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Mechanobiology of femoral neck structure during adolescence

M.C.H. van der Meulen, PhD; M. Moro, MS; B.J. Kiratli, PhD; R. Marcus, MD; L.K. Bachrach, MD
Sibley School of Mechanical and Aerospace Engineering, Cornell University, Ithaca, NY 14850 and Biomedical Mechanics and Biomolecular Design, Hospital for Special Surgery, New York, NY 10021; Agilent Technologies, Andover, MA 01810; Spinal Cord Injury Center and Geriatric Research, Education and Clinical Center, Department of Veterans Affairs, Palo Alto, CA 94304; Departments of Medicine and Pediatrics, School of Medicine, Stanford University, Stanford, CA 94305.

Abstract—Understanding femoral neck structure may be critical to preventing fractures at this site. We examined the correlates of changes in the femoral neck during adolescence. Dual energy x-ray absorptiometry measurements of proximal femora were made in 101 Caucasian youths (ages 9 to 26 years). Relationships were examined between developmental parameters (age, pubertal stage, height, body mass, lean mass, and fat mass) and femoral structure (bone mineral content, bone mineral density, neck width, cross-sectional area, and cross-sectional strength). Lean body mass was the best predictor of femoral neck structure, explaining 53–87 percent of the variance, and was independent of gender. Body mass only explained 51–79 percent of the variance. Previously we found body mass to be the strongest predictor of femoral mid-diaphyseal cross-sectional properties. These findings suggest that trabecular bone of the femoral neck may be more responsive to its mechanical environment than the cortical diaphysis. In addition, lean body mass may be a more reliable predictor of muscle loading than body mass.

Key words: *adolescence, body mass, bone mineral content, DXA, femoral neck, mechanical loading.*

INTRODUCTION

Hip fractures are a common manifestation of osteoporosis, occurring in a large portion of the elderly population (1,2). Currently, hip fracture risk is predicted by comparing areal bone mineral density (BMD) measured by dual energy x-ray absorptiometry (DXA) to reference values (3,4). However, the ability of the hip to bear functional loads is determined not only by the bone mass represented by BMD, but also by material quality and distribution. Because BMD only partially discriminates individuals who will or will not fracture (5), we need to understand the geometry of the hip and how this structure contributes to the ability to withstand loading (6–8). The adult skeletal form is the product of an exquisite growth and development process, so understanding the development of femoral neck structure will provide insights into adult pathologies and treatments. During

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Dr. van der Meulen is affiliated with Cornell and HSS; Ms Moro works for Agilent Technologies; Dr. Kiratli is affiliated with the VA Palo Alto Health Care System; Dr. Marcus with Stanford and the VA Palo Alto Health Care System; and Dr. Bachrach with Stanford.

Address all correspondence and requests for reprints to: Marjolein C.H. van der Meulen, PhD, Sibley School of Mechanical and Aerospace Engineering, Cornell University, 219 Upson Hall, Ithaca, NY 14853; email: mcv3@cornell.edu

skeletal growth and development, adolescence is a critical period of bone mineral acquisition and much remains to be understood regarding the factors controlling these skeletal processes.

We previously examined the relationships between femoral mid-diaphyseal structure and developmental parameters during adolescence (9,10). We hypothesized that the appositional growth of the long bones, which produces the cross-sectional morphology, is strongly driven by mechanical stimuli (11). For a group of adolescents, mid-diaphyseal linear bone mineral content (BMC) and femoral width were obtained directly from DXA scans. Using the method of Martin and Burr (12), femoral cross-sectional and structural properties, including cortical cross-sectional area, polar moment of inertia, and section modulus, were calculated from the bone mineral properties. Of age, pubertal stage, body mass, and height, body mass was shown to be the strongest predictor of femoral cross-sectional properties, and the relationship was independent of gender and ethnicity. We concluded that body mass was the strongest predictor of femoral cross-sectional properties, supporting our hypothesis regarding the importance of mechanical stimuli.

While our results in the femoral diaphysis were significant and conclusive, few clinical problems arise at this skeletal site. In contrast, the structure and strength of the femoral neck is of great interest clinically, particularly because age-related changes in femoral neck structure have been suggested as a cause for hip fractures (13). Both developmentally and structurally, the femoral neck and diaphysis have several important differences. While the diaphysis consists entirely of cortical bone, the femoral neck contains approximately 75 percent cancellous bone surrounded by a cortical shell. These morphologies arise by two different developmental processes: the cortical bone of the diaphysis is formed by direct bone apposition while the cancellous bone of the epiphyses is formed by endochondral ossification of the cartilaginous growth plate. The dense cortical bone in the shaft primarily provides structural support while the epiphyseal cancellous bone also serves a critical metabolic function. In the spine, for example, different developmental factors influence the density of the cortical and cancellous envelopes, and mechanical influences have been suggested to play a lesser role in cancellous bone density than hormonal factors (14). Therefore, the factors influencing midfemoral bone structure might not apply to the femoral neck.

In this study, we asked the following research question: what factors control skeletal changes in the femoral neck during adolescence? Applying a similar approach to that used for the femoral diaphysis, we examined the geometry and structure of the femoral neck in the same adolescent and young adult population studied previously. The relationships between developmental determinants and femoral neck structure were investigated. Based on our femoral diaphysis results, we hypothesized that the development of femoral neck structure would be strongly related to increases in mechanical loading and, therefore, would correlate strongly with body mass.

METHODS

Experimental Subjects and Physical Characteristics

One hundred and one healthy Caucasian subjects ranging in age from 9 to 26 years (48 males and 53 females) were recruited from the Stanford University community. The details of the subject recruitment, femoral neck bone mass, and hip axis length are presented elsewhere (15,16). Subjects included in this analysis were limited to individuals whose parents were both of Caucasian background. Telephone interviews were performed to exclude subjects with a history of systemic disease or medication known to affect bone mineralization, including amenorrhea. Height and body mass were measured for each subject.

Pubertal stage was determined using a self-assessment questionnaire based upon Tanner classifications of pubertal development (17). Radiologic examination of skeletal maturity could not be ethically justified in this population of young individuals. Females were given drawings and written descriptions of the five stages of breast and pubic hair development and were asked to select the drawings that most accurately reflected their own stage of development. Males ranked their own pubertal stage in a similar manner, using photographs of genital and pubic hair development. This self-assessment method has been shown to correlate well with pubertal staging as determined by a physician examination (18). The values for breast/genital and pubic hair Tanner Stages were added and a combined Tanner Score ranging from 2 to 10 was determined. Each subject was sorted into one of three categories: early puberty (combined Tanner Score 2–5), midpuberty (combined Tanner Score 6–8), and mature (combined Tanner Score 9–10).

The influence of diet, particularly calcium, was accounted for by estimating dietary calcium intake normalized by total caloric consumption (calcium/energy) (see detailed methodology in 15). The subjects' daily activities were expressed as the average number of hours of weightbearing activity per week. Activities generating at least one body weight were included (15). The study protocol was approved by the Stanford University Institutional Review Board. Written consent was obtained from each subject and from a parent of minors.

Femoral Analyses

The BMC of the left proximal femur and the whole body was measured by DXA (Hologic QDR 1000/W; Hologic, Waltham, MA). Whole body DXA scans were used to determine lean mass (LM, kg) and fat mass (FM, kg). Femoral neck linear BMC (g), BMD (g/cm^2), and hip axis length (HAL, cm) were obtained directly from the proximal femur scans using standard scanner software. The scan protocol and HAL determination are described elsewhere (16).

The areal properties of a single central scan line in the femoral neck region were obtained using the approach of Martin and Burr and implemented as follows (12,19). The attenuation plot was output for a single scan line from the femoral neck subregion (**Figure 1**). The attenuation values were divided by the density of cortical bone (1.85 g/cm^3) to obtain the beam path lengths along the scan line. From this data, the femoral neck bone width was determined directly (W, cm), and the area (A, cm^2) and moments of inertia (I, cm^4) were obtained by integrating the area underneath the x-ray absorption curve. The section modulus, (Z, cm^3) a geometry-based indicator representing the strength of a cross section, was calculated from the moment of inertia divided by half the bone width (2I/W). Finally, an index of neck strength was formulated based on the bone strength index proposed by Selker and Carter (20) by dividing the section modulus by the HAL (Z/HAL, cm^2). This value is representative of the bending force required to fracture the neck; therefore, a longer HAL or a lower section modulus would reduce Z/HAL, indicating a lower strength. Clinical studies have demonstrated an association between longer HAL and femoral neck fracture risk (21).

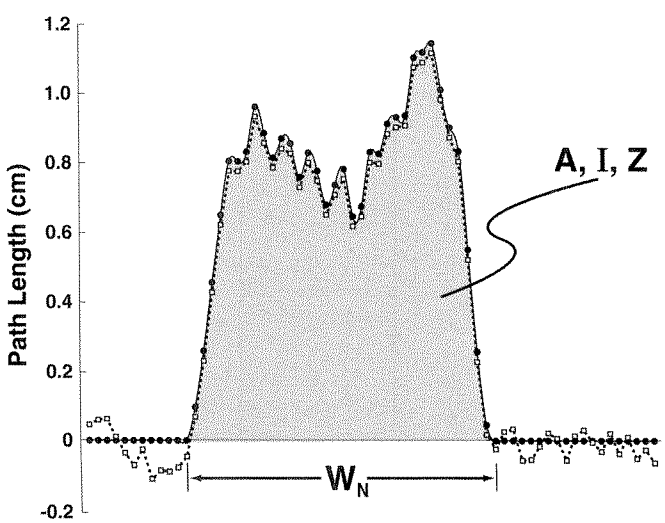

Figure 1.
Femoral neck DXA scan line data for raw unprocessed scan (dashed line, open square data points) and adjusted splined scan with bone data points only (solid line, solid circle data points). Shaded region is bone area, bone width (W) as indicated.

Statistical Analysis

All data were analyzed using StatView and SuperANOVA (Abacus Concepts, Berkeley, CA). First mean values were determined for BMD, W, A, I, and Z. The effect of gender was determined for each pubertal group by an analysis of variance. When the ANOVA was significant, the Fisher PLSD post-hoc was used to compare groups.

Regression analyses were performed to examine the influence on femoral neck development of age, pubertal stage, height, body mass, lean mass, and fat mass. Simple linear regressions were performed between these developmental parameters and each femoral neck structural measurement: BMC, BMD, W, A, I, and Z. Multiple regressions were performed for each developmental parameter including gender as a factor. Finally, a saturated model including age, pubertal stage, height, body mass, lean mass, and gender was examined. The different regression models were compared for predictive power based on the amount of data variance each explained (indicated by the coefficient of determination).

Correlations were examined among related femoral neck parameters. Significance was determined by Fisher's r to z test. For all tests, differences were considered statistically significant if $p<0.05$.

RESULTS

During development there were no gender differences in age, body mass, or height until maturity, as reported previously (9). At maturity the males were significantly taller and heavier than the females. Lean mass and lean mass/body mass showed no difference at early puberty but were significantly greater at midpuberty and maturity in males than in females. Fat mass only showed significant differences at midpuberty; midpubertal females had significantly more fat mass, but this difference disappeared at maturity.

All femoral neck measurements demonstrated significant increases with age and pubertal stage. In the males, there were very significant increases in all parameters both between early puberty and midpuberty ($p<0.001$) and between midpuberty and maturity ($p<0.01$; see **Figure 2**). In the females, however, significant increases were only present from early puberty to midpuberty; none of the changes from midpuberty to maturity were significant. At early puberty, there were no significant gender differences. Consistent with the taller stature and larger body size of mature males, the mature male values were significantly greater than those of the females for all femoral neck measurements ($p<0.0005$) and the midpuberty male values were significantly greater than the female for BMC, A, I, and Z. A similar pattern was observed previously for HAL, which increased significantly between each stage in males, but only from early to midpuberty in females; males had significantly greater HAL at maturity (16).

All simple linear regressions of the femoral neck measurements on the developmental parameters were significant. Lean body mass had the strongest relationships with all femoral neck measurements, explaining 53–87 percent of the variance in the parameters (**Table 1, Figure 3**). Body mass and height showed moderate relationships, explaining 51–79 percent and 42–77 percent, respectively. Body mass explained more variance (2–9 percent more) than height for all measurements except femoral neck width. Pubertal group explained 27–46 percent of the data variance, and age explained 22–34 percent. Fat mass showed the weakest relationships, explaining only 4–14 percent of the variance in the data. For the regressions on age, height, body mass, and lean mass, section modulus showed the strongest relationship of the six parameters investigated.

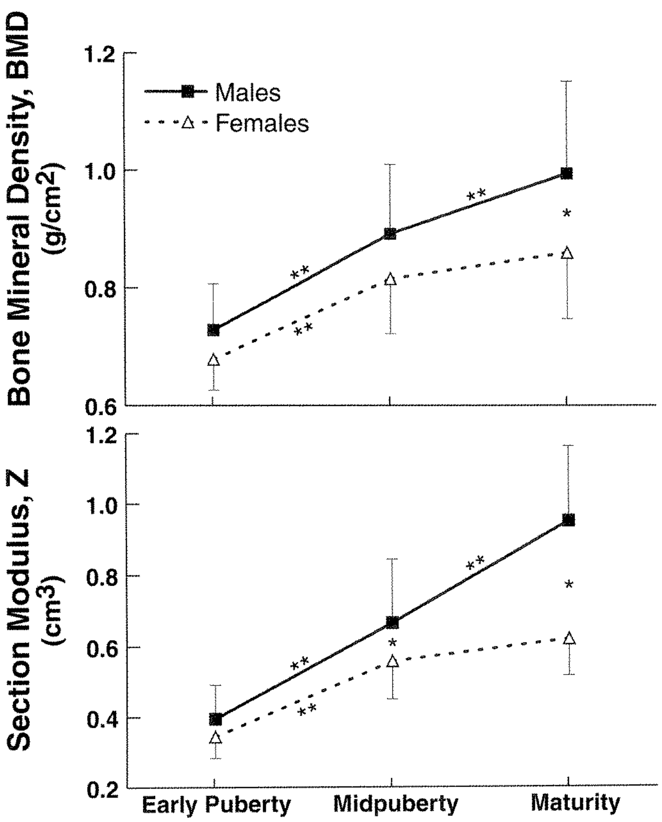

Figure 2.
Comparison of mean (SD) BMD and section modulus values for the femoral neck by pubertal stage between males and females. * indicates significant difference between genders at a given stage; ** indicates significant difference between pubertal stages for a given gender.

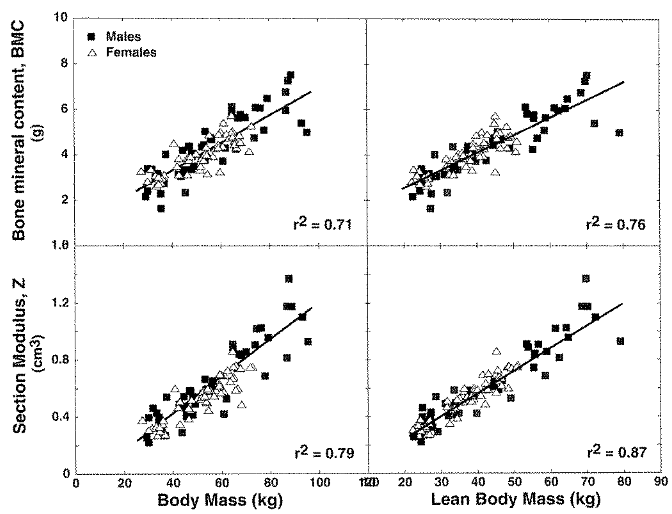

Figure 3.
Relationships between BMC (top) and section modulus (bottom) and body mass (left) and lean body mass (right). All regressions are significant and independent of gender.

The regressions on the environmental factors (calcium intake and weightbearing activity) had very poor explanatory power. Calcium intake was significantly related to W, I, and Z, but only explained 2–3 percent of the variance in these parameters. Our measure of weightbearing activity had no significant relationship with any femoral neck measures.

When gender was included in the regressions, lean body mass still had the strongest relationships with the

Table 1.
Coefficients of determination (adjusted r^2) for simple linear regressions of femoral neck measures on developmental parameters. Bold indicates strongest relationships. All regressions are significant.

Measure	Age	PG	Height	BM	LM	FM
BMC	0.26	0.46	0.66	0.71	**0.76**	0.13
BMD	0.25	0.33	0.42	0.51	**0.53**	0.11
W	0.22	0.27	0.60	0.56	**0.63**	0.04
A	0.28	0.44	0.70	0.76	**0.80**	0.14
I	0.30	0.36	0.72	0.74	**0.83**	0.07
Z	0.34	0.43	0.77	0.79	**0.87**	0.10
Z/HAL	0.31	0.46	0.65	0.71	**0.75**	0.12

Measure = femoral neck measure; PG = pubertal group; BM = body mass; LM = lean mass; FM = fat mass; BMC = bone mineral content, in g; BMD = bone mineral density, in g/cm^2; W = width, in cm; A = area, in cm^2; I = moment of inertia, in cm^4; Z = section modulus, in cm^3; Z/HAL = section modulus divided by hip axis length, in cm^2.

femoral neck measures (**Table 2**). The relationships with lean mass, fat mass, and body mass were independent of gender. Gender significantly improved all regressions on pubertal group and some regressions on age and height, increasing the explanatory power up to 23 percent. For height, both gender and the interaction between age and gender were significant for the BMC, I, and Z regressions. The age relationships for BMC, A, I, and Z were significantly influenced by gender, and there was a significant interaction between age and gender. Although gender was not significant for BMD and W, the interaction between age and gender was significant. When gender was accounted for, the regressions on height and body mass were very similar for all femoral neck measures, and height explained more variance for femoral width, moment of inertia, and section modulus.

Table 2.
Coefficients of determination (adjusted R^2) for multiple linear regressions with gender of femoral neck measures on individual developmental parameters and for saturated regression. Bold indicates strongest relationships. All regressions are significant.

Measure	Age	PG	Height	BM	LM	ALL
BMC	0.39*	0.62*	0.70*	0.71	**0.76**	0.79
BMD	0.26	0.45*	0.45	0.51	**0.53**	0.56
W	0.36	0.46*	**0.64**	0.56	0.63	0.65
A	0.41*	0.62*	0.73	0.76	**0.80**	0.82
I	0.49*	0.62*	0.79*	0.74	**0.83**	0.84
Z	0.52*	0.66*	0.81*	0.79	**0.87**	0.88
Z/HAL	0.44*	0.59*	0.68	0.71	**0.75**	0.76

Measure = femoral neck measure; PG = pubertal group; BM = body mass; LM = lean mass; ALL = cumulation of age, pubertal group, height, body mass, lean mass, and gender; BMC = bone mineral content, in g; BMD = bone mineral density, in g/cm^2; W = width, in cm; A = area, in cm^2; I = moment of inertia, in cm^4; Z = section modulus, in cm^3; Z/HAL = section modulus divided by hip axis length, in cm^2. Significant effect of gender on regression.

Accounting for all the contributing developmental variables in a saturated regression (age, pubertal group, height, body mass, lean mass, and gender) only increased the explanatory power by 1–3 percent over lean body mass alone.

Where relationships were expected, correlations were examined among independent femoral neck measures from the DXA data (**Table 3**). There was a strong correlation between the section modulus and both femoral neck BMC (r=0.863) and BMD (r=0.754). When examined by gender, this correlation with BMD was stronger in males (r=0.803) than females (r=0.660), at least partially due to the large data range of the males. Section modulus and HAL were also strongly correlated (r=0.811, $p<0.0001$).

Table 3.
Correlations among femoral neck measures. All correlations are significant ($p<0.0001$).

Measure	BMC	BMD	W	A	I	Z
Z	0.863	0.754	0.863	0.955	0.990	.
HAL	0.741	0.528	0.758	0.749	0.796	0.811
Z/HAL	0.911	0.777	0.825	0.951	0.960	.

Measure = femoral neck measure; BMC = bone mineral content, in g; BMD = bone mineral density, in g/cm^2; W = width, in cm; A = area, in cm^2; I = moment of inertia, in cm^4; Z = section modulus, in cm^3; HAL = hip axis length; Z/HAL = section modulus divided by hip axis length, in cm^2.

DISCUSSION

When the predictive power of age, pubertal stage, height, body mass, lean mass, and fat mass were compared, we found that lean mass was the strongest correlate of femoral neck structure in adolescents and this relationship was independent of gender. Lean mass explained from 2 to 9 percent more data variance than body mass, the next strongest individual correlate in most cases. When gender was taken into account, body mass and height demonstrated similar relationships. A saturated regression containing age, pubertal group, height,

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body mass, lean mass, and gender only provided 1–3 percent more explanatory power than lean mass alone, not a practically relevant improvement.

These findings contrast with our earlier results in the femoral diaphysis (9,10). At the mid-diaphysis, all femoral cross-sectional measures correlated most strongly with body mass, and these relationships were independent of gender. The relationships with lean mass were weaker than those with body mass and were also strongly dependent on gender, with greater values in females than males at any given lean mass. With the exception of femoral length, all body mass relationships were much stronger than the relationships with height, explaining 6–17 percent more variance in mid-diaphyseal measures. These results, combined with the current findings, suggest that lean mass may be a more reliable indicator of mechanical loading than total body mass at this skeletal site. The cancellous structure of the femoral neck is more metabolically active and may be more sensitive to mechanical loading than the cortical mid-diaphysis.

We focused on structure of the midsection of the femoral neck. Most other analyses have focused solely on bone mineral acquisition at the femoral neck during growth. Our values of BMD and BMC at the femoral neck are consistent with measurements reported by others at similar stages of development (22–26). Gender-based examinations of BMC or BMD acquisition at the femoral neck have consistently revealed similarly rapid changes in bone mass from early to midpuberty in both sexes, followed by a slowdown in women from midpuberty to maturity (22,25,27). Estimates of volumetric bone density from bone mineral apparent density (BMAD) do not change in the femoral neck during adolescence, suggesting that gains in BMD can be explained by increases in bone size alone (16). Similar strong associations have been reported for femoral bone mass with body mass and height (24,28).

In our study, the lack of association of femoral neck structure with weightbearing activity may be due to several factors, including the strong relationship with body mass and particularly with lean body mass, difficulties in quantifying activity information, and lack of variance within this population. In this active young population, body mass and lean muscle mass may already account for the majority of differences in physical activity, leaving little further explanatory power for activity measures (29). Weak or no relationships were found previously in this cohort; weightbearing activity correlated weakly with femoral BMD and BMAD in the females of this study (30) and with femoral BMD in early pubertal males of this study (16).

Two other groups have examined the structural behavior of the femoral neck, focusing on age-related changes. Using a more complex structural model, Beck et al. (13,31) characterized gender differences in femoral structure with aging. They showed significant gender differences in age-related changes in the femoral neck, but only examined adult and elderly subjects and focused on relationships of neck structure with age. Mourtada et al. (8) validated this curved beam approach to the structural behavior of the proximal femur. The femoral neck showed the smallest cross-sectional area and lowest moment of inertia. Under loading conditions simulating a fall on the greater trochanter, the greatest stresses were present in the femoral neck. Yoshikawa et al. (7) used a structural approach similar to ours. In their calibration study, the correlations between the mineral measurements and the moment of inertia are similar to ours. They examined a series of normal adult subjects and found no relationship between the cross-sectional moment of inertia and age, but did not fully examine other possible explanatory characteristics such as body mass and height. They did observe age-related gender differences in femoral stresses, safety factor, and fall index, which might indicate increased fracture risk.

The advantage of these approaches (6–8) and the work presented here is that they provide a mechanistic characterization of femoral neck structure. Although BMD correlates well with the structural parameters we examined, BMD alone cannot account for differences in mineral distribution and load-bearing ability and is known to be insufficient for predicting fracture risk (5). Structural parameters such as cross-sectional moment of inertia and section modulus provide insight into the response of the femoral neck when a force is applied. More widespread implementation of structural approaches is necessary, however, to validate their utility.

The significance of lean body mass to femoral structure may have important consequences in understanding hip fracture risk later in life. Increased hip fracture risk has been associated with low body mass in studies of ethnic differences in hip fracture rates (32). Longer HAL is also associated with increased hip fracture risk (21). Understanding how these influences interact during development may provide insights into age-related changes and benefit predictions of fracture risk. Our results demonstrate lean body mass to be a powerful, independent predictor of femoral neck structure during development, but these results cannot address whether a causal relationship exists. Lean body mass is a measure of the skeletal loading created by the local actions of muscles. The strong relationship with lean body mass and weaker correlations with general indicators of growth such as height, therefore, suggest that the developing femoral neck is very responsive to its mechanical environment. Further investigation of femoral neck structure and lean body mass in longitudinal studies may provide insights into this load-based adaptation and identify a role for loading and exercise in femoral neck fracture risk prevention.

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REFERENCES

1. Gullberg B, Johnell O, Kanis JA. World-wide projections for hip fracture. Osteoporos Int 1997;7:407–13.
2. Melton LJ 3rd, Thamer M, Ray NF, Chan JK, Chestnut CH 3rd, Einhorn TA, et al. Fractures attributable to osteoporosis: report from the National Osteoporosis Foundation. J Bone Miner Res 1997;12:16–23.
3. Cummings SR, Black DM, Nevitt MC, Browner W, Cauley J, Ensrud K, et al. Bone density at various sites for prediction of hip fractures. The Study of Osteoporotic Fractures Research Group. Lancet 1993;341:72–5.
4. Kanis JA. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis: synopsis of a WHO report. Osteoporos Int 1994;4:368–81.
5. Riggs BL, Wahner HW, Seeman E, Offord KP, Dunn WL, Mazess RB, et al. Changes in bone mineral density of the proximal femur and spine with aging. Differences between the postmenopausal and senile osteoporosis syndromes. J Clin Invest 1982;70:716–23.
6. Beck TJ, Ruff CB, Warden KE, Scott WW Jr, Rao GU. Predicting femoral neck strength from bone mineral data: A structural approach. Invest Radiol 1990;25:6–18.
7. Yoshikawa T, Turner CH, Peacock M, Slemenda CW, Weaver CM, Teegarden D, et al. Geometric structure of the femoral neck measured using dual-energy x-ray absorptiometry. J Bone Miner Res 1994;9:1053–64.
8. Mourtada FA, Beck TJ, Hauser DL, Ruff CB, Bao G. Curved beam model of the proximal femur for estimating stress using dual-energy x-ray absorptiometry derived structural geometry. J Orthop Res 1996;14:483–92.
9. van der Meulen MCH, Ashford MW Jr, Kiratli BJ, Bachrach LK, Carter DR. Determinants of femoral geometry and structure during adolescent growth. J Orthop Res 1996;14:22–9.
10. Moro M, van der Meulen MCH, Kiratli BJ, Marcus R, Bachrach LK, Carter DR. Body mass is the primary determinant of midfemoral bone acquisition during adolescent growth. Bone 1996;19:519–26.
11. van der Meulen MCH, Beaupre GS, Carter DR. Mechanobiologic influences in long bone cross-sectional growth. Bone 1993;14:635–42.
12. Martin RB, Burr DB. Non-invasive measurement of long bone cross-sectional moment of inertia by photon absorptiometry. J Biomech 1984;17:195–201.
13. Beck TJ, Ruff CB, Bissessur K. Age related changes in female femoral neck geometry: Implications for bone strength. Calcif Tissue Int 1993;53:S41–6.
14. Mora S, Goodman WG, Loro ML, Roe TF, Sayre J, Gilsanz V. Age-related changes in cortical and cancellous vertebral bone density in girls: Assessment with quantitative CT. AJR Am J Roentgenol 1994;162:405–9.
15. Bhudhikanok GS, Wang M-C, Eckert K, Matkin C, Marcus R, Bachach LK. Differences in bone mineral in young Asian and Caucasian Americans may reflect differences in bone size. J Bone Miner Res 1996;11:1545–56.
16. Wang M-C, Aguirre M, Bhudhikanok GS, Kendall CG, Kirsch S, Marcus R, et al. Bone mass and hip axis length in healthy Asian, black, Hispanic, and white American youths. J Bone Miner Res 1997;12:1922–35.
17. Tanner JM. Growth at adolescence. 2nd ed. Oxford: Blackwell; 1962. p. 28–39.
18. Duke PM, Litt IF, Gross RT. Adolescents' self-assessment of sexual maturation. Pediatrics 1980;66:918–20.
19. Myers ER, Hecker AT, Rooks DS, Hipp JA, Hayes WC. Geometric variables from DXA of the radius predict forearm fracture load in vitro. Calcif Tissue Int 1993;52:199–204.
20. Selker F, Carter DR. Scaling of long bone fracture strength with animal mass. J Biomech 1989;22:1175–83.
21. Faulkner KG, Cummings SR, Black D, Palermo L, Gluer CC, Genant HK. Simple measurement of femoral geometry predicts hip fracture: The Study of Osteoporotic Fractures. J Bone Miner Res 1993;8:1211–7.
22. Bonjour JP, Theintz G, Buchs B, Slosman D, Rizzoli R. Critical years and stages of puberty for spinal and femoral bone mass accumulation during adolescence. J Clin Endocrinol Metab 1991;73:555-63.
23. Southard RN, Morris JD, Mahan JD, Hayes JR, Torch MA, Sommer A, et al. Bone mass in healthy children: Measurement with quantitative DXA. Radiology 1991;179:735–8.
24. Henderson NK, Price RI, Cole JH, Gutteridge DH, Bhagat CI. Bone density in young women is associated with body weight and muscle strength but not dietary intake. J Bone Miner Res 1995;10:384–93.
25. Zanchetta JR, Plotkin H, Alvarez Filgueira ML. Bone mass in children: Normative values for the 2–20-year-old population. Bone 1995;16(4 Suppl):393S–9S.
26. Morris FL, Naughton GA, Gibbs JL, Carlson JS, Wark JD. Prospective ten-month exercise intervention in premenarcheal girls: Positive effects on bone and lean mass. J Bone Miner Res 1997;12:1453–62.

27. Theintz G, Buchs B, Rizzoli R, Slosman D, Clavien H, Sizonenko PC, et al. Longitudinal monitoring of bone mass accumulation in healthy adolescents: Evidence for a marked reduction after 16 years of age at the levels of lumbar spine and femoral neck in female subjects. J Clin Endocrinol Metab 1992;75:1060–5.
28. Pockock N, Eisman J, Gwinn T, Sambrook P, Kelly P, Freund J, et al. Muscle strength, physical fitness, and weight but not age predict femoral neck bone mass. J Bone Miner Res 1989;4:441–8.
29. Kroger K, Kotaniemi A, Kroger L, Alhava E. Development of bone mass and bone density of the spine and femoral neck—a prospective study of 65 children and adolescents. Bone Miner 1993;23:171–82.
30. Matkin CC, Bachrach L, Wang M-C, Kelsey J. Three measures of physical activity as predictors of bone mass in a young cohort. Clin J Sport Med 1998;8:201–8.
31. Beck TJ, Ruff CB, Scott WW Jr, Plato CC, Tobin JD, Quan CA. Sex differences in geometry of the femoral neck with aging: a structural analysis of bone mineral data. Calcif Tissue Int 1992;50:24–9.
32. Pruzansky ME, Turano M, Luckey M, Senie R. Low body weight as a risk factor for hip fracture in both black and white women. J Orthop Res 1989;7:189–97.