Reviewer's report

Title: Relationship between apolipoprotein(a) size polymorphism and coronary heart disease in overweight subjects

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Reviewer: Abayomi Akanji

Reviewer's report:

General

This paper reviews apo(a) polymorphism in groups of normal and over-weight subjects with and without CHD and concludes that the smaller sized phenotypes may be important in ascertaining CHD risk in overweight subjects. The manuscript is not original as many other reports are published on the utility of Lp(a) and apo(a) polymorphism in assessing CHD risk - the subject of Lp(a) has even become less fascinating these days in light of problems with assay comparability. The authors claim novelty in assessing its risk in overweight subjects, but even that is not strictly correct.

There are some important problems in subject categorization:

1. Recent evidence suggests that generalised obesity may not be as important as central obesity in assessing cardiovascular risk. It would have been much more useful to assess the importance of varying WHR and/or waist circumferences in the subjects studied.

2. many would be surprised at the use of the cut-off point of BMI > 27, as indicative of moderate obesity in Caucasians (p 4, ref 22). Obesity is only considered when BMI > 30 conventionally - and 27 would simply be overweight.

3. dyslipidaemia (which is really what should have been addressed especially in the diabetic population rather than simply hypercholesterolaemia) is more than a total cholesterol of >5.2 mM. The authors should probably have considered values for LDL, TG and HDL as well.

4. units for age and BMI should have been indicated in the text (p 4,5)

5. Were all the ‘normal’ control subjects and the overweight without CHD subjected to exercise stress tests to exclude CHD or the diagnosis was excluded only on clinical grounds? The authors were ambiguous on this in the manuscript.

Discretionary Revisions (which the author can choose to ignore)

1. The apo(a) phenotyping technique should have been described in greater detail, moreso as it was developed in the authors’ labs. It is unclear if the results and deductions have been replicated by other workers. And in dividing the apo(a) size polymorphism, reference should have been made to many more previous works where there were at least 5 polymorphs described.

2. A photograph of a typical gel would have helped in the discussion

Minor Compulsory Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1. numerous typographical errors
2. ref 22 cited for cut-off points on obesity is not the gold standard for such categorization
3. ref 23 on classification of DM is old and antiquated - the more recent WHO/ADA classification should have been referred to.
4. the author is at liberty to refer to a similar publication on the same subject: Ann Clin Biochem 2000, 37, 360-66, which comes to different conclusions

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. Tables 1 and 2 are at variance regarding the median and range of values for Lp(a) in the overweight subjects: Table 1: 8 (2.5-19.3) and Table 2: median 12.6/20(2.6-50.3). This would have to be adjusted and also in the text.
2. If there is a preponderance of low m.wt isoforms in overweight CHD patients, and these determine Lp(a) levels, why is there no difference in Lp(a) levels between patients with CHD and controls?
3. Tables 3 and 4 should probably be combined to reduce redundancy
4. table 5: what are the significant predictors in normal weight subjects with CHD and how is the pattern different in the overweight
5. the authors should refer to recent attempts at standardising Lp(a) assays and indicate if their assay controls are referrable to any international standards.

Advice on publication: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: A paper of limited interest

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

Declaration of competing interests:

None