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Reply to: Systematic review and meta-analysis for the association of bone mineral density and osteoporosis/osteopenia with vascular calcification in women

Alexander J. Rodríguez^{1*}, David Scott^{1,2}, Peter Ebeling^{1,2} & B Abrahamsen³

¹Bone and Muscle Health Research Group, Department of Medicine, School of Clinical Sciences at Monash Health, Faculty of Medicine, Nursing and Health Sciences, Monash University, Clayton, Australia

²Melbourne Medical School (Western Campus), Department of Medicine, The University of Melbourne, St Albans, Australia

³Research Centre for Ageing and Osteoporosis, Glostrup Hospital, University of Southern Denmark Copenhagen, Denmark

*Corresponding Author:

Mr Alexander Rodriguez B.MedSc (Hons), M.TransMed

Bone and Muscle Health Research Group, Department of Medicine, School of Clinical Sciences at Monash Health, Faculty of Medicine, Nursing and Health Sciences, Monash University

Monash Medical Centre, 246 Clayton Road,
Clayton, Victoria,
Australia 3168.

Ph: + 61 3 8572 2574 Fax: + 61 3 9594 6437 Email: alexander.rodriquez@monash.edu

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To the Editor,

We read with interest the study by Zhang and Feng on the association between bone mineral density (BMD) and vascular calcification in post-menopausal women [1]. The results of their meta-analysis of four studies (n=1666 vascular calcification cases and n=1190 controls) demonstrated that both hip and spine BMD were significantly lower in women with vascular calcification. Further, in those with vascular calcification, there was an approximate four and a half-fold increased likelihood of having osteoporosis, and an approximate two-fold increased likelihood of having osteopenia.

The authors conclude that patients with vascular calcification “have lower lumbar spine and hip BMD and increased risk for developing osteoporosis or osteopenia”. Whilst it is possible that aspects of increased vascular calcification may contribute to declines in bone density (through common risk factors such as age, smoking, low levels of physical activity and chronic inflammation), this conclusion potentially ignores evidence that vascular calcification can also result from dysregulated bone metabolism in ageing [2-4].

A longitudinal study in postmenopausal women has shown that progression of aortic calcification is greater in those who demonstrate bone loss, compared to those who experience no bone loss [5]. In a Japanese sample of older men and women, ectopic calcium deposition in mitral and aortic valves was related to the severe bone loss attributed to osteoporosis [6]. Furthermore, studies conducted in patients with chronic kidney disease (a condition characterised by bone mineral derangement) demonstrate that vascular calcification is a common feature in this population [7]. Additionally, important catabolic bone metabolites such as phosphate (hyperphosphatemia), calcium (hypercalcemia) and FGF23 are all elevated in chronic kidney disease further suggestive of a role for bone dysregulation [8].

Thus, vascular calcification may well be a consequence of age-related declines in bone density, in addition to the possibility that cardiovascular diseases, including vascular calcification, contribute to bone loss. Other consequences of ageing may also explain the lower BMD of those with vascular calcification, particularly given that the included cross-sectional cohort study by El Maghraoui et al. (which contributed over 50% of participants to the meta-analysis), demonstrated that participants with abdominal aortic calcification were approximately 10 years older than those without calcification [9]. A meta-regression accounting for age was not performed in the article by Zhang and Feng and thus one may speculate that the findings may be confounded by the effects of age.

A previous study (not included in the present meta-analysis) of Japanese-American women has conversely reported no association between BMD and aortic calcification [10], and thus prospective studies investigating associations between bone loss and vascular calcification are needed to clarify the relationship between these conditions. Nevertheless, Zhang and Feng's study highlights the increasing research interest in mechanisms that may lead to both osteoporosis and cardiovascular disease in ageing populations.

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Author/s:

Rodriguez, AJ;Scott, D;Ebeling, P;Abrahamsen, B

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