Reviewer's report

Title: A 12-week after-school physical activity programme improves endothelial cell function in overweight and obese children: a randomised controlled study

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Reviewer: Kevin R Short

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General
In response to the prior comments the revised paper is improved. I have some remaining comments and suggestions as noted.

Specific comments

Introduction
The authors wrote: “Furthermore, the study of Le and colleagues found that the carotid artery intima-media thicknesses of obese children were more typical of those of a 45-year-old and these children had high levels of LDL and triacylglycerol and low levels of HDL [1].” The authors should clarify whether they mean that the obese children had cIMT values that were similar to normal healthy adults, or adults with obesity or related metabolic disorders. Please revise this sentence to be more specific.

Methods
The authors wrote: “In addition, our power calculation assumed at least a 70% increase in CD34, CD133, CD34/CD133 and CIMT.” Did the authors really expect to observe a 70% increase in EPCs and cIMT? Those seem like pretty large changes to predict. More importantly, please either explain why you expected cIMT to increase since this was the opposite effect of what was observed and what has been shown in the literature for people who exercise and/or lose weight. Perhaps this was not written as clearly as intended and should be revised.

The authors wrote: “Participants were advised to avoid physical activity for 48 hours and to fast for at least 10 hours prior to sample collection.” This new sentence was added in response to a comment made in the prior review, which is good. However, it would be even better to clarify whether this timing applied to both the beginning and end of the study and for all of the tests besides blood collection. That is, once the child had finished the last supervised exercise session in week 12, how much time passed until each of the outcome tests was performed: cIMT, blood for EPC, and the body composition and treadmill tests? This type of detail is important for exercise intervention studies because it allows the reader to decide whether the changes observed are due to adaptations to training, rather than the residual effect of the last exercise session.
In response to a prior comment from this reviewer the authors stated that the two study groups were matched for the distribution of boys and girls. This clarifying reply appeared in their letter to the reviewers but the details were not added to the Methods. This information should be stated, along with any other stratification approaches that were used to balance the groups at the beginning.

Results

Tables 1 and 2 have duplicate information on the outcome variables and could be combined into a single table. Add the first 3 lines in Table 1 (variables: sex, OW/Ob, age) to Table 2. Age and sex wouldn’t change during the study of course, but since BMI did change, it would be useful to list the number of OW/Ob at both the beginning and the end of the study, and add a comment on whether any children changed BMI categories. For example, in the exercise group did any OW children move into the normal weight BMI as a result of weight loss? Or children in the obese range move into overweight. Another suggestion is to revise the title of Table 2 to be more descriptive and accurate of the results presented. The data shown are pre-post intervention results, rather than “change” values as stated, and there is more than body composition and VO2max as listed in the title. A broader, perhaps more general title as in Table 1 would be better.

It would be a good idea to clarify whether the waist circumference and VO2max showed statistically significant changes within either group. It is unclear whether the significant interaction effect is due only to the opposite direction of changes in the two study groups or whether the exercise group experienced an increase in VO2 and decline in waist size, independent of the control no-exercise group.

Discussion

The authors wrote: “However, we failed to find the relationship between endothelial progenitor cells and carotid intima-media thickness (r = - 0.118, p = 0.329) (Data not shown).” This is an important comment in the discussion because although the rationale for including cIMT measurements should be somewhat obvious, the authors did not explicitly state that their goal was to look for association between changes in cIMT and EPCs. This could have been more clearly stated in the introduction; without providing a rational or statement of purpose about cIMT, non-specialist readers may view the inclusion of cIMT as somewhat secondary. As a technical comment, the actual statistical results should be moved to the Results and interpretation of those results should be within the Discussion. Also, the finding that changes in cIMT and EPCs were not related is interesting but it would also be valuable for the authors to also comment in the Results about whether there was a correlation at baseline between these two variables (i.e., was the beginning value of cIMT correlated with EPC number?).

The authors wrote: “In addition, differences in diet might also be a confounding factor [41].” This comment would be improved if the authors expanded it to state that they did not provide specific dietary advice to the children, teachers or
families (is this correct?) but that unmeasured changes in diet could have contributed to the weight loss in the exercise group. It is possible that because these children had been selected for the intervention that either their own eating behavior or the diet provided and the behavior of their parents or school staff was affected. The literature supports that interventions with exercise-only (without structured nutritional approach for weight loss) typically result in little or no change in body weight or BMI in adults or children over 12 weeks (although body composition can and does change in some studies). Although the change in EPCs reported in the current study is most likely due to the exercise per se, the impact of body fat reduction secondary to dietary changes may also potentially contribute and this should be acknowledged.

Another limitation (or opportunity for future research) that should be stated in the final paragraph of the discussion is that the authors have not examined the separate effects of the aerobic versus resistive exercise. It is unclear whether these overweight children would have the same response if they only did one type of exercise.