Reviewer’s report

Title: Association of plasma osteoprotegerin levels with the severity of lower extremity arterial disease in patients with type 2 diabetes

Version: 2
Date: 3 June 2015

Reviewer: Mads Nybo

Reviewer’s report:

This is a study on a potential association between plasma OPG and lower extremity arterial disease in T2DM patients. As described by the authors there are not many studies on peripheral artery disease, and this study, which do find a significant association between plasma OPG and a Doppler investigation, therefore seems relevant. Overall, I therefore find the study interesting and well-described.

Major compulsory revisions:
In the Statistical section it is stated how data is expressed depending on their distribution: How was the distribution tested? This should be stated in the manuscript.
Also, OPG concentrations are throughout the manuscript reported as mean +/- SD. But OPG concentrations almost always have a skewed distribution – which also looks to be the case for these data when looking at Figure 1: Please explain this discrepancy.

Minor essential revisions:
In general, the manuscript is well-written, but there are some language flaws, especially in the Discussion section, which must be re-read.

Background
At the end of the Background section, the authors state that little is known about the association between plasma OPG levels and lower extremity arterial disease. The information may be scarce, but there are a number of studies looking at the association between OPG and peripheral artery disease (PAD) that must be mentioned, namely a review by Hosbond et al (2012), a study by Poulsen et al on T2DM patients (2011) and finally a study by O’Sullivan et al (2010). Please incorporate these in the Background and later in the Discussion when comparing with earlier findings.

Methods
It is stated that the T2DM patients was selected. How was this done?

The authors erroneously use the term Triacylglycerol, where I suppose they should have used Triglycerides (page 6 and Table 3). Please correct this.
Discussion

Line 171: I do not see how the demonstrated association between OPG and the severity of lower arterial extremity stenosis provides an explanation for the increased vascular events in patients with high plasma OPG. As we know nothing certain about the mechanism through which OPG increases the risk (is it just an epiphenomenon?), I find the authors must settle with the potential use of plasma OPG as a biomarker for this condition, not an explanation for any forthcoming events. Please adjust this.

If the Tables are not a part of the manuscript, main numbers must be presented in the text in order to facilitate the reading of the paper.

Discretionary revisions:

In the Methods chapter, section “Determination of lower …” (p. 6), the phrase “Doppler examination can accurately …” should be erased. This is a statement, which does not belong in the method section.

Also, please omit the phrase “We compared the degree of …”, which if necessary can be incorporated in the statistical section. The final sentence belongs to the section regarding the Patients (p. 4). Also, please correct the plurals form used here (histories (history), backgrounds (background), medications (…)).

Results, Baseline characteristics, line 1: … patients with … (not had).

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