did not reach statisitical significance". If it does not reach statistical significance it is not significant. The authors appropriately mention small sample size in the limitations.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.
No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.
Yes
Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.
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