Identification of vertebral fractures: a moderately severe solution?

E. V. McCloskey^{1,2,3}

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Vertebral fractures, arguably the most common osteoporotic fracture, have long featured at the heart of the diagnosis and treatment of osteoporosis, with many authorities recommending the presence of a spine fracture as an eligibility criterion for intervention or reimbursement [1–3]. The visual and quantitative methods involved in their characterization have achieved much attention over the last 25 years [4–8]. Despite this, and in the face of initiatives by organizations such as the International Osteoporosis Foundation to improve their detection and reporting [9], they frequently remain undiagnosed, with only about one third or even less coming to clinical attention [10]. However, both radiographically detected (incorrectly termed asymptomatic fractures) and clinical vertebral fractures are associated with significant future fracture risk [11], morbidity [12–14] and mortality [15, 16]. Vertebral fracture assessment (VFA), using lateral spine images acquired with a bone densitometer, is increasingly being advocated for clinical use. It has the advantage of being performed alongside DXA measurement of BMD, thus offering greater convenience for the patient and a substantially lower radiation dose than lateral radiographs [17]. VFA classification of vertebra as normal or fractured shows good concordance with lateral radiograph diagnosis [18–22]. This technique therefore facilitates improved detection of vertebral

fracture. A recent article by Cosman and colleagues in *Osteoporosis International* reminds us of some important issues that are at least partially independent of the imaging technique used.

Self-reporting of vertebral fractures is unreliable, in contrast to self-recall of previous hip and forearm fractures [23]. As reported by Cosman and colleagues [24], the majority (80%) of participants in NHANES reporting a previous vertebral fracture was subsequently found to have no fractures on VFA, with the caveat that the upper reaches of the thoracic spine were poorly visualised by VFA. Furthermore, of those with a fracture on VFA, only 8% had a self-reported vertebral fracture. Interestingly, in a study of women aged 75 years and over in the UK, using a similarly stringent definition of fracture and VFA imaging, we found a prevalence of 14.5%, not dissimilar to that reported by Cosman and colleagues in the USA. In the UK study, only 1.1% of the UK women had a self-reported vertebral fracture, and over half (58%) of these had a fracture confirmed on VFA. In contrast, the prevalence of vertebral fracture in those reporting no history of vertebral fracture was 14%; i.e., the yield in terms of total fractures is greatest when the whole population is imaged, at least at older ages.

Algorithms to target imaging of the spine to individuals deemed to have characteristics associated with their presence have been proposed [25, 26]. For example, height loss, history of back pain, low BMD, past non-vertebral fracture and older age have been identified in various studies. The association of height loss and back pain is greater in those with underlying multiple vertebral fractures, but they perform poorly in identifying individuals with a single vertebral fracture. While the application of criteria such as that from NOF and ISCD does identify a fracture-enriched population, as seen in the study by Cosman and colleagues, sensitivity remains relatively low, particularly in relatively young population samples as seen

✉ E. V. McCloskey
e.v.mccloskey@sheffield.ac.uk

¹ Mellanby Centre for Bone Research, University of Sheffield, Sheffield, UK

² Centre for Integrated research in Musculoskeletal Ageing (CIMA), Mellanby Centre for Bone Research, University of Sheffield, Sheffield, UK

³ Metabolic Bone Centre, Northern General Hospital, S5 7AU, Sheffield, UK

in NHANES (mean age 65 years). Indeed, some have proposed the use of VFA in older age groups regardless of the presence of specific vertebral fracture predictive factors [27], and this can certainly be actioned in clinical referral populations as opposed to population screening [28]. To my knowledge, only one randomised controlled study of screening for vertebral fractures has been published to date, with encouraging results, and more studies are needed [29].

Finally, and perhaps the most important reminder provided by Cosman et al.'s study relates to the classification of the severity or grade of the prevalent vertebral fracture. The technique used in the Cosman study [24], and probably one of the most widely used in epidemiological studies and clinical trials, is the semi-quantitative method of Genant [4]. As stated in the paper, this method examines the vertebrae not just for height loss but additional features including end-plate deformity and buckling of cortices to discriminate from non-fracture vertebral deformities. Such subtleties may be difficult to detect on VFA imaging and, indeed, even on traditional radiographs, and this is particularly true in the setting of grade 1 or mild vertebral fractures. In expert hands such fractures can be identified, but even when images are evaluated by those trained in the technique, there is a significant false positive rate largely due to confusion with non-fracture deformities such as short vertebral height [30, 31]. Indeed, this was observed in the Cosman study, where one third of those identified as having a fracture were subsequently reclassified as non-fractured; importantly, these mis-called events were reported to be mostly mild wedge deformities [24]. There is good evidence that such fractures are not always associated with low BMD or future non-vertebral fracture risk, unlike moderate (grade 2) or severe (grade 3) vertebral fractures [30, 32]. Further evidence suggests that short vertebral height, a common reason for non-expert definition of mild vertebral fractures, shows little relationship with age [33]. Interestingly, even in the study by Cosman and colleagues [24], the prevalence of such fractures only increased from 1.7% in women aged 40–64 years to 4.2% in those aged over 80 years, with overlapping confidence intervals. This 2.5-fold increase contrasts with the 12.4-fold increase in moderate or severe vertebral fractures over the same age intervals. Importantly, these mild fractures comprised 61% of the total vertebral fractures at the younger ages in women. That these mild or grade 1 vertebral fractures are frequently contaminated by non-fracture deformities is even more likely in daily clinical practice of clinicians or general radiologists and may lead to significant over-investigation and unnecessary treatment. The latter is contrasted with the known under-diagnosis and treatment of patients with existing moderate and severe vertebral fractures [34]. Near-term future strategies should probably focus on identifying those men and women with un-diagnosed moderate or severe vertebral fractures; such approaches might lend themselves more easily to automated or semi-automated

detection of vertebral fractures on VFA, radiographs and other imaging modalities, such as CT and MRI.

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