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Difference in the Trajectory of Change in Bone Geometry as Measured by Hip Structural Analysis in the Narrow Neck, Intertrochanteric Region, and Femoral Shaft between Men and Women Following Hip Fracture

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Abstract

Prior studies have shown that women have declines in bone structure and strength after hip fracture, but it is unclear whether men sustain similar changes. Therefore, the objective was to examine sex differences in proximal femur geometry following hip fracture. Hip structural analysis was used to derive metrics of bone structure and strength: aerial bone mineral density, cross-sectional bone area (CSA), cortical outer diameter, section modulus (SM), and buckling ratio (BR) from dual-energy x-ray absorptiometry scans performed at baseline (within 22 days of hospital admission), two, six, or twelve months after hip fracture in men and women (n=282) enrolled in the Baltimore Hip Studies 7th cohort. Weighted estimating equations were used to evaluate sex differences at the narrow neck (NN), intertrochanteric (IT), and femoral shaft (FS). Men had significantly different one year NN changes compared to women in CSA: −6.33% (−12.47, −0.20) vs. 1.37% (−3.31, 6.43), *P*=0.049; SM: −4.98% (−11.08, 1.10) vs. 3.94% (−2.51, 10.42), *P*=0.042; and BR: 7.50% (0.65, 14.36) vs. −1.20% (−6.41, 4.00), *P*=0.044. One year IT changes displayed similar patterns, but the sex differences were not statistically significant for CSA: −4.07% (−10.83, 2.67) vs. 0.41% (−3.41, 4.24), *P*=0.252; SM: −4.78% (-12.10, 5.53) vs. −0.31 (−4.74, 4.11), *P*=0.287; and BR: 4.59% (−0.65, 9.84) vs. 1.52% (−4.23, 7.28), *P*=0.425.

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Conflicts of Interest

Dr. Jay Magaziner has consulting agreements with Ammonett, Novartis, Sanofi, and Viking. Dr. Denise Orwig has consulting agreements with Kinexum and Viking. Dr. Thomas J. Beck is CEO of Beck Radiological Innovations Inc. Drs. Alan M. Rathbun, Michelle Shardell, J. Richard Hebel, Gregory E. Hicks, and Marc C. Hochberg have no conflicts of interest to declare.

Differences in FS geometric parameters were even smaller in magnitude and not significantly different by sex. Women generally experienced non-significant increases in bone tissue and strength following hip fracture, while men had structural declines that were statistically greater at the NN region. Reductions in the mechanical strength of the proximal femur after hip fracture could put men at higher risk for subsequent fractures of the contralateral hip.

Keywords

Aging; DXA; Osteoporosis; Injury/Fracture healing; Fracture Prevention

1.0 Introduction

Osteoporosis is a systemic condition characterized by a reduction in the structural strength of bones. The most significant consequence of the disease is often hip fracture, which is associated with excess mortality, morbidity, and health care expenditures [1,2]. Rates of bone fragility and hip fracture are higher in women compared to men, in part, due to the larger skeletal size and bone mass of men and bone loss that occurs in women during menopause [3–5]. Most prior research examining skeletal determinants of hip fracture risk and recovery have focused on bone mineral density, which is a surrogate marker for mechanical strength and not a uniquely distinct geometric property of bone tissue [6–8]. Geometric parameters capture the spatial distribution of bone tissue in ways that are relevant to strength in bending, axial compression, and cortical instability and are independently predictive of hip fracture even after accounting for aerial BMD and other clinical risk factors [9–11]. Geometric properties of bone tissue can be used to understand how changes in bone structure and strength during the natural course of aging contribute to sex differences in the pathogenesis of osteoporosis and hip fracture [1].

Studies of sex differences in bone geometry across adult lifespan have consistently demonstrated that compared to women, men have greater aerial BMD, cross-sectional bone areas (CSA), bone diameters, section moduli (bending strength; SM), and lower buckling ratio (cortical instability; BR) at the narrow neck (NN), intertrochanteric region (IT), and femoral shaft (FS) [1,5,11–16]. Cross-sectional investigations indicate that BMD decreases with age in both men and women but expansions in outer diameter serve to preserve bending strength and compensate for net BMD decline [1,12,15,17]. However, alterations in bone structure and strength among women are accompanied by greater increases in indices of cortical instability compared to men [13]. Moreover, these sexual dimorphisms in bone geometry start earlier in women and continue to occur at greater rates in old-old age at common fracture sites at the NN and IT regions [15,17]. The combination of bone mineral loss, thinning of cortex regions, increases in outer diameter, and consequent susceptibility to local buckling among women during aging contribute to their higher likelihood of hip fracture [9–11].

Also of clinical relevance is an understanding of changes in bone structure and strength that occur after hip fracture because such information is necessary for the design and optimization of treatment strategies to maximize recovery and minimize the risk for

subsequent fractures. After hip fracture, women experience profound declines in BMD, particularly at the femoral neck, and these declines are greater than observed in unfractured community-dwelling older women [7,18–20]. Women sustaining hip fracture have comparatively lower BMD not only due to their femurs having less bone (lower CSA) but also because the bone is distributed in a large bone diameter at the contralateral non-fractured hip compared to similar postmenopausal women with osteoporosis [21]. They also experience significantly greater declines in bending strength and increases in cortical instability [21]. Thus, increases in bone fragility may occur rapidly after hip fracture and greatly inflate the risk of a second fracture during the recovery period. As existing research is limited to women, no studies have evaluated sex differences in changes to bone geometry that occur after hip fracture, and such differences may potentially affect recovery in different ways between men and women [22]. Research recently reported that men experience clinically significant greater decrements in BMD after hip fracture than women [23]. The objective of this study was to compare temporal patterns in bone geometry measured in men and women in the year following hip fracture.

2.0 Materials and Methods

2.1 Study Data & Sample

The Baltimore Hip Studies 7th cohort (BHS-7) was an observational study designed to compare the metabolic, physiologic, neuromuscular, functional, and clinical consequences of hip fracture between men and women. Patients hospitalized for hip fracture were recruited from one of eight BHS network hospitals in the Baltimore metropolitan area and included those 65 years or older at the time of hospital admission for hip fracture (ICD-9 codes 820.00–820.9). Men were continuously enrolled into the study; women were frequency matched with men on fracture timing within each hospital, which ensured recruitment of an equal number of men and women and minimized any impact of secular changes in care and hospital practice differences. Exclusion criteria were: pathologic fracture, not community-dwelling at the time of fracture, non-English speaker, being bedbound for 6 months before fracture, residence > 70 miles from the hospital, weight > 300 pounds, no surgery, and hardware in the contralateral hip.

A total of 362 hip fracture patients were enrolled (180 males and 182 females). Five participants did not provide data at the baseline or 2-month follow-up visit and another 18 participants were removed as a result of an IRB-requested post procedure audit (6 participants were subsequently found to be ineligible because they did not meet study inclusion criteria and 12 participants were determined to be ineligible secondary to failures of the informed consent process), leaving a sample of 339 participants. Study visits were conducted at baseline (within 22 days of admission) and at two, six, and twelve months after admission, and included questionnaires and measures of body composition and functional performance. Study protocols were reviewed and approved by the University of Maryland, Baltimore IRB and the review boards of participating hospitals. The analytic sample included 282 participants with at least one dual-energy x-ray absorptiometry (DXA) scan that could be used to derive geometric measures of hip structural strength (Figure 1).

2.2 DXA Measurement

DXA scans of the total hip were used to evaluate BMD (grams per centimeter squared) longitudinally at the non-fractured hip using either a Lunar Prodigy machine (four sites; Madison, WI, USA) or Hologic machine (three sites; Waltham, MA, USA) at one of seven study DXA facilities. Standardized methods were used for quality control, certification of DXA operators, and scanning procedures to guarantee the reproducibility of results. DXA machines were calibrated daily using a phantom to ensure that no significant measurement drift occurred over time. While it was not always possible to image patents on the same scanner, care was taken to ensure that a scanner from the same manufacturer was consistently used. To account for any inter-machine differences, statistical models included an indicator to capture the type of DXA machine that a given patient was scanned on throughout participation in the study. The estimated sex differences were an average that represented a marginal effect across men and women who used the same type of scanner at each time point.

2.3 Structural Parameters

HSA software used for this study was developed at The Johns Hopkins University and re-analyzes conventional DXA image data to obtain geometric properties of bone cross-sections [8]. Any DXA scans that were judged to be of insufficient quality (e.g., poor image, lack of anatomical coverage) were excluded. The validated HSA algorithm was used to establish three cross-sectional analysis regions on femur DXA images: (1) narrow neck (NN), the narrowest point of the femoral neck; (2) intertrochanteric (IT), along the bisector of the neck-shaft angle; and (3) femoral shaft (FS), a distance of approximately 1.5 times the narrowest neck diameter that is distal to the intersection of neck-shaft axes [24]. The HSA software generates five parallel, pixel mineral mass profiles, along lines that traverse the femur at each of the three regions. From each region: areal BMD (grams per centimeter squared); cross-sectional area (CSA; a measure of bone surface area); outer diameter (OD; a measure of outer cortical width); section modulus (SM; a measure of bending strength); and buckling ratio (BR; a measure of bone instability) were derived from the five profiles and averaged for reporting [8].

2.4 Predictor Variables

All covariates included in multivariable regression models were measured at study enrollment. These variables were selected *a priori* based on factors that were associated with changes in BMD among women and men in the Study of Osteoporotic Fractures and the Study of Osteoporotic Fractures among Men, respectively [25,26]. Demographic and anthropometric determinants included sex, age (years), race (white or non-white), height (meters), and weight (kilograms). Behavioral factors were smoking (never, past, current) and alcohol consumption (none, minimal, moderate). Clinical characteristics included comorbidity, assessed using a modified version of the Charlson Comorbidity Index that omitted liver disease [27]; depressive symptoms, measured with the Center for Epidemiological Studies Depression Scale [28]; functional limitations, evaluated with the Instrumental Activities of Daily Living (IADL) with a modified version of the Older Americans Resources and Services Instrument [29]. Concomitant medications (never, past,

or current) were assessed via patient-reported survey questions and included bone-active drugs, glucocorticoids, hormone therapy, and calcium supplements. Bone-active drugs included Etidronate, Alendronate, Risedronate, Ibandronate, Teriparatide, Calcitonin, Zoledronic Acid, and Pamidronate. Glucocorticoid medications included Prednisone, Cortisone, Hydrocortisone, Dexamethasone, or other steroids. Hormone therapy was dichotomized into binary categories of “ever” and “never” and defined as the use of Estrogen (pill, vaginal cream, suppository, or patch) in women and Testosterone (injection, patch, and gel) in men. Calcium supplements were measured as the daily consumption of Caltrate, Citracal, Os-Cal, or Tums.

2.5 Statistical Analysis

Baseline characteristics were compared between men and women using chi-square tests for categorical covariates and t-tests for continuous variables. Inverse probability of observation weights (IPW) were used to account for missing baseline covariate data, missing longitudinal outcome data, and truncation due to death [30–32]. The weights were the inverse probability of observation given predictors of missing data chosen from the study covariates selected a priori. The IPW approach is used to reweight the analytic sample to be representative of the overall cohort, and more detailed information about the computation and construction of the missing data weights is provided in Appendix A.

Weighted generalized estimating equations (WEE) assuming an independent variance-covariance matrix were fit with robust standard error estimators to account for within-patient clustering of observations. Multivariable models adjusted for the previously described covariates were used to estimate the association between sex and changes in geometric parameters of hip bone strength: aerial BMD, CSA, OD, SM, and BR. Time was modeled as a categorical index to allow for non-linear functional forms. The primary parameter of interest was the interaction between sex and follow-up time that tested whether change from baseline in the geometric structural parameters differed between men and women overall and at each follow-up time point. Multivariable WEE were used to estimate adjusted sex-specific baseline geometric structural parameters, which were calculated holding all covariate values at their sample mean, as well as the corresponding absolute changes and percent changes during follow-up with 95% confidence intervals (95% CI). Statistical significance was set at an alpha level of 0.05 for primary outcome models, and all analyses were conducted using Stata (Version 13, Stata Corp, College Station, Texas, USA).

3.0 Results

3.1 Descriptive Characteristics

The study sample was mostly white with an average age of approximately 80 years (Table 1). Men were significantly heavier and taller than women and were more likely to be smokers and to consume alcohol. Men also had significantly greater levels of comorbidity and functional limitations compared to women. Baseline aerial BMD at the NN, IT, and FS were higher in males and among those participants scanned with a Lunar machine (Supplementary Table 1). Women had a significantly higher likelihood of reporting past or current utilization of bone-active drugs, glucocorticoids, hormone therapy, and calcium

supplements. Bisphosphonates, particularly alendronate, were the most frequently reported bone-active drugs that participants disclosed to have ever been taken (Supplementary Table 2).

3.2 Narrow Neck (NN)

Men had lower adjusted baseline NN aerial BMD and CSA than women but greater OD, SM, and BR (Table 2). Relative to baseline, aerial BMD and CSA declined in men at the NN from two to twelve months: −0.87% (5.54, 3.78) to −6.36% (−12.81, 0.06) and −1.52% (−6.17, 3.11) to −6.33% (−12.47, −0.20), respectively (Figure 2). In contrast, women experienced non-monotone changes: aerial BMD increased by 0.82% (−2.84, 4.51) at two months but decreased by −0.14% (−4.05, 3.74) at twelve months; and CSA decreased at two months (−0.52%; 95% CI: − 4.01, 2.96) but increased by twelve months (1.37%; 95% CI: −3.31, 6.43). The twelve-month difference in change in NN CSA change (−6.33% vs. 1.37%) was significantly different between men and women (P=0.049), but the global test of the interaction was not statistically significant (P=0.26). There were similar overall changes in OD (P=0.80). However, men experienced greater reductions in SM and increases in BR compared to women. Men had an average decrease in SM of −2.48% (−7.63, 2.64) at two months, −3.76% (−9.64, 2.10) at six months, and −4.98% (−11.08, 1.10) at twelve months. Average twelve month SM change in women (3.94%; 95% CI: −2.51, 10.42) was statistically different compared to men (P=0.042). The twelve-month increase in BR among men of 7.50% (0.65, 14.36) was also significantly different (P=0.044) than the observed decline of −1.20% (−6.41, 4.00) in women. The overall sex differences for SM (P=0.245) and BR (P=0.176) did not reach statistical significance.

3.3 Intertrochanteric (IT)

Adjusted baseline IT aerial BMD, CSA, OD, SM, and BR were greater in men than women (Table 3). Estimated geometric parameters at the IT in men displayed a non-linear pattern of change, specifically, decreases at two months, which were attenuated by six months, but eventually reoccurred in greater magnitude at twelve months (Supplementary Figure 1). These patterns are illustrated by changes in CSA in men: −2.66% (−7.90, 2.56) at two months, 0.61% (−5.15, 6.39) at six months, and −4.07% (−10.83, 2.67) at twelve month; and estimates of SM: −4.32% (−10.49, 1.83) at two months, 1.14% (−5.37, 7.66) at six months, and −4.78% at twelve months (−12.10, 5.53). There were similar trends for IT aerial BMD, OD, and BR. Changes in geometric parameters at the IT in women, with the exception of SM, were largest in magnitude at two months but smaller by twelve months. For instance, aerial BMD increased by 2.63% (−1.58, 6.89) at two months; however, at twelve months, the improvement was minimal (0.43%; 95% CI: −3.73, 4.61). Similarly, OD decreased by −0.85% (−1.94, 0.23) at two months, but this change decreased in magnitude to −0.02% by twelve months. IT CSA and BR displayed comparable longitudinal trends. Average percent change in SM was 0.61 % (−3.13, 4.36) at two, −2.89% (−7.07, 1.28) at six, and −0.31% (−4.75, 4.11) at twelve months; this trajectory of change was significantly different compared to men (P=0.048). None of the other time-specific differences or global sex by time interactions were statistically significant.

3.4 Femoral Shaft (FS)

Men had significantly greater baseline FS aerial BMD, CSA, cortical width, and SM compared to women (Table 4). Men experienced non-linear changes for all FS geometric parameters, where the average percent changes generally declined from baseline to two months, increased from baseline to six months, and decreased again by twelve months (Supplementary Figure 2). For example, estimated percent changes in FS CSA and SM at two, six months, and twelve months were: −0.94% (−5.23, 3.33), 2.28% (−2.97, 7.54), and 0.13% (−5.38, 5.66); and −1.53% (−6.07, 3.00), 1.28% (−4.30, 6.88), and 0.37% (−5.33, 6.09), respectively. Analogous patterns of change were observed for aerial BMD, OD, and BR. The trajectories of change for FS geometric parameters in women were more stable and showed less longitudinal variation. Average percent change in FS CSA was 2.19% (−1.51, 5.90) at two months, 1.70% (−2.26, 5.69) at six months, and 2.48% (−2.29, 7.27) at twelve months. Likewise, estimates of percent change in FS SM were 2.71% (−1.51, 6.94), 1.32% (−2.72, 5.37), and 2.64% (−1.85, 7.15). Aerial BMD, cortical width, and BR showed comparable prospective trends. Neither the time-specific differences nor the global interactions for any of the geometric parameters at the FN were statistically significant.

4.0 Discussion

The results showed that men had significantly different patterns of change in proximal femur structural strength compared to women after hip fracture. Women in BHS-7 generally experienced negligible changes with respect to the spatial distribution of bone tissue influencing structural strength. By contrast, men showed declines in CSA, SM, and increases in BR, particularly at the NN, where the estimated twelve-month differences in change reached statistical significance. In context, normal aging among women is associated with greater aerial BMD loss and increases to cortical outer diameter compared to men, as well as greater corresponding declines in bending strength and increases in susceptibility to local buckling [1,12,15,17]. However, our results imply that in the year following hip fracture the structural advantage of males may be reversed.

The findings from the current study suggest that women had non-significant increases in bone tissue, and in some instances, these changes to the spatial distribution of bone mineral were accompanied by minimal increases in bending strength and cortical stability. Previous BHS research has shown that women experience significant declines in BMD at the intertrochanteric region and femoral neck after hip fracture that are greater compared to community-dwelling older women [7,18–20]. Further, one study found decreases in cross-sectional bone area, bending strength, and cortical stability among women following hip fracture that were significantly greater compared to similar postmenopausal women with osteoporosis [21]. Current guidelines recommend long-term bisphosphonate treatment for osteoporosis, and bone-active drug use after hip fracture has increased since research has demonstrated decreases in the risk of subsequent fracture, mortality, and further BMD loss [33–35]. Prior BHS research used data from earlier cohorts, for example, the BHS 3rd cohort who were recruited from 1992 to 1995 [21]. During the BHS-7 recruitment time period from 2006 to 2010, prescriptions of bone-active drugs in the US increased from 21 million in 2002 to 31 million in 2007, and hip fracture incidence among American women decreased

over this same interval through 2012 [36,37]. Thus, more favorable bone geometry outcomes among women in BHS-7 may reflect improvements in osteoporosis management prior to and after hip fracture. Cohort effects and differences in study inclusion and exclusion criteria could also contribute to the divergence in results of the current study compared to previous research [21,23]. Specficially, differences in cohort characteristics or patient case mix may account for the observed findings because women experiencing hip fractures in the 21st century could have had different pre-fracture lifetime exposures compared to women who fractured when earlier BHS studies were conducted.

Men had significantly greater twelve-month decreases at the NN in the amount of cross-sectional bone area and declines in bending strength and increases in cortical instability that were significantly different compared to changes in women. Despite decreases in BMD over time, men have stable NN SM throughout life course, a result of enlargements to outer diameter that offset these decrements in the amount of bone tissue [1,12]. Unlike men, compensatory changes in bone structure among women that maintain bending strength occur in conjunction with significant increases in BR [13,17]. However, the findings of this study illustrate a different pattern of change in bone geometry in men who have sustained hip fracture compared to the changes associated with normal aging. The results of the current study are congruent with data suggesting greater post-fracture declines in total hip and femoral neck BMD in men compared to women and more closely resembles the documented patterns in bone geometry among women that occur in the context of aging [23]. The finding that these changes occurred disproportionately at the narrow neck are consistent with previous research indicating that long bone ends sustain more age-related BMD loss [38]. Aging predominantly impacts men at the neck region in the context of bone structure and strength, whereas women are affected at both the neck and intertrochanteric region, and low impact fractures at the NN are most common under the lowest structural mechanical strength levels [15,39]. Changes to bone geometry may put men at higher risk for subsequent fracture of the neck region at the contralateral hip, but what remains unclear from this study are the mediating mechanisms responsible for the greater losses in bone tissue, bending strength, and cortical stability.

Several factors may contribute to sex differences in hip bone geometry following hip fracture. Men have age-related accelerations in BMD decline later in life, while women experience attenuations in decline that may be due to prior decrements that start after menopause, and this divergence may affect the spatial distribution of bone tissue [23,40–42]. There also are hormonal changes in factors known to influence bone mineralization that occur post-fracture, such as Insulin-like growth hormone-1, parathyroid hormone, and osteocalcin, which could differentially affect bone formation and structure between men and women [22,43–45]. Further, osteoporosis is under-recognized in men and does not receive the same level of clinical attention [46]. Men are 10–20 times more likely to be under-treated with bisphosphonates and have lower rates of DXA referral and osteoporosis treatment initiation after hip fracture [47,48]. Disproportionately better osteoporosis care prior to and after hip fracture may lead to differences in musculoskeletal outcomes. Likewise, femoral bone structure and strength adapts to skeletal loading; that is, increases in weight loss and declines in physical performance are associated with poorer mechanical homeostasis [14,49,50]. Men are also generally in poorer health at the time of fracture (i.e.,

greater comorbidity), and if frailty following hip fracture occurs more frequently in men, physiological changes and a deconditioning of the body could result in losses to bone mass and strength. The pathways leading to sex differences in hip bone geometry are likely heterogeneous and comprised of a multitude of mechanisms.

There are limitations that should be considered when interpreting the results. Two types of DXA scanners were used, and this could have influenced the magnitude of the estimated percent changes within-sex. However, male and female hip fracture patients were matched on clinical site and thus DXA manufacturer; longitudinal sex differences were therefore independent of machine effects. The HSA method for measuring femur geometry has a number of intrinsic limitations, which have been described previously in detail elsewhere, and they are mainly a consequence of the two-dimensional nature of DXA images [24]. Femurs are three-dimensional objects, but the dimensions and the distribution of the mineral mass in the DXA scan depend strongly on how the femur is positioned in the projected image. Positioning uncertainties require larger samples and longer observation periods to detect subtle differences or changes in hip bone structure. The buckling ratio is, at best, a crude index of cortical instability based on an estimate of the average cortical thickness. It is well recognized that the femoral neck cortex is highly asymmetric and favors the physiologically loaded medial surface [51]. Use of the average cortex probably underestimates the contribution of local buckling to failure in a fall to the side, however, failure mechanisms cannot be reliably predicted from the rudimentary structural information present in a DXA scan. Concomitant medication use data was captured using self-reported questionnaires and information on compliance and adherence was not collected. The BHS-7 cohort primarily recruited white men and women from Baltimore metropolitan area and may lack generalizability to more ethnically and regionally diverse hip fracture samples. Last, there is the potential for confounding by unmeasured factors not included in the analysis.

Nonetheless, the various strengths of the study mitigate any potential sources of bias. BHS-7 is one of the largest cohorts of men and women hip fracture patients that was specifically designed to examine sex differences in the sequelae of hip fracture. Thus, comprehensive and relevant information was collected from clinical and patient-reported measures on a multitude of important confounders: body size and mass, comorbidity, physical function, and bone-active medications. The analytical approach also utilized methods to account for missing covariate and outcome data and truncation due to death. Our research is the first to evaluate sex differences in bone geometry after hip fracture and has yielded new information on how patterns of change in bone structure and strength differ between men and women.

5.0 Conclusions

The findings from the current study build upon previous research. First, women were shown to have minimal increases in bone structure and strength that were not significantly different from zero. Second, men experienced declines in the spatial distribution of bone tissue and reductions in mechanical bone strength at the NN region that were significantly different compared to women. The evidence indicates that men may be at greater subsequent risk for low impact fractures of the contralateral non-fractured hip and underscores the necessity for better clinical management of osteoporosis among men prior to and after hip fracture in

order to improve post-fracture musculoskeletal outcomes. Future research should ascertain how changes in hip bone geometry in men after hip fracture compare to the normal variation associated with aging and also attempt to identify the mediating mechanisms responsible for the observed sex differences in bone structure and strength.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Abbreviations

HSA	hip structural analysis
BMD	bone mineral density
CSA	cross-sectional area
OD	outer diameter
SM	section modulus
BR	buckling ratio
NN	narrow neck
IT	intertrochanteric region
FS	femoral shaft
BHS	Baltimore hip studies
DXA	dual-energy x-ray absorptiometry
IPW	inverse probability of observation weights
WEE	weighted generalized estimating equations

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Highlights

- Women generally showed non-significant increases in bone tissue, bending strength, and cortical stability following hip fracture
- Men experienced statistically greater one-year declines in cross-sectional bone area, bending strength, and cortical stability than women after hip fracture
- Men may be at increased risk for subsequent fracture of the non-fractured contralateral after incident hip fracture
- Findings underscore the need for better osteoporosis care among men prior to and after hip fracture

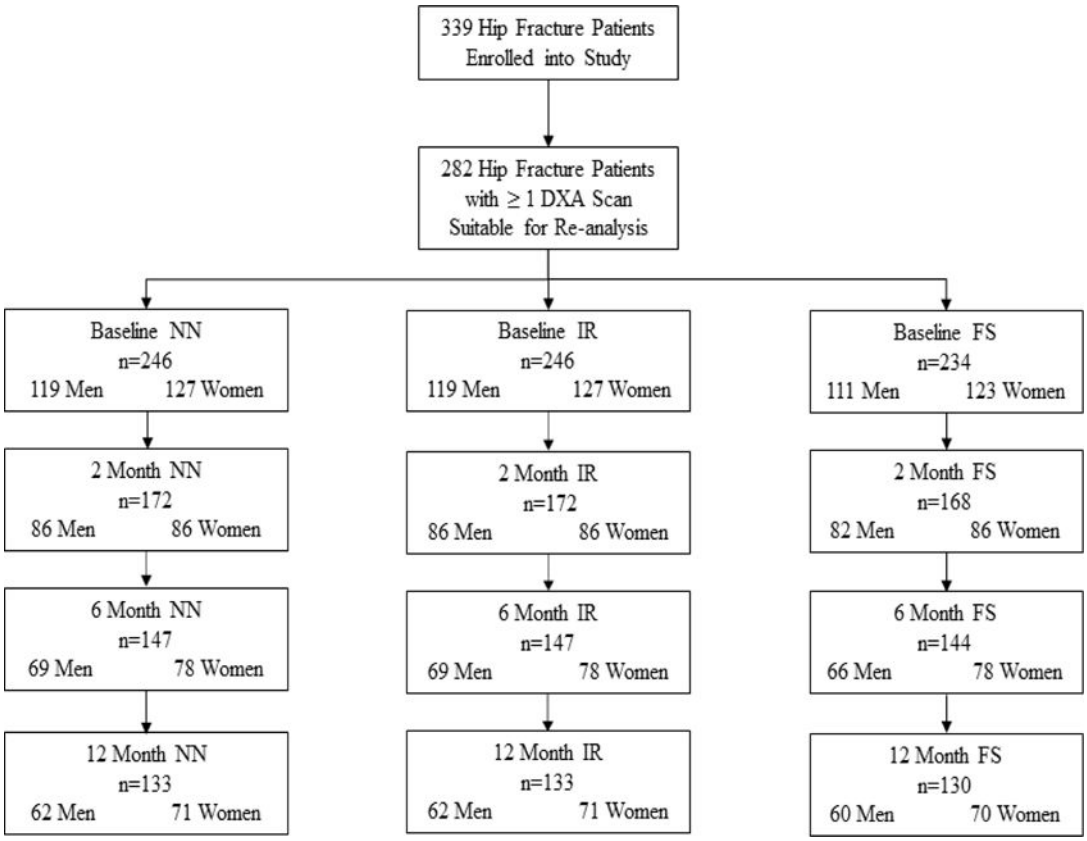

Figure 1.

Flow chart for HSA data in the three regions at each time point in the Baltimore Hip Studies 7th cohort.

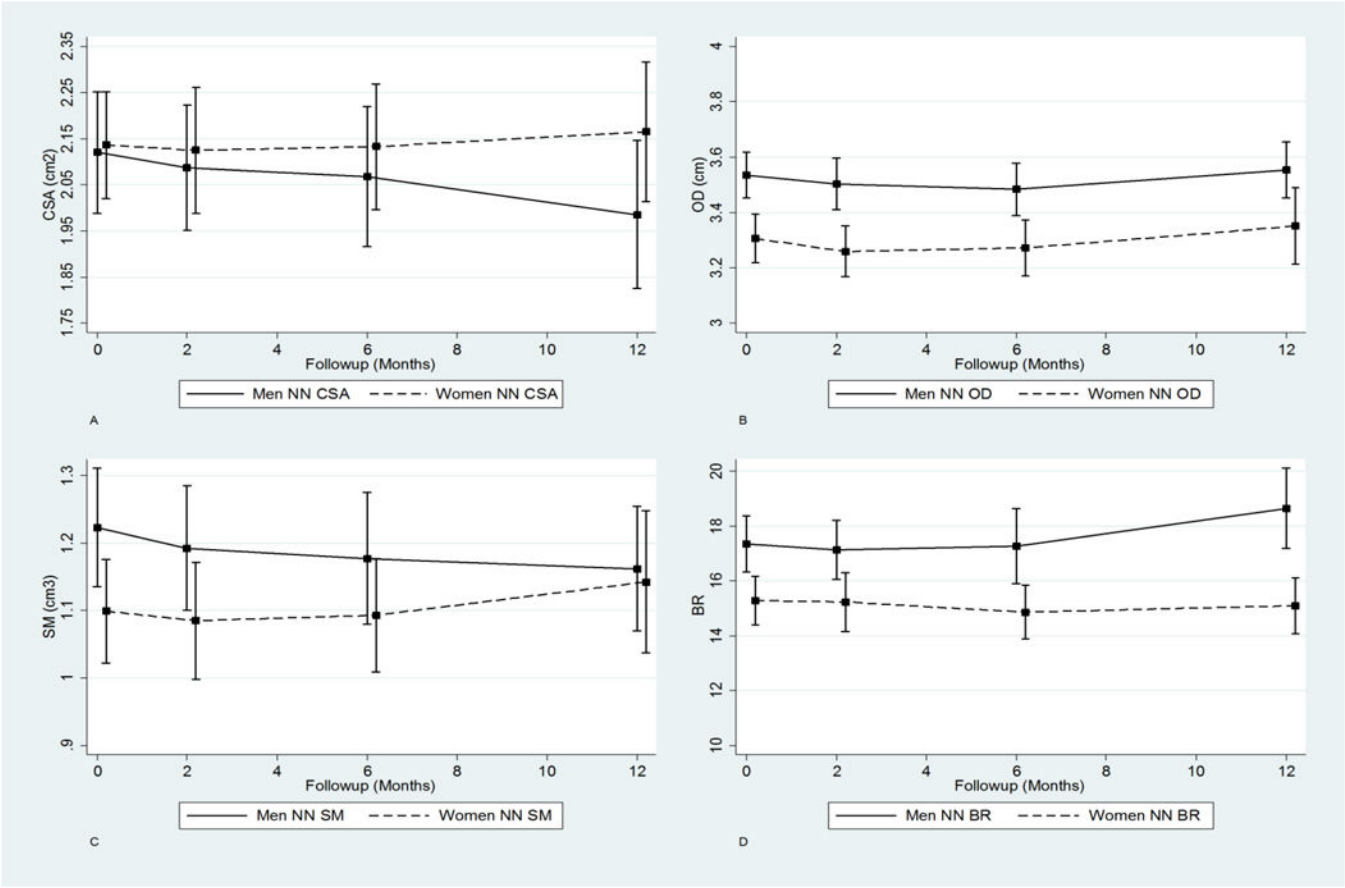

Figure 2.

Trajectory plots of adjusted absolute values for the one-year post fracture recovery period for NN CSA (A), OD (B), SM (C), and BR (D).

Table 1

Baseline characteristics among men and women with HSA data.

	Analytic Sample		
Variable	**Men (n=137)**	**Women (n=145)**	**P Value**
White (n, %)	123 (90.5%)	134 (93.7%)	0.32
Age (m, SD)	80.3 ± 7.7	81.0 ± 7.7	0.48
Weight (m, SD)	79.5 ± 14.1	63.4 ± 14.3	<0.0001
Height (m, SD)	1.8 ± 0.08	1.6 ± 0.08	<0.0001
Smoking (n, %)			
Never	30 (22.1%)	67 (46.5%)	<0.0001
Past	95 (69.9%)	68 (47.2%)	
Present	11 (8.1%)	9 (6.3%)	
Alcohol Use (n, %)			
None	53 (40.0%)	72 (50.0%)	0.089
Minimal	79 (58.1%)	65 (45.1%)	
Moderate	4 (2.9%)	7 (4.9%)	
Bone-Active Drugs (n, %)			
Never	123 (91.1%)	84 (58.3%)	<0.0001
Past	1 (0.7%)	21 (14.6%)	
Current	11 (8.2%)	39 (27.1%)	
Glucocorticoids			
Never	106 (80.3%)	91 (64.1%)	0.009
Past	17 (12.9%)	29 (20.4%)	
Current	9 (6.8%)	22 (15.5%)	
Hormone Therapy	4 (2.9%)	54 (37.5%)	<0.0001
Calcium Supplements (n, %)			
Never	96 (71.1%)	45 (31.5%)	<0.0001
Past	14 (10.4%)	17 (11.9%)	
Current	25 (18.5%)	81 (56.6%)	
Comorbidity (M, IQR)	2.5 ± 1.9	1.7 ± 1.6	0.0001
IADL (M, IQR)	2.2 ± 1.5	1.7 ± 1.5	0.0099
CES-D (m, SD)	17.0 ± 9.6	17.7 ± 11.2	0.55

Table 2

Adjusted baseline estimates and relative mean percent change at two, six, and twelve months follow-up in hip structural analysis narrow neck geometric parameters.

Time Point		Men			Women			
Aerial BMD	**% Change**	**95% CI**	*** P**	**% Change**	**95% CI**	*** P**	**** P**	***** P**
Baseline	0.62	(0.59, 0.66)	REF	0.67	(0.64, 0.70)	REF	0.109	0.418
Δ T2	−0.87	(−5.54, 3.78)	0.71	0.82	(−2.84, 4.51)	0.655	0.559	
Δ T6	−0.90	(−6.40, 4.55)	0.742	0.60	(−2.85, 4.10)	0.728	0.643	
Δ T12	−6.36	(−12.81, 0.06)	0.052	−0.14	(−4.05, 3.74)	0.939	0.11	
CSA								
Baseline	2.11	(1.98, 2.25)	REF	2.13	(1.98, 2.25)	REF	0.882	0.265
Δ T2	−1.52	(−6.17, 3.11)	0.518	−0.52	(−4.01, 2.96)	0.768	0.739	
Δ T6	−2.47	(−7.75, 2.80)	0.357	−0.14	(−3.95, 3.66)	0.941	0.491	
Δ T12	−6.33	(−12.47, −0.20)	0.043	1.37	(−3.31, 6.43)	0.565	0.049	
OD								
Baseline	3.53	(3.45, 3.61)	REF	3.30	(3.21, 3.39)	REF	0.004	0.807
Δ T2	−0.88	(−2.44, 0.66)	0.261	−1.42	(−2.92, 0.07)	0.063	0.683	
Δ T6	−1.46	(−3.25, 0.32)	0.109	−1.03	(−2.76, 0.69)	0.239	0.694	
Δ T12	0.52	(−1.32, 2.38)	0.575	1.35	(−1.38, 4.08)	0.332	0.649	
SM								
Baseline	1.22	(1.13, 1.31)	REF	1.09	(1.02, 1.17)	REF	0.087	0.245
Δ T2	−2.48	(−7.63, 2.64)	0.341	−1.27	(−5.14, 2.58)	0.515	0.678	
Δ T6	−3.76	(−9.64, 2.10)	0.207	−0.53	(−5.03, 3.95)	0.813	0.371	
Δ T12	−4.98	(−11.08, 1.10)	0.108	3.94	(−2.51, 10.42)	0.23	0.042	
BR								
Baseline	17.34	(16.31, 18.37)	REF	15.27	(14.40, 16.15)	REF	0.012	0.176
Δ T2	−1.20	(−6.22, 3.81)	0.636	−0.32	(−6.04, 5.38)	0.909	0.795	

Time Point	Men			Women				
Aerial BMD	**% Change**	**95% CI**	***P**	**% Change**	**95% CI**	***P**	****P**	*****P**
Δ T6	−0.47	(−6.87, 5.92)	0.884	−2.74	(−6.96, 1.46)	0.2	0.609	
Δ T12	7.50	(0.65, 14.36)	0.032	−1.20	(−6.41, 4.00)	0.65	0.044	

BMD: Bone Mineral Density; CSA: Cross Sectional Area; SM: Section Modulus; BR: Buckling Ratio.

*
P value for sex- and time-specific changes;

**
P values for the time-specific differences in change;

***
P value for the global test of the sex by time interaction.

Table 3

Adjusted baseline estimates and relative mean percent change at two, six, and twelve months follow-up in hip structural analysis intertrochanteric region geometric parameters.

Time Point		**Men**			**Women**			
Aerial BMD	**% Change**	**95% CI**	*** P**	**% Change**	**95% CI**	*** P**	**** P**	***** P**
Baseline	0.66	(0.62, 0.70)	REF	0.64	(0.61, 0.68)	REF	0.668	0.382
Δ T2	−1.26	(−6.22, 3.67)	0.613	2.63	(−1.58, 6.89)	0.221	0.235	
Δ T6	0.71	(−5.04, 6.48)	0.807	0.86	(−2.96, 4.69)	0.658	0.971	
Δ T12	−4.23	(−10.94, 2.44)	0.214	0.43	(−3.73, 4.61)	0.836	0.246	
CSA								
Baseline	3.80	(3.56, 4.03)	REF	3.5193	(3.33, 3.70)	REF	0.11	0.232
Δ T2	−2.66	(−7.90, 2.56)	0.317	1.89	(−1.84, 5.63)	0.319	0.164	
Δ T6	0.61	(−5.15, 6.39)	0.834	0.35	(−3.25, 5.63)	0.847	0.933	
Δ T12	−4.07	(−10.83, 2.67)	0.236	0.41	(−3.41, 4.24)	0.831	0.252	
OD								
Baseline	5.99	(5.88, 6.10)	REF	5.69	(5.59, 5.78)	REF	0.002	0.775
Δ T2	1.22	(−2.66, 0.20)	0.092	−0.85	(−1.94, 0.23)	0.124	0.64	
Δ T6	0.09	(−1.47, 1.66)	0.906	−0.41	(−1.70, 0.88)	0.532	0.628	
Δ T12	0.56	(−0.83, 1.96)	0.429	−0.02	(−1.48, 1.44)	0.976	0.562	
SM								
Baseline	3.91	(3.64, 4.19)	REF	3.28	(3.10, 3.46)	REF	0.001	0.048
Δ T2	−4.32	(−10.49, 1.83)	0.168	0.61	(−3.13, 4.36)	0.745	0.162	
Δ T6	1.14	(−5.37, 7.66)	0.730	−2.89	(−7.07, 1.28)	0.174	0.342	
Δ T12	−4.78	(−12.10, 5.53)	0.199	−0.31	(−4.75, 4.11)	0.888	0.287	
BR								
Baseline	13.47	(12.59, 14.34)	REF	13.18	(12.38, 13.99)	REF	0.703	0.571
Δ T2	0.86	(−3.54, 5.27)	0.70	2.51	(−4.40, 9.44)	0.474	0.689	

Time Point	Men			Women				
Aerial BMD	% Change	95% CI	* P	% Change	95% CI	* P	** P	*** P
Δ T6	−0.67	(−5.90, 4.54)	0.799	1.85	(−3.27, 6.97)	0.477	0.494	
Δ T12	4.59	(−0.65, 9.84)	0.086	1.52	(−4.23, 7.28)	0.602	0.425	

BMD: Bone Mineral Density; CSA: Cross Sectional Area; SM: Section Modulus; BR: Buckling Ratio.

*
P value for sex- and time-specific changes;

**
P values for the time-specific differences in change;

***
P value for the global test of the sex by time interaction.

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Table 4

Adjusted baseline estimates and relative mean percent change at two, six, and twelve months follow-up in hip structural analysis femoral shaft geometric parameters.

Time Point		**Men**			**Women**			
Aerial BMD	**% Change**	**95% CI**	*** P**	**% Change**	**95% CI**	*** P**	**** P**	***** P**
Baseline	1.27	(1.19, 1.34)	REF	1.12	(1.05, 1.19)	REF	0.025	0.813
Δ T2	−0.72	(−5.12, 3.64)	0.741	1.27	(−2.75, 5.31)	0.533	0.514	
Δ T6	2.27	(−2.91, 7.47)	0.388	1.31	(−2.71, 5.35)	0.521	0.727	
Δ T12	0.21	(−5.46, 5.90)	0.939	1.17	(−3.92, 6.29)	0.649	0.822	
CSA								
Baseline	3.87	(3.64, 4.10)	REF	3.33	(3.12, 3.53)	REF	0.005	0.526
Δ T2	−0.94	(−5.23, 3.33)	0.662	2.19	(−1.51, 5.90)	0.245	0.299	
Δ T6	2.28	(−2.97, 7.54)	0.394	1.70	(−2.26, 5.69)	0.398	0.798	
Δ T12	0.13	(−5.38, 5.66)	0.96	2.48	(−2.29, 7.27)	0.307	0.568	
OD								
Baseline	3.19	(3.13, 3.24)	REF	3.07	(3.02, 3.13)	REF	0.019	0.406
Δ T2	−0.40	(−1.77, 0.96)	0.557	1.96	(−1.48, 5.41)	0.263	0.208	
Δ T6	−0.07	(−1.49, 1.33)	0.912	0.76	(−0.51, 2.04)	0.242	0.406	
Δ T12	0.12	(−1.61, 1.87)	0.883	1.85	(0.29, 3.42)	0.02	0.167	
SM								
Baseline	2.35	(2.21, 2.49)	REF	1.99	(1.87, 2.10)	REF	0.002	0.447
Δ T2	−1.53	(−6.07, 3.00)	0.507	2.71	(−1.51, 0.694)	0.208	0.196	
Δ T6	1.28	(−4.30, 6.88)	0.651	1.32	(−2.72, 5.37)	0.52	0.96	
Δ T12	0.37	(−5.33, 6.09)	0.896	2.64	(−1.85, 7.15)	0.248	0.596	
BR								
Baseline	3.85	(3.52, 4.18)	REF	4.38	(4.05, 4.72)	REF	0.076	0.713
Δ T2	−0.18	(−6.14, 5.76)	0.95	6.57	(−6.24, 19.39)	0.313	0.336	

Time Point	Men			Women				
Aerial BMD	% Change	95% CI	* P	% Change	95% CI	* P	** P	*** P
Δ T6	−1.00	(−7.45, 5.45)	0.76	−2.17	(−7.68, 3.34)	0.439	0.741	
Δ T12	0.88	(−6.39, 8.18)	0.81	2.68	(−4.46, 9.83)	0.461	0.695	

BMD: Bone Mineral Density; CSA: Cross Sectional Area; SM: Section Modulus; BR: Buckling Ratio.

* P value for sex- and time-specific changes;

** P values for the time-specific differences in change;

*** P value for the global test of the sex by time interaction.