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Questions Regarding Conclusions Reached in "Age Dependence of Femoral Strength in White Women and Men"

Jonathan J Kaufman

Department of Orthopedics, Mount Sinai School of Medicine and CyberLogic, Inc., New York, NY, USA

To the Editor:

The paper by Keaveny and colleagues[1] entitled, "Age-Dependence of Femoral Strength in White Women and Men," provides interesting data and analysis related to the use of biomechanical computed tomography (BCT) for estimating femoral strength (FS). In the BCT technique, quantitative CT scans are used at a given anatomic site (in this article at the proximal femur) in conjunction with sophisticated computational techniques (finite-element analyses) to estimate the biomechanical properties associated with the femur. Based on the data and analysis described in the article, Keaveny and colleagues present two main conclusions. The first is that age-related declines in femoral strength are much greater than suggested by age-related declines in femoral neck areal bone mineral density (aBMD). The second is that far more of the elderly may be at high risk of hip fracture because of low femoral strength than previously assumed based on the traditional classification of osteoporosis (ie, T-score < -2.5). Implicit in these conclusions is that BCT is superior to aBMD in terms of identifying individuals at increased risk of fracture. In the following it will be shown that the first conclusion does not adequately explain the data and that the second is a useful observation but can be incorporated into standard aBMD analyses.

Regarding the first conclusion, the data demonstrate that age-related declines in femoral strength (as estimated by BCT) are much larger than age-related declines in femoral neck aBMD. For example, in women, the decline in femoral strength over five decades of life was 55%, whereas the decline in aBMD was only 26%. The implication is that femoral strength, as estimated by BCT, would be a much better quantity to estimate fracture risk than aBMD. However, the percent decline of a parameter is not necessarily relevant in terms of its potential utility as a proxy for fracture risk. To see this, it is useful to plot femoral strength versus aBMD (Fig. 1)[1]. As may be seen, there is a strong linear relationship between femoral strength and aBMD, with R^2 values equal to 0.98 for women and 0.96 for men. In addition, the equation relating FS to aBMD is $FS = \alpha \times aBMD - \beta$, with $\alpha = 10{,}530$ and $\beta = 5680$ for women and with $\alpha = 8956$ and $\beta = 4326$ for men. While it is true that percentage changes in aBMD over a period of time are less than the percentage changes in FS over the same time period, the relevant comparison is to examine the relative change in femoral strength that results from a relative change in aBMD. This can be computed according to the following formula:

$$\frac{\Delta FS}{FS} = \left(\frac{1}{1 - \frac{\beta}{\alpha \times aBMD}}\right)\frac{\Delta aBMD}{aBMD}$$

In this formula, ΔFS and ΔaBMD are the absolute changes in FS and aBMD, respectively, whereas the term in parentheses is a sensitivity coefficient relating the relative change in aBMD to the relative change in FS. Figure 2 displays the sensitivity coefficients for men and women over the range of mean aBMD values from Keaveny and colleagues. As may be seen, the sensitivity coefficients ranges from a low of about 1.8 (at the highest value of aBMD for men) to a high of about 3.6 (at the lowest value of aBMD for women). This latter result means, for example, that for a woman having an aBMD of 0.75 g/cm^2, a change in aBMD of 1% will lead to a change in FS of about 3.6 times more, or 3.6%.

This analysis has demonstrated two key points: First and perhaps foremost is the fact that aBMD of the femoral neck is an excellent proxy for femoral strength, at least as estimated by BCT. This was shown by the exceptionally high R^2 values between FS and aBMD (Fig. 1). The second point is that a sensitivity analysis shows that small changes in aBMD are magnified by about 2 to 3.5 times in terms of their effect on femoral strength. The fact that relative changes in FS are larger (by about a factor of 2) than relative changes in aBMD is of little consequence.[2]

The second conclusion of Keaveny and colleagues was that a standard T-score-based diagnosis of osteoporosis would miss a

Address correspondence to: Jonathan J Kaufman, PhD, CyberLogic, Inc., 611 Broadway, Suite 707, New York, NY 10012, USA. E-mail: jjkaufman@cyberlogic.org

[1]The data values in Fig. 1 were estimated from the graphs in Fig. 2 in the paper by Keaveny et al.[1]

[2]This analysis does not address the issue of precision, but given the high levels of performance of present-day densitometers, this would not be expected to affect the fundamental results.

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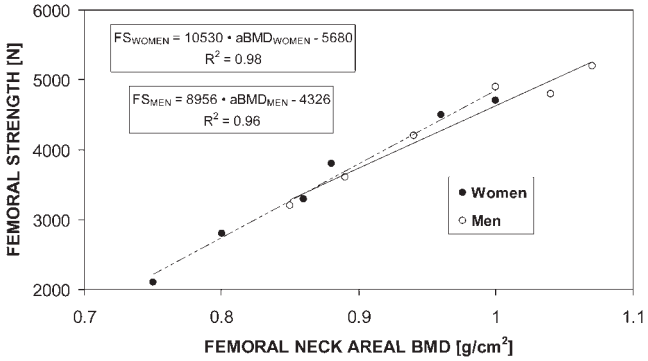

Fig. 1. Femoral strength versus femoral neck aBMD for women and men.

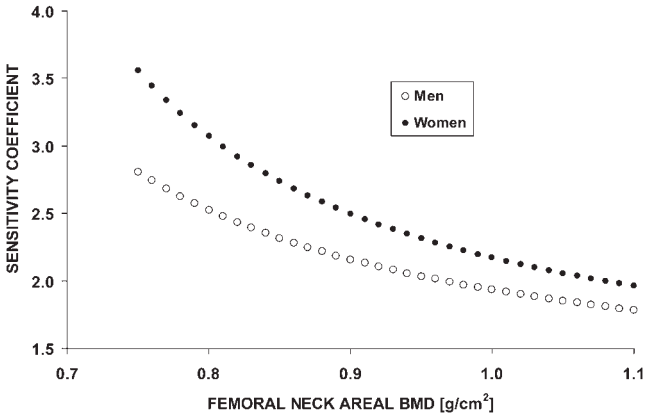

Fig. 2. Sensitivity coefficients for relative change in femoral strength owing to a relative change in femoral neck areal BMD.

large number of individuals who were identified by BCT as being at high risk of fracture. In particular, Keaveny and colleagues defined a cutoff for femoral strength of 3000 N; that is, any individuals with a BCT-determined FS of less than 3000 N are classified as "osteoporotic." The *T*-score-based classification (*T*-score < -2.5) led to a much lower prevalence of osteoporosis compared with the FS-based classification (FS < 3000 N). For example, for women older than 80 years of age, the prevalence of osteoporosis based on *T*-score was about 28%, whereas that based on FS was about 89%. However, this discrepancy is artificial because it is based on the largely arbitrary cutoff of 3000 N for FS. By increasing the *T*-score cutoff or, equivalently, by lowering the FS cutoff, the prevalence of osteoporosis will become about the same. For example, using the relationship for women FS $= 10{,}530 \times$ aBMD $- 5680$ (Fig. 1), it can be shown that the prevalence of osteoporosis can be made essentially identical by retaining the 3000 N cutoff for FS and increasing the *T*-score cutoff to -2.1 for women; for men, the *T*-score cutoff would have to be increased to -1.3.

In conclusion, the implication that BCT provides superior information on bone strength and fracture risk at the proximal femur as that provided by aBMD is questionable at least based on the data provided in the article by Keaveny and colleagues. Smaller percentage reductions in aBMD over time compared with the larger percentage reductions in BCT-determined femoral strength are simply indicative of the specific affine relationships that exist between aBMD and FS. Finally, the demonstration that the standard *T*-score cutoff of -2.5 appears to miss individuals at substantial risk of fracture is in agreement with the present trend toward risk-based assessments.[2,3]

Reference

1. Keaveny TM, Kopperdahl DL, Melton LJ III, et al. Age-dependence of femoral strength in white women and men. J Bone Miner Res. 2010;25:994–1001.
2. Kanis JA, McCloskey EV, Johansson H, Oden A, Ström O, Borgström F. Development and use of FRAX in osteoporosis. Osteoporos Int. 2010;21:S407–413.
3. Schechner Z, Luo G, Kaufman JJ, Siffert RS. A poisson process model for hip fracture risk. Med Biol Eng Comput. 2010;48:799–810.