Iranian J Publ Health, 2007, A supplementary issue on Osteoporosis, pp.70-74

Relationship between Family History of Osteoporotic Fracture and Femur Geometry

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Abstract

Background: The principal aim of this study was therefore to investigate association between family history of osteoporotic hip fracture, BMD and femur geometry in Bushehr city in South of Iran.

Methods: In this cross-sectional study, data were obtained from Iranian Multi-center Osteoporosis Study (IMOS) in Bushehr. Healthy men and women aged 50 to 75 years were selected based on randomized clustered sampling of all regions of the corresponding city.

BMD was measured once at the lumbar spine (L2-L4) and proximal femur with dual X-ray absorptiometry using Lunar DPX densitometers. From the DXA image the operator manually determines the hip axis length (HAL) and femoral neck-shaft angle. The HAL was measured from the inner pelvic brim to the lateral side of the femur .The femoral neck–shaft angle was defined as the angle between the femoral neck axis and the femoral shaft axis .

Results: There were no significant differences between the family fracture history groups with regard to the potential confounders of age and body mass index (BMI).

HAL of women with history of hip fracture was greater but history of hip fracture showed no significant relation with other variables.

Conclusion: These findings suggest that individuals with a positive family history may be at higher risk of osteoporotic hip fracture because they have greater HAL and more prone to buckle at the femur neck.

Keyword: *Osteoporosis, Bone fracture, Hip axis length (HAL), Femoral neck-shaft angle*

Introduction

Low bone mineral density (BMD) is an important risk factor for hip fractures (1), although geometry of the hip may also play a role (2-4). Family and twin studies have demonstrated that osteoporosis is under strong genetic control, with female first-degree relatives of women with osteoporosis having reduced BMD at both the spine and hip when compared with healthy controls (5-9). Maternal history of fracture at the hip and wrist has recently been shown to be a positive risk factor for fracture in elderly women (10, 11).

The principal aim of this study was therefore to investigate association between family history of osteoporotic hip fracture, BMD and femur geometry in Bushehr city in south of the Iran.

Materials and Methods

In this cross-sectional study, data were obtained from Iranian Multi-center Osteoporosis Study (IMOS) in Bushehr. Healthy men and women aged 50 to 75 yr were selected based on randomized clustered sampling of all regions of the corresponding city.

To confirm inclusion of healthy participants to the study, subjects with following diseases or conditions were excluded before densitometry: known history or evidence of rheumatoid arthritis, thyroid, parathyroid or adrenal disease, hepatic

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or renal failure, metabolic bone disease, type I diabetes mellitus, sterility, oligomenorrhea, malignancy, malabsorption, immobility for more than one week, pregnancy, lactation, smoking more than 10 cigarettes per day, alcoholism, and medications influencing bone metabolism.

Written informed consent was obtained from all participants and the study protocol was approved by the research ethics committee of the Tehran University of Medical Sciences and Iranian Ministry of Health and Medical Education, Iran.

BMD was measured once at the lumbar spine (L2-L4) and proximal femur with dual X-ray absorptiometry using Lunar DPX densitometers (Lunar 7164, GE, Madison, WI). The procedure was carried out by a trained operator according to the manufacturer's instruction. Machine calibration was done daily. Daily and weekly quality assurance tests were performed as recommended by the DXA machine manufacturers.

Precision errors for BMD measurements were 1–1.5% in the lumbar and 2-2.5% in the femoral regions. These precision errors were obtained in each center from precision studies according to standard methods.

From the DXA image the operator manually determines the hip axis length (HAL) and femoral neck-shaft angle. The HAL was measured from the inner pelvic brim to the lateral side of the femur. The femoral neck-shaft angle was defined as the angle between the femoral neck axis and the femoral shaft axis (geo14-21). All measurements were undertaken by one of the authors.

Results

Two hundred fifty six participants (134 male, mean age 58.25±6.79 yr and 122 female, mean age 57.27±6.09 yr) were included in the analyses. A history of hip fracture in females and males was reported in 15 and13 subjects, respectively. There were no significant differences between the family fracture history groups with regard to the potential confounders of age and body mass index (BMI).

Relations between sex with other variable are shown in Table1. Males had greater hip axis length and BMD in all regions than females. Femural neck-shaft angle in men and women was not significant.

Correlation of women HAL with lumbar BMD (r =0.2, *P*= 0.02) and age(r= 0.2, *P*= 0.01) was weakly positive, but not correlated with total BMD, neck BMD and BMI. In men HAL was not correlated with lumbar BMD, total BMD, neck BMD, BMI and age but weakly correlated with femoral area (r= 0.17, *P*= 0.04).

Relations between history of hip fracture in men and women age greater than 50 yr with other variable are shown in Table 2. HAL of women with history of hip fracture was greater but history of hip fracture showed no significant relation with other variables. History of hip fracture in men had not significant relation with other variables.

Table 1: Relationship between sex and variable of hip geometry

BMI	**Men**	**Women**	***P***
	26/16 ± 3/65	**27/66 ± 4/55**	**0/005**
Age	58/25 ± 6/76	57/27 ± 6/09	0/001
Total femur BMD	0/776 ± 0/16 g/m^2	0/709 ± 0/13 g/m^2	0/001
Neck BMD	0/753 ± 0/133 g/m^2	0/691 ± 0/109 g/m^2	0/001
Neck BMD	0/917 ± 0/166 g/m^2	0/838 ± 0/136 g/m^2	0/001
Area of femur	5/25 ± 0/905 g/m^2	4/48 ± 0/83 g/m^2	0/001
HAL	11/39 ± 0/67 cm	10/29 ± 0/55 cm	0/001
Neck shaft angle	129/18 ± 12/27^o	128/16 ± 5/93^o	0/4

Table 2: Relationship between family history of hip fracture and hip geometric parameter and BMD

	Women			Men		
	With family history of fracture	**With out family history of fracture**	***P***	**With family history of fracture**	**With out family history of fracture**	***P***
BMI	29/42±4/22	27/4±4/56	0/1	25/6±2/65	26/22±3/74	0/5
Total femur BMD	0/728±0/13	0/706±0/13	0/5	0/732±0/146	0/781±0/166	0/3
Neck BMD	0/712±0/12	0/688±0/106	0/4	0/719±0/124	0/757±0/133	0/3
HAL	10/57±0/67	10/25±0/52	0/04	11/4±0/48	11/39±0/69	0/9
Neck shaft angle	127/26±6/12^o	128/29±5/92^o	0/5	128/6±4/21^o	129/24±12/18	0/8

Discussion

Our findings suggest that there is a strong familial predisposition to the risk of osteoporotic fractures. The risk of fracture appears to operate, in large part, independently of bone density and may be mediated by characteristics besides BMD such as femur geometry.

In our study HAL of women with family history of hip fracture was greater than others. Hip axis length was one of the first geometric measures proposed as an indicator of hip fracture risk for females independent of BMD at the femoral neck. An increase in HAL equivalent to 1 SD was associated with a 1.8-fold increase in the risk of hip fracture in women enrolled in the study of osteoporotic fractures (12). Following that report,

a number of other studies have appeared in support of HAL (13-15), with a few questioning its predictive significance (16-18).

Arden et al demonstrated that Hip axis length had major genetic components with estimates of 0.61, which remained virtually unchanged after adjustment for bone mineral density and suggests that a combination of different genetic factors acting on the structure, dimensions and density of bone may explain the importance of family history as a risk factor for hip fracture.

Looker et al did not find differences in hip axis length by family history. This suggests that family history may not influence osteoporotic fragility via lever mechanics (19). Fox et al. also reported no difference in hip-axis length by maternal history of hip fracture in a subset of elderly women from the Study of Osteoporotic Fractures (11). The lack of relationship was somewhat surprising in light of the high heritability reported for these measures of neck length in some (5, 20), but not all (21), twin studies. These measurements have also been found to be sensitive to the position of the patient during imaging (22), so technical differences in the measurements might account for the discrepancy in results.

Our data suggest that family history of hip fracture was unrelated to BMD. Keen et al suggest that family history is site-specific, as a positive family history for appendicular fracture was associated with wrist and/ or hip fractures but not with spinal fractures. The finding that the increase in fracture risk associated with a positive family history was unaltered after adjustment for BMD suggests that common, within-family factors (both genetic and environmental) other than BMD may be contributing to this familial clustering of fracture risk (23). Bone structure and architecture have been shown to be under genetic control independent of BMD (5), and have also been demonstrated to be independent predictors of hip fracture in elderly populations (24, 25). The finding that the increase in risk was independent of BMD may also indicate a possible familial component to the risk of falling, with the genetic effect being

mediated through factors such as muscle strength and proprioception (26).

In conclusion, our results provide insight into skeletal differences that may underlie the relationship between family history of hip fracture and geometry. In specific, in addition to BMD, femur geometry such as HAL in the femur neck differed between those with and without a family history of hip fracture. These findings suggest that individuals with a positive family history may be at higher risk of osteoporotic hip fracture because they have greater HAL and more prone to buckle at the femur neck. Additional studies with more thoroughly documented family history of osteoporotic hip fracture seem warranted to confirm these findings; such work may help identify an important surrogate phenotype to be used in future genetic studies of osteoporosis.

Acknowledgements

We would like to thank all colleges in the endocrine department of Bushehr. This study was supported by the research grant of Endocrinology and Metabolism Research center.

References

1. Cummings SR, Black DM, Nevitt MC, et al. (1993). Bone density at various sites for prediction of hip fractures. *Lancet*, 341(8850):72-5.
2. Gluer CC, Cummings SR, Pressman A, et al. (1994). Prediction of hip fractures from pelvic radiographs: the study of osteoporotic fractures. *J Bone Miner Res*, 9(4): 671-77.
3. Faulkner KG, Cummings SR, Black D, Palermo L, Gluer CC, Genant HK (1993). Simple measurement of femoral geometry predicts hip fracture: the study of osteoporotic fractures. *J Bone Miner Res*, 8(10):1211-17.
4. Gnudi S, Ripamonti C, Gualtieri G, Malavolta N (1999). Geometry of proximal femur in the prediction of hip fracture in osteoporotic women. *Br J Radiol*, 72(860): 729-33.
5. Arden NK, Baker J, Hogg C, Baan K, Spector TD (1996). The heritability of bone mineral density, ultrasound of the calcaneus and hip axis length: a study of postmenopausal twins. *J Bone Miner Res*, 11(4): 530-34.
6. Flicker L, Hopper JL, Rodgers L, Kaymakci B, Green RM, Wark JD (1995). Bone density determinants in elderly women: a twin study. *J Bone Miner Res*, 10(11): 1607-13.
7. Pocock NA, Eisman JA, Hopper JH, Yeates MG, Sambrook PN, Eberl S (1987) Genetic determinants of bone mass in adults: a twin study. *J Clin Invest*, 80 (3):706–10.
8. Seeman E, Hopper JH, Bach LA, et al. (1989). Reduced bone mass in daughters of women with osteoporosis. *N Engl J Med*, 320 (9): 554-58.
9. Evans RA, Marel GM, Lancaster EK, Kos S, Evans M, Wong SYP (1988). Bone mass is low in relatives of osteoporotic patients. *Ann Intern Med*, 109(11): 870-73.
10. Cummings SR, Nevitt MC, Browner WS, et al. (1995). Risk factors for hip fracture in white women. *N Engl J Med*, 332(12): 767-73.
11. Fox KM, Cummings SR, Powell-Threets K, Stone K (1998). Family history and risk of osteoporotic fracture. *Osteoporos Int*, 8(6): 557-62.
12. Martin R, Burr D (1984). Non-invasive measurement of long bone cross-sectional moment of inertia by photon absorptiometry. *J Biomech*, 17(3):195-201.
13. Crabtree NJ, Kroger H, Martin A, Pols HAP, Lorenc R, Nijs J, Stepan JJ, et al. (2002). Improving risk assessment: hip geometry, bone mineral distribution and bone strength in hip fracture cases and controls. The EPOS study. *Osteoporos Int*, 13 (1):48-54.

14. Boonen S, Koutri R, Dequeker J, Aerssens J, Lowet G, Nijs J, Berbeke G, Lesaffre E, Geusens P (1995). Measurement of femoral geometry in type I and type II osteoporosis: differences in hip axis length consistent with heterogeneity in the pathogenesis of osteoporotic fractures. *J Bone Miner Res*, 10(12): 1908-12
15. Gnudi S, Malavolta N, Testi D, Viceconti M (2004). Differences in proximal femur geometry distinguish vertebral from femoral neck fractures in osteoporotic women. *Br J Radiol*, 77(915): 219-23.
16. Gomez Alonzo C, Diaz Curiel M, Hawkins Carranza F, Perez Cano R, Diez Perez A (2000). Femoral bone mineral density, neck-shaft angle and mean femoral neck width as predictors of hip fracture in men and women. *Osteoporos Int*, 11(8): 714-20.
17. Dretakis EK, Papakitsou E, Kontakis GM, Dretakis K, Psarakis S, Asteriopoulos KA (1999). Bone mineral density, body mass index, and hip axis length in postmenopausal Cretan women with cervical and trochanteric fractures. *Calcif Tissue Int*, 64 (3): 257-58
18. Pande I, O'Neill TW, Pritchard C, Scott DL, Woolf AD (2000). Bone mineral density, hip axis length and risk of hip fracture in men: results from the Cornwall Hip Fracture Study. *Osteoporos Int*, 11(10): 866-70.
19. Looker AC, Beck TJ (2004). Maternal history of osteoporosis and femur geometry. *Calcify tissue Int*, 75: 277-85.
20. Flicker L, Faulkner KG, Hopper JL, Green RM, Kaymakci B, Nowson CA, Young D, Wark JD (1996). Determinants of hip axis length in women aged 10–89 years: a twin study. *Bone*, 18 (1): 41-5
21. Slemenda CW, Turner CH, Peacock M, Christian JC, Sorbel J, Hui SL, Johnston CC (1996). The genetics of proximal femur geometry, distribution of bone mass and bone mineral density. *Osteoporos Int*, 6 (2): 178-82.
22. Michelotti J, Clark J (1999). Femoral neck length and hip fracture risk. *J Bone Miner Res*, 14 (10): 1714-20.
23. Keen RW, Hart1 DJ, Arden NK, Doyle DV and Spector1 TD (1999). Family History of Appendicular Fracture and Risk of Osteoporosis: A Population-Based Study. *Osteoporos Int*, 10(2): 161-66.
24. Faulkner KG, Cummings SR, Black D, Palermo L, Gluer CC, Genant HK (1993). Simple measurement of femoral geometry predicts hip fracture: the study of osteoporotic fractures. *J Bone Miner Res*, 8(10): 1211-17.
25. Hans D, Dargent-Molina P, Schott AM, et al. (1996). Ultrasonographic heel measurements to predict hip fracture in elderly women: the EPIDOS prospective study. *Lancet*, 348(9026): 511-4.
26. Arden NK, Spector TD (1997). Genetic influences on muscle strength, lean body mass, and bone mineral density: a twin study. *J Bone Miner Res*, 12(12): 2076-81.