Reviewer's report

Title: Association between UCP2 polymorphism A55V and risk of cardiovascular events in patients with multi-vessel coronary arterial disease.

Version: 1 Date: 5 March 2012

Reviewer: Gilberto Velho

Reviewer's report:

To authors
Sugaya and co-workers investigated the association of A55V polymorphism of UCP2 with secondary cardiovascular events in a group of subjects with previous coronary artery disease enrolled in a prospective randomized trial that compared different treatments. They report an association of A55V with increased cardiovascular risk in the first 2 years of follow-up in the subset of patients with dysglycaemia, but not in normoglycaemic subjects. No association was observed after 5 years of follow-up.

Comments:
- Major Compulsory Revisions
  1. Methods / Statistical analysis. The authors have not adjusted the threshold of statistical significance to take into account stratification by glycaemic status. This point deserves justification and discussion.

  2. Methods / Statistical analysis. The sample size of this investigation is small for an association study, specially considering the low incidence of cardiovascular events during the follow-up. Authors should present a power calculation.

- Minor Essential Revisions
  3. The introduction section could be more concise. There is too much general information that is not necessarily needed to introduce the present work.

  4. Methods / Data collection. The criteria (and methods) used for classifying the glycaemic status should be given.

  5. Methods / A55V genotyping. This is another section that could be more concise. There is a long paragraph that could be replaced by something much more simple such as "Genotyping was performed with an Array Tape technology (Douglas Scientific, Alexandria MN) (reference or web site)." The manufacturer of the allele-specific PCR assay that was used could be given.

  6. Methods / A55V genotyping. It would be important to present the rational for selecting the A55V polymorphism of UCP2 (as opposed to others that have been reported).

  7. Results. What is the rational for grouping Ala/Ala and the Ala/Val genotypes?
When considering the frequency of cardiovascular events according to genotype, is there any evidence for a dominant Ala effect?

8. Results. Tables 2, 3 and 4 could be combined into a single table. Moreover, those p-values are redundant with those of Cox analysis shown in the text and figures. I would suggest keeping the genotype frequencies and giving the hazard ratios (95% C.I.) and p-values of the Cox regression analyses. Cox is more appropriate than chi-square for incidence studies.

9. Discussion. Authors could include a paragraph with strengths / weaknesses of the study.

10. Discussion. Please discuss clearly the reasons you believe may underline the lack of association after 5 years of follow-up. Is there any experimental evidence that the duration of diabetes plays a role as you suggested? What about mortality related bias?

11. General comment: The manuscript needs a writing revision. There are several awkward and wordy sentences and many typos.

- Discretionary Revisions
12. Methods / Patients selection. One sentence summarising the main results of MASS II would be welcome.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

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

**Declaration of competing interests:**

I declare that I have no competing interests.