Reviewer's report

Title: A Follow-Up Study for Left Ventricular Mass on Chromosome 12p11 Identifies Potential Candidate Genes

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Reviewer: Carlos Pirola

Reviewer's report:

The manuscript of Della-Morte et al about the potential association between LVM and candidate genes located in Chr 12p11 in a particular population of Caribbean Hispanics is on an issue of scientific interest and public Health impact. There are, however, several methodological and design concerns and this are major compulsory revisions.

Genotyping was performed by GW Human SNP 6.0 chip from Affimatrix. As stated by the manufacturer, “the new Affymetrix Genome-Wide Human SNP Array 6.0 features 1.8 million genetic markers, including more than 906,600 single nucleotide polymorphisms (SNPs) and more than 946,000 probes for the detection of copy number variation”. So, this reviewer feels that the total tests performed a priori is much higher than the restricted numbers (7085 or 4334 SNPs used for multiple testing correction and, then, for defining the statistical significance threshold, even admitting that the strategy of using a less conservative approach such as SimpleM is correct) and the authors have made a post-hoc analysis for the region of chr12p11. Taking into account the above consideration there are non significant results to be described.

For the association test, the adjustment for covariates using SBP is not appropriated, because 64% of the subjects are hypertensive and them probably medicated, It seems that no effort has been made for controlling this problem. Even worse, the population has a mean age of 70.8 years meaning that there is a potential bias for studying “survivors”, in particular for a risk factor for CVD. At best, the results of the study are exclusively limited to this particular population subset.

In addition, this reviewer feels that there is not a clear cutoff for the effect of WC on CVD or LVH risk and the effect of WC is, as for other traits, continous. Therefore, it would have more power and be more logical to include WC as a continous covariate in the model, instead of BMI (of course these are two very, but not perfectly, related variables).

Minor Essential Revisions

Finally, it would be important, though not strictly essential, to replicate the findings in an independent sample because the number of the sample is rather modest.

The discussion at light of concerns described above should be more conservative and easily shortened.
Level of interest: An article of limited interest

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests