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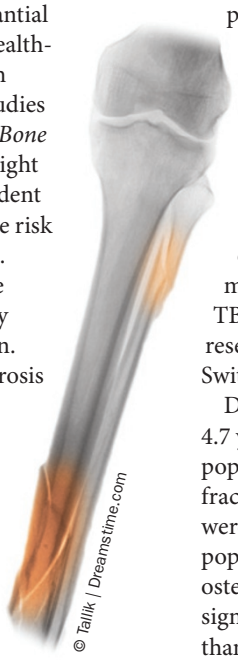
BONE

Fracture risk prediction—beyond BMD assessment

The search for easy-to-use, cost-effective strategies to predict the risk of fracture associated with osteoporosis has been the focus of much attention, fuelled by concerns about the increasing number of people with osteoporosis and the substantial morbidity, mortality and health-care burden associated with this condition. Two new studies published in the *Journal of Bone and Mineral Research* highlight the value of BMD-independent strategies to predict fracture risk in postmenopausal women.



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BMD is calculated on the basis of a dual-energy X-ray absorptiometry (DXA) scan. The WHO defines osteoporosis as a BMD 2.5 SD below the average BMD of a young adult healthy population. "In many countries, patients have access to antiosteoporotic drug prescription and/or reimbursement only if they fall within the 'operational' WHO definition of osteoporosis," comments Jean-Yves Reginster, from the University of Liège, Belgium, who was not involved in the two studies. However, "whereas this definition is practical and easy to use for prescribing physicians, many patients who experience spinal or peripheral fracture do not meet these criteria". Therefore, several approaches have been and continue to be developed to predict fracture risk beyond calculation of BMD.

Bone strength is influenced by a variety of factors in addition to BMD, including the microarchitecture of the trabecular bone. Some methods for assessing bone microarchitecture, such as quantitative CT and MRI, are costly and time-consuming. In the first study, Didier Hans and colleagues tested a method for trabecular bone evaluation that does not require the patient to undergo multiple tests and that can be applied retrospectively to a previously performed DXA exam. The researchers calculated a 'trabecular bone score' (TBS) and assessed whether it could be used to predict fractures independent of BMD in a cohort of 29,407 postmenopausal women aged ≥50 years (mean age 65.4 years) who were registered in the public health-care system of the Province of Manitoba, Canada, and in whom DXA testing had been performed. Health registry data were used to collect information about the occurrence of nontraumatic osteoporotic fractures after BMD measurement. The calculation of spine TBS was done in a blinded fashion by researchers at the University of Lausanne, Switzerland, on the basis of DXA images.

During the follow-up period (mean 4.7 years), 1,668 women (5.7% of the population) had a major osteoporotic fracture; 439 of these were spinal and 293 were hip fractures (1.5% and 1.0% of the population, respectively). Women with osteoporotic, spinal and hip fractures had significantly lower spine TBS and BMD than women with no fractures. A model that combined TBS and BMD assessment significantly improved fracture prediction compared with either TBS or BMD assessment alone.

"The interest of this technology is that it does not need any additional measurement or radiation exposure, TBS being calculated directly on the BMD measurement printout or screen," comments Reginster. "If confirmed in other studies, this new technology might significantly improve the assessment of fracture risk in one single individual. This is the first time that a noninvasive measurement provides information on bone microarchitecture in a way that is cheap, fast and harmless for the patient."

In the second study, Philip Sambrook and colleagues compared several fracture prediction models, including the WHO Fraction Risk Assessment Tool (FRAX®), the Garvan Fracture Risk Calculator (FRC) and a model based on age and fracture history alone, in an international cohort of 19,586 women aged ≥60 years who were enrolled in the GLOW study and who were not receiving antiosteoporotic medication. All data collected were self-reported; BMD data were not considered. During the 2 years of follow-up, 880 women reported the occurrence of fractures, including 69 hip fractures, 468 major fractures as defined by the FRAX® model and 583 osteoporotic fractures as defined by the FRC model.

The researchers observed that FRAX® and FRC were not superior to the model based on age plus fracture history alone in predicting fracture risk. Therefore, the researchers suggest that, in the absence of BMD data, the consideration of clinical factors in addition to age and fracture history does not substantially alter fracture risk prediction. They also propose that clinical factors alone can be used to predict the absolute risk of fracture in primary care populations, without BMD.

Reginster finds these results interesting, but points out that they are probably biased by the short duration of the trial (a limitation acknowledged by the authors). "The main objective of FRAX® is to predict the 10-year fracture risk in an untreated population; FRAX® was not designed to calculate short-term fracture risk," says Reginster, who stresses the value of FRAX® as a tool to identify patients who should receive treatment as well as those who should not. "From a cost-conscious perspective, the identification of the patients who really deserve to be treated appears to be a social, economic and ethical priority."

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Original articles Hans, D. *et al.* Bone micro-architecture assessed by TBS predicts osteoporotic fractures independent of bone density: the Manitoba study. *J. Bone Miner. Res.* doi:10.1002/jbmr.499 | Sambrook, P. N. *et al.* Predicting fractures in an international cohort using risk factor algorithms, without bone mineral density. *J. Bone Miner. Res.* doi:10.1002/jbmr.503