Reviewer's report

Title: Low bone mineral density is related to atherosclerosis in postmenopausal women

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Reviewer: Teresa Adragao

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This study is a cross-sectional analysis, performed in a group of 72 post-menopausal women, showing an association between low femoral bone mineral density and carotid IMT. I think that this finding is once again a demonstration of the existence of a link between bone disease and vascular disease and other studies in larger populations have already shown an association between higher IMT and lower BMD. The association of vascular disease (IMT, vascular calcifications, pulse wave velocity) with bone disease has been described in several studies in general population and also in the subgroup population of chronic kidney disease patients. The reason for this association is unknown yet and it is possible that a common mechanism affecting bone and vessel might be the cause for this apparent association. It is however interesting to consider the existence of a possible causal mechanism relating these two entities.

In all these previous studies the results are generally presented in a different direction: the vascular disease is the outcome and the bone disease is the predictor factor. Namely, in the case of chronic kidney disease patients, it is postulated that bone disease prevents the bone to capture calcium. Calcium in association with phosphorus is responsible for stimulating vascular calcification by an active cellular mechanism. The interest of this approach is the possibility of reducing vascular risk by treating bone disease. This remains to be demonstrated.

The authors suggest that bone disease must be looked for in patients with vascular disease but the opposite, in my opinion, is more interesting: to look for occult vascular disease in patients with low bone mineral density. However, this kind of analysis can only show an association between low femoral BMD and CA IMT and any approach is valid if well explained.

In this study, in univariate analysis it could be interesting to compare two groups defined by the diagnostic criteria of femoral osteoporosis; Tscore<-2.5 SD vs. Tscore#-2.5 SD. All the variables presented for the general population should be compared between these two groups. Calcium, phosphorus, Vit D, osteocalcin, PTH levels and urine CTX should be also presented, if available. It should also be interesting to see the distribution of the 4 types of plaques between these two groups. The lack of correlation verified in this study may be the result of the sample dimension but is possible that an association might be verified between
plaques and presence or absence of osteoporosis.

I also suggest trying multivariate analysis in the opposite direction: dependent variable as femoral BMD and lumbar BMD, in a linear regression or diagnosis of osteoporosis (yes, no) in a binary regression. If this kind of approach does not increase the amount of information, the previous approach could be maintained.

In the discussion, the lack of association between lumbar BMD and vascular disease also deserves to be referred to. Previous studies have shown a negative association between lumbar BMD and IMT but this lack of association has also been described in hemodialysis patients.

In summary, the presentation of these results do not constitute a novelty but they are a once again a confirmation of an association that is not fully understood. In my opinion a different direction in the statistical analysis should be tried.

**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