COMMENTARIES

The Importance of Calculating Absolute Rather Than Relative Fracture Risk

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Commentary on: Tucker G, Metcalfe A, Pearce C, Need AG, Dick IM, Prince RL, Nordin BE. The importance of calculating absolute rather than relative fracture risk. *Bone*. 2007 Dec;41(6):937-41.

Until recently, current guidelines make recommendations for the management of postmenopausal women based on the T score. The rationale of this advice is the relationship between the decrease in bone mineral density (BMD) and the increase in fracture risk. The relative risks of fractures have been calculated in prospective studies for each standard deviation (*i.e.*, T score unit) decrease in spine and/or hip BMD. The paper by Tucker *et al*. challenges the relevance of this "relative risk" dogma in the management of patients (1).

The rationale of the paper is the difference between a relative risk (odds ratio), derived from logistic regressions, and absolute risk, calculated from the actual proportion of cases with fractures in a given cohort. The practice assumes that risk increases multiplicatively with each unit fall in bone density. Consider a patient with T = - 3 at the femoral neck. Prospective data have shown that the relative risk of hip fracture, for a decrease of 1 SD at the same site, is 2.6. Thus the risk for this patient is $2.6^3 = 17.5$ times higher than the risk of a patient with normal BMD. Absolute risk (calculated as odds/(1 + odds)) lies between 0 and 1 and cannot do so. For the authors, a multiplicative relation of fracture risk to BMD is acceptable for low risk, but not for moderate/high risk. This observation is in line with the estimation of Kanis *et al*. (2) showing that absolute risk increases linearly with RR in young women (*i.e*., multiplicatively), but slower than RR in older women.

The authors studied a cohort of 1098 women, 75 years old on average, who completed a 6-year follow-up. They were receiving either calcium or placebo, but results were analyzed for the entire cohort as the effect of calcium was not significant in the ITT analysis. Baseline hip T score was – 1.07 (-4.15, 2.77), 27.6% of patients had a prevalent fracture, and 18.1% an incident one. Results of logistic regression showed that, at zero BMD SD, the calculated fracture odds was 0.208 (constant of the logistic regression of incident fracture on negative hip BMD SDs and T scores), with a fracture probability of 0.172 (17.2%, close to the observed 18.1%). The calculations based on T scores showed that the odds rose from 0.055 to 0.732, and the absolute risk from 0.052 to 0.4223 at T = + 2 and T = - 4, respectively, so following 2 divergent lines at T score below 0. Multiple logistic regression yielded significant odds ratios of 1.47 for each 5-year increase in age and for prevalent fracture, and 1.49 for each unit fall in hip T score. The main conclusion of the paper is that odds and risk are similar at very low risk, but in other situations, risk does not rise multiplicatively. Thus multipliers of risk tend to overstate the effect of continuous variables such as age and T score.

The authors' conclusion is that absolute risks, rather than relative risks, are closer to the reality and of more value to clinicians. Indeed, in the same paper, Tucker *et al*. provide a nomogram showing the probability of fracture over 6 years as a function of hip T score for postmenopausal women without fracture. This is exactly in line with the recommended use of the WHO fracture

prediction algorithm to determine the patient's absolute, as opposed to relative, fracture risk.

Beyond the wording, these concepts represent a considerable change for physicians, and economists as well, providing appropriate interpretation and use of these data (3). First of all, the use of risk does not change the definition of osteoporosis based on T < -2.5, just as the use of Framingham data to estimate the risk of stroke did not change the definition of hypertension. This definition was an important clarification, and is still relevant. However, BMD is measured not only to provide a diagnosis, but also to give information on fracture risk. Clinical risk factors for fractures improve the sensitivity of BMD measurement and fracture risk is different for a given T score depending on age and additional risk factors. This is the rationale for the development of the fracture risk assessment tool (FRAX^{TM}) recently published that gives on an individual basis the probability of fracture (4). We have now a better basis to provide advice and share decisions with patients at risk for fracture. It is very reassuring to observe that absolute fracture risk reporting is well-received by physicians, and is strongly preferred to traditional T score-based reporting (5).

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References

1. Tucker G, Metcalfe A, Pearce C, Need AG, Dick IM, Prince RL, Nordin BE. The importance of calculating absolute rather than relative fracture risk. *Bone*. 2007 Dec;41(6):937-41.

2. Kanis JA, Johnell O, Oden A, De Laet C, Oglesby A, Jönsson B. Intervention thresholds for osteoporosis. *Bone*. 2002 Jul;31(1):26-31.

3. Dawson-Hughes B, Tosteson AN, Melton LJ 3rd, Baim S, Favus MJ, Khosla S, Lindsay RL; National Osteoporosis Foundation Guide Committee. Implications of absolute fracture risk assessment for osteoporosis practice guidelines in the USA. *Osteoporos Int*. 2008 Apr;19(4): 449-58.

4. Kanis JA, Johnell O, Odel A, Johansson H, McCloskey E. FRAX and the assessment of fracture probability in men and women from the UK. *Osteoporos Int*. 2008 Apr;19(4):385-97.

5. Leslie WD; Manitoba Bone Density Program Committee. Absolute fracture risk reporting in clinical practice: a physician-centered-survey. *Osteoporos Int*. 2008 Apr;19(4):459-63.