Reviewer's report

**Title:** Serum 25-hydroxyvitamin D levels is associated with carotid atherosclerosis in normotensive and euglycemic Chinese postmenopausal women: The Shanghai Changfeng Study

**Version:** 7  
**Date:** 15 September 2014

**Reviewer:** Marc Blondon

**Reviewer's report:**

Strong points of the manuscript
- Well written manuscript
- Large and contemporary sample of Asian women
- Good definitions for CIMT measures and plaques
- Good definitions and measures of covariates

Major Compulsory Revisions

1. A comparison with the current literature on the topic is missing.

This study builds on multiple previous studies examining the association of 25-OH-D with carotid IMT or plaque, which have been mostly null. Two recent examples, along several other, include Deleskog A (ATVB 2013) and Blondon M (ATVB 2013). The manuscript would be much improved by adding a thorough discussion of differences between the presented positive findings and the overall null results from the literature.

2. Low levels of 25(OH)D

About 75% of subjects in this sample have 25(OH)D levels below 50nmol/L, which has been defined by many, including the Institute of Medicine, as deficient levels (mostly based on Caucasian populations, though). This is even more surprising as the studied sample appears very healthy and non-obese. Further, I anticipated a stronger association between 25(OH)D levels and BMI. Authors should make a convincing point in explaining these somewhat unexpected data.

3. Statistical handling / models

A few points need to be enhanced or revised:
- No information is available about possible missing data.
- If authors want to use analysis of covariance, some assumptions of this method, in particular homoskedasticity, should be tested. I'd personally advise using linear regression with robust standard errors instead of analysis of
covariance for alleviance of such assumptions and to come up with more meaningful results (differences in cIMT per one unit increase in 25(OH)D or doubling of 25(OH)D [if log2-transformed]).

- The potential for residual confounding remains, regardless of the restriction to non-hypertensive and non-diabetic women. Why did the authors not consider socio-economic status and physical activity as possible confounding variables? The rationale to include liver enzymes levels in covariates appears low, on the other hand.

(4) Lack of basic description of cIMT and plaques

It would really help to have complete descriptions of mean cIMT, including some measures of its dispersion, and prevalences of plaques, including their numbers per individual. Do the authors have any data on plaque surface?

(5) Abstract

Please report results from the main analysis. Readers will not be interested about association with 25(OH)D here, but will be interested about inference from the main analysis (25(OH)D with cIMT and with plaque).

Discretionary Revisions

Line 184 – what does the ICC of 95% relate to (plaque, pathological IMT, other)? Given the difficulty in measuring ICC, more data on reliability of the measures of this study would be valuable.

The 25(OH)D assay is not the gold-standard (mass spectrometry). Do the authors believe this may have influenced their results?

The significance of IMT measured in the CCA remains to be clarified. Although many use it as a marker of atherosclerosis, it may be more related to hypertensive remodeling. I have less worries about plaques. Overall, I’d advise to at least use « markers of atherosclerosis » more than « atherosclerosis » throughout the manuscript.

Minor Essential Revisions

Title – « are » instead of « is »

Line 101 - Reference [7] appears to be wrong.

Line 222 – « fourth » instead of « forth »

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

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests.