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Hip Geometry in Diabetic Women: Implications for Fracture Risk

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Abstract

Objective—Women with type 2 diabetes mellitus (T2DM) have a higher risk of fractures despite increased bone mineral density (BMD) as compared to women without diabetes. We hypothesized that bone strength is diminished in women with T2DM after accounting for lean body mass, which may contribute to their increased fracture risk.

Methods—Participants from Women's Health Initiative Observational Study were included in this cross-sectional study. These analyses include 3 groups of women: 1) T2DM women on diet or oral hypoglycemic agents (n=299); 2) T2DM women on insulin therapy (with or without oral agents) (n=128); and 3) Non-diabetic control women (n=5497). Hip structural analyses were done using the validated Beck's method on hip scans from dual energy x-ray absorptiometry (DXA). We compared BMD and section modulus (bending strength) at the narrow neck with and without correcting for total body DXA lean body mass.

Results—Women in all three groups were of similar ages (63.7, 64.6 and 64.2 years, respectively) and heights, but those with T2DM were heavier, with greater lean body weight vs. controls (p<0.001). In both diabetic groups, absolute BMD and section modulus were higher compared with controls. However, after adjusting for total lean body weight, diabetic women on insulin had significantly lower BMD and section modulus.

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Disclosure Statement: TB is co-founder of Quantum Medical metrics LLC which is developing technology and software for evaluating bone structure. His former employer, the Johns Hopkins University receives royalties from Hologic Inc. on the HSA software used in this study with a share to TB. Other authors have no conflict of interest.

Author contributions: RG and MSL conceived the idea, interpreted data and wrote the manuscript; TB conducted bone structural analysis; GW performed statistical analyses; ZC, JAC, DN, BL and AL helped in interpretation of data and reviewed the manuscript.

Conclusion—Adjusted for lean body weight, the BMD and bending strength in the femoral neck are significantly lower in insulin - treated diabetic women vs. controls. This may represent altered adaptation of bone modeling and explain the higher fracture risk in patients with T2DM.

Keywords

Bone Geometry; Diabetes mellitus; Hip structural analysis; Women's Health Initiative Study

Introduction

Diabetes and osteoporosis are major public health problems that affect 220 million and 200 million individuals, respectively, worldwide [1, 2]. Among diabetic patients, 90% have type 2 diabetes mellitus (T2DM) [1]. Although, the risk of both T2DM and osteoporosis increases with age, individuals with T2DM tend to have a higher bone mineral density (BMD) and higher body mass index, both of which should be protective against fractures [3, 4]. However, recent large studies and a meta-analysis showed that compared with non-diabetic controls, individuals with T2DM have a greater fracture risk that suggests reduced bone strength despite the higher BMD [3, 5–9]. In addition, the FRAX score used to clinically indicate projected fracture risk is increased regardless of hip BMD in subjects with T2DM compared to those without diabetes [10].

While BMD is a useful measure in clinical practice it does not actually measure the property of bone that determines its mechanical strength and it is not helpful in determining the underlying causes of bone fragility in T2DM. Bones fracture when loading forces cause stresses (force concentrations) to exceed the stress limits of the bone tissue. Bones may be relatively weak in T2DM if the bone dimensions (structural geometry) are insufficient to support the skeletal loads in these subjects or if the bone tissue degrades so that it fails at lower levels of stress [11]. Although tissue material properties can only be measured by invasive (biopsy) methods, bone geometry can be measured by several imaging methods. One such method, Hip Structure Analysis (HSA), provides limited geometry of bone cross-sections to be derived from the data generated by dual energy X-ray absorptiometry (DXA) used for BMD measurements.

Forces on the femur generated by physiological activities and common trauma generate a combination of axial compression and bending stresses. Two important parameters that define resistance of a cross-section of bone to these stresses are the bone cross-sectional area (CSA) and the section modulus which can be extracted from DXA data by the HSA program. The CSA is a measure of the total bone surface in the cross-section excluding marrow and other soft tissue and spaces. Section modulus is computed from the second moment of area (SMA) which is the surface area of the cross-section weighted by the square of distance from the center of mass of the cross-section. Section modulus is then the SMA divided by the distance from the center of mass to the farthest outer cortical margin. Geometric parameters measured by the HSA method have been previously demonstrated to be predictive of fracture risk [12].

Despite the high prevalence of diabetes and concomitant increased fracture risk, there are very few studies that have evaluated hip structure in women with T2DM [13]. In this study, we tested whether there were alterations in hip structure among women with T2DM compared with non-diabetic, control women enrolled in the large Women's Health Initiative Observational Study (WHI-OS).

Methods

This study includes 5924 postmenopausal women who were part of the WHI-OS bone density cohort. Women were recruited for this cohort at three of the forty WHI clinical centers, Tucson and Phoenix AZ, Pittsburgh PA and Birmingham AL between 1993 and 1998. Informed consent was obtained from all of the participants. Women were 50–79 years of age at study entry. Study inclusion criteria included a self-reported positive history of diabetes or a history of treatment with an anti-diabetic medication. T2DM was defined as a diagnosis at age >20 years with no history of diabetic coma. Use of insulin or pills for diabetes was provided by self-report.

Baseline hip bone density and body composition were measured using conventional DXA scans (Hologic, Bedford MA) and image data were archived at the WHI coordinating center. All scan data were stored in computers and available for this study. Validated HSA was performed at Johns Hopkins University on nearly all of the available DXA scans in WHI, and results have been presented in several previously published analyses [14–16]. The HSA program processes the DXA image to remove soft tissue and organic material from within and surrounding the bone leaving only bone mineral mass. The program uses the principle that a line of pixels traversing the bone axis is a projection of the cross-section at that point and can be used to compute certain geometric dimensions of the cross-section [17]. Bone geometry is computed from averages of 5 parallel lines ~1mm apart traversing the bone axis at 3 femur regions. The three regions include: femur neck at its narrowest point, the shaft at a distance of 1.5 times the minimum neck width distal to the intersection of neck and shaft axes and the intertrochanter region across the angle bisector of the neck and shaft axes. For each region, the distribution of the bone mass across the bone is extracted; the outer diameter (OD cm) is measured from the blur corrected outer margins of the profiles. Bone cross-sectional area (CSA, cm²), and second moment of area (SMA, cm⁴), are measured directly from mass profile integrals. Section modulus, an indicator of *bending strength*, is calculated as SMA divided by the maximum distance from the center of mass to the outer cortical margin. BMD (g/cm²) is calculated in the conventional manner, although these regions of interest do not have exact counterparts in the conventional BMD analyses provided by the manufacturer. Therefore, absolute BMD values may differ. The program also computes the neck-shaft angle and femoral neck length, as well as a number of other parameters not used in this report.

Statistical Analyses

Differences in baseline characteristics between diabetic and non-diabetic women were analyzed with ANOVA or Chi square tests as appropriate. Primary analysis was the comparison of section modulus for all regions of study between the 3 groups, non-diabetic women, diabetic women not on insulin and diabetic women on insulin unadjusted and after adjusting for age, height, weight, lean body weight, alcohol intake, race, use of other drugs including calcium and vitamin D, neck-shaft angle (in degrees), femur neck length, physical activity and HT usage. In evaluation of potential confounding factors, models with and without the covariate were compared to examine the change of regression coefficient after considering the biological plausibility. A 10% of relative change in coefficient was used as statistical standard to select the covariates.

Since BMD and bone strength are proportional to lean body mass and the lean body mass differs between diabetic vs. non-diabetic women, we also compared the ratios of BMD, CSA and section modulus to lean body mass as previously reported [18]. All continuous data are presented as means with standard deviation (SD) and categorical data are presented as number and percentage. Significance level for all analysis was set at $p < 0.05$.

Results

Baseline characteristics of the 3 groups are shown in Table 1. Of the 5924 women included in our study, 427 women had a history suggestive of T2DM, 128 women were on insulin and 5497 women had no history of diabetes. Women with diabetes were older, had higher body weight and BMI, were more likely to belong to black race and had lower calcium and vitamin D intake. Bone density and bone geometry data are shown in Table 2. Overall spine and hip BMD were higher in diabetic women compared with non-diabetic women. Similarly many of the bone geometry measures that depend on body and bone size were higher in the diabetic women, irrespective of their insulin use. After adjusting for multiple risk factors for osteoporosis, the differences between non-diabetic women and insulin-treated, diabetic women disappeared (Table 2). As noted in Table 1, diabetic women have more lean mass than non-diabetic women but it is a relatively smaller fraction of their total body mass. When section modulus, CSA and BMD were scaled to lean body mass, the ratios were significantly lower in the insulin treated women as compared to the non-diabetic women (Figure 1).

Discussion

Diabetes mellitus is a highly prevalent disease that is associated with an increased risk of fragility fractures [9]. In the WHI-OS, the relative risk of incident fractures in women with T2DM was significantly higher when compared with non-diabetic women even after adjusting for age, weight, height, falls and poor vision [8]. Our data show that absolute BMD was higher in women with T2DM as compared to non-diabetic control women as were most of the geometry variables. However, section modulus, CSA and BMD each normalized to lean body mass were lower in diabetic women on insulin compared with controls or non-insulin treated women with T2DM. This may be a particularly important finding as it suggests that there may be a defect in the relationship between bone strength and mechanical load among diabetic women on insulin.

Bone health depends muscle contraction from physical activity and femur geometry scales in proportion to lean mass [18, 19]. Lean body mass is predominantly muscle and this is consistent with the theories that bone adapts primarily to dynamic muscle loads [20] and that the size of those loads are approximated by the size (mass) of muscle. In our study insulin treated women had significantly higher BMD and stronger bone geometries in absolute terms, consistent with their heavier bodies. However when BMD and geometries were expressed relative to their lean masses, the relationship reversed. BMD and geometric indices of bone resistance to axial (CSA) and bending (section modulus) forces were significantly lower than in non-diabetic women. These data also indicate that this relative bone structural weakening is evident only in the presence of a more severe disease, i.e. when insulin is required for treatment of diabetes. Since insulin is an anabolic hormone, weaker bones in women with T2DM treated with insulin are probably indicative of more severe disease. A recent study found that lean mass was associated with hip strength in women and men with non-insulin dependent T2DM [21]. In addition, in a pilot study of 19 subjects enrolled from a diabetes outpatient setting, use of high resolution, peripheral computed tomography showed that cortical porosity was significantly higher in women with T2DM as compared to matched non-diabetic control women [22]. These data suggest that bones of diabetic women are relatively weaker than those of non-diabetic women. Although the mechanism and the details remain unclear it does appear that the disease tends to diminish the response of bone to mechanical stimuli. This may help to explain the consistent reports showing that unadjusted clinical BMD is higher among diabetics despite their clearly increased fragility.

Mechanisms of increased fracture risk in diabetes are likely to be multi-factorial. One study suggested decreased muscle strength and quality despite increased lean body mass in patients with T2DM [23]. Therefore, bones may be subjected to reduced muscle loads in T2DM compared to non-diabetic subjects for the same lean body mass. Moreover, diabetes may affect physical activity and therefore weaken bone structure. Autonomic neuropathy in patients with more severe T2DM may mechanistically contribute to reduced bone strength or the presence of peripheral neuropathy may impair their ability to prevent a fall [24, 25]. Patients with T2DM also have several systemic changes that could affect bone formation especially in response to load stimuli [26]. Changes in adipokine levels e.g. adiponectin and leptin may also affect bone formation but the available data are contradictory [27–31]. Another potential mechanism for reduced bone strength and skeletal fragility in patients with advanced T2DM may be an increase in circulating cytokines and activation of NF κ B [32]. Increased levels of circulating cytokines are associated with increased risk of fractures [33]. Glycation end products in the bone may be another mechanism of impaired bone strength in advanced diabetes [34]. Association of low levels of endogenous receptor for advanced glycation end products with vertebral fractures in diabetic patients is consistent with the role of glycation end products in causing bone damage [35]. Diabetic patients may also have lower calcium intake and are more likely to have renal insufficiency and less likely to exercise. In this study, diabetic patients had lower intake of calcium and vitamin D and lower alcohol intake. They were also less likely to have a history of HT usage. All these factors except lower alcohol intake may contribute to lower bone strength. Thiazolidinedione drugs are associated with adverse bone effects but are unlikely to affect the results of this study because our study participants were enrolled before these drugs became commercially available for clinical use.

A limitation of our study is that it may be difficult to translate to the clinical setting with current technologies. First it requires measurement of lean body mass thus requiring a DXA scanner with that capability. Secondly while two different manufacturers of DXA scanners provide software for measuring proximal femur geometry (Hologic and GE/Lunar), the method is relatively imprecise. This is mainly because the hip is 3-dimensional but the image is 2-dimensional. Due to anatomical variations and other factors it is difficult to consistently position the proximal femur in the clinical setting for geometry measurements. A measurement reliable enough for clinical use may ultimately require improvements in the scanner technology. . In addition, some insulin requiring women may actually have type 1 diabetes but this number is likely to be small because the majority of women were relatively old, obese and started taking insulin after the age of 40 years. Because they were not screened for diabetes, some women in the non-diabetic group may have unrecognized diabetes. However, this will make the differences between the two groups less significant. Therefore, we believe that our findings are applicable to women with T2DM.

In conclusion, women with insulin treated T2DM have lower BMD and bone strength relative to their lean body mass when compared with non-diabetic women. This finding in conjunction with other factors may explain their high risk for fractures.

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Abbreviations

T2DM	Type 2 diabetes mellitus
BMD	Bone mineral density
HSA	Hip structural analysis
DXA	Dual energy x-ray absorptiometry
NN	Narrow neck
PRA	Plasma renin activity
HOMA	Homeostasis model assessment
WHI-OS	Women's Health Initiative Observational Study
CSA	Cross-sectional area
SMA	Second moment of area

References

1. <http://www.who.int/mediacentre/factsheets/fs312/en/>
2. <http://www.iofbonehealth.org/health-professionals/about-osteoporosis/epidemiology.html>
3. de L II, van der Klift M, de Laet CE, et al. Bone mineral density and fracture risk in type-2 diabetes mellitus: the Rotterdam Study. *Osteoporos Int.* 2005; 16(12):1713–1720. [PubMed: 15940395]
4. Strotmeyer ES, Cauley JA, Schwartz AV, et al. Diabetes is associated independently of body composition with BMD and bone volume in older white and black men and women: The Health, Aging, and Body Composition Study. *J Bone Miner Res.* 2004; 19(7):1084–1091. [PubMed: 15176990]
5. Strotmeyer ES, Cauley JA, Schwartz AV, et al. Nontraumatic fracture risk with diabetes mellitus and impaired fasting glucose in older white and black adults: the health, aging, and body composition study. *Arch Intern Med.* 2005; 165(14):1612–1617. [PubMed: 16043679]
6. Robbins J, Aragaki AK, Kooperberg C, et al. Factors associated with 5-year risk of hip fracture in postmenopausal women. *JAMA.* 2007; 298(20):2389–2398. [PubMed: 18042916]
7. Lipscombe LL, Jamal SA, Booth GL, et al. The risk of hip fractures in older individuals with diabetes: a population-based study. *Diabetes Care.* 2007; 30(4):835–841. [PubMed: 17392544]
8. Bonds DE, Larson JC, Schwartz AV, et al. Risk of fracture in women with type 2 diabetes: the Women's Health Initiative Observational Study. *J Clin Endocrinol Metab.* 2006; 91(9):3404–3410. [PubMed: 16804043]
9. Vestergaard P. Discrepancies in bone mineral density and fracture risk in patients with type 1 and type 2 diabetes--a meta-analysis. *Osteoporos Int.* 2007; 18(4):427–444. [PubMed: 17068657]
10. Schwartz AV, Vittinghoff E, Bauer DC, et al. Association of BMD and FRAX score with risk of fracture in older adults with type 2 diabetes. *JAMA.* 2011; 305(21):2184–2192. [PubMed: 21632482]
11. Bouxsein ML. Mechanisms of osteoporosis therapy: a bone strength perspective. *Clin Cornerstone.* 2003; (Suppl 2):S13–S21. [PubMed: 15035555]
12. Melton LJ 3rd, Beck TJ, Amin S, et al. Contributions of bone density and structure to fracture risk assessment in men and women. *Osteoporos Int.* 2005; 16(5):460–467. [PubMed: 15688123]
13. Ishii S, Cauley JA, Crandall CJ, et al. Diabetes and femoral neck strength: findings from the Hip Strength Across the Menopausal Transition Study. *J Clin Endocrinol Metab.* 2012; 97(1):190–197. [PubMed: 22072739]
14. Beck TJ, Ruff CB, Warden KE, et al. Predicting femoral neck strength from bone mineral data. A structural approach. *Invest Radiol.* 1990; 25(1):6–18. [PubMed: 2298552]
15. Chen Z, Qi L, Beck TJ, et al. Stronger bone correlates with African admixture in African-American women. *J Bone Miner Res.* 2011; 26(9):2307–2316. [PubMed: 21590740]

16. Nelson DA, Beck TJ, Wu G, et al. Ethnic differences in femur geometry in the women's health initiative observational study. *Osteoporos Int.* 2011; 22(5):1377–1388. [PubMed: 20737265]
17. Martin RB, Burr DB. Non-invasive measurement of long bone cross-sectional moment of inertia by photon absorptiometry. *J Biomech.* 1984; 17(3):195–201. [PubMed: 6736056]
18. Beck TJ, Petit MA, Wu G, et al. Does obesity really make the femur stronger? BMD, geometry, and fracture incidence in the women's health initiative-observational study. *J Bone Miner Res.* 2009; 24(8):1369–1379. [PubMed: 19292617]
19. Travison TG, Araujo AB, Esche GR, et al. Lean mass and not fat mass is associated with male proximal femur strength. *J Bone Miner Res.* 2008; 23(2):189–198. [PubMed: 17922610]
20. Beck TJ, Oreskovic TL, Stone KL, et al. Structural adaptation to changing skeletal load in the progression toward hip fragility: the study of osteoporotic fractures. *J Bone Miner Res.* 2001; 16(6):1108–1119. [PubMed: 11393788]
21. Moseley KF, Dobrosielski DA, Stewart KJ, et al. Lean mass predicts hip geometry in men and women with non-insulin-requiring type 2 diabetes mellitus. *J Clin Densitom.* 2011; 14(3):332–339. [PubMed: 21652249]
22. Burghardt AJ, Issever AS, Schwartz AV, et al. High-resolution peripheral quantitative computed tomographic imaging of cortical and trabecular bone microarchitecture in patients with type 2 diabetes mellitus. *J Clin Endocrinol Metab.* 2010; 95(11):5045–5055. [PubMed: 20719835]
23. Park SW, Goodpaster BH, Strotmeyer ES, et al. Decreased muscle strength and quality in older adults with type 2 diabetes: the health, aging, and body composition study. *Diabetes.* 2006; 55(6):1813–1818. [PubMed: 16731847]
24. Eleftheriou F, Ahn JD, Takeda S, et al. Leptin regulation of bone resorption by the sympathetic nervous system and CART. *Nature.* 2005; 434(7032):514–520. [PubMed: 15724149]
25. Patel S, Hyer S, Tweed K, et al. Risk factors for fractures and falls in older women with type 2 diabetes mellitus. *Calcif Tissue Int.* 2008; 82(2):87–91. [PubMed: 18175036]
26. Schwartz AV, Sellmeyer DE. Diabetes, fracture, and bone fragility. *Curr Osteoporos Rep.* 2007; 5(3):105–111. [PubMed: 17925191]
27. Barbour KE, Zmuda JM, Boudreau R, et al. Adipokines and the risk of fracture in older adults. *J Bone Miner Res.* 2011; 26(7):1568–1576. [PubMed: 21312272]
28. Napoli N, Pedone C, Pozzilli P, et al. Adiponectin and bone mass density: The InCHIANTI study. *Bone.* 2010; 47(6):1001–1005. [PubMed: 20804877]
29. Kanazawa I, Yamaguchi T, Sugimoto T. Baseline serum total adiponectin level is positively associated with changes in bone mineral density after 1-year treatment of type 2 diabetes mellitus. *Metabolism.* 2010; 59(9):1252–1256. [PubMed: 20045535]
30. Kontogianni MD, Dafni UG, Routsias JG, et al. Blood leptin and adiponectin as possible mediators of the relation between fat mass and BMD in perimenopausal women. *J Bone Miner Res.* 2004; 19(4):546–551. [PubMed: 15005840]
31. Vasilkova O, Mokhort T, Sharshakova T, et al. Leptin is an independent determinant of bone mineral density in men with type 2 diabetes mellitus. *Acta Diabetol.* 2011
32. Pieper GM, Riaz ul H. Activation of nuclear factor-kappaB in cultured endothelial cells by increased glucose concentration: prevention by calphostin C. *J Cardiovasc Pharmacol.* 1997; 30(4):528–532. [PubMed: 9335415]
33. Cauley JA, Danielson ME, Boudreau RM, et al. Inflammatory markers and incident fracture risk in older men and women: the Health Aging and Body Composition Study. *J Bone Miner Res.* 2007; 22(7):1088–1095. [PubMed: 17419681]
34. Tang SY, Vashishth D. Non-enzymatic glycation alters microdamage formation in human cancellous bone. *Bone.* 2010; 46(1):148–154. [PubMed: 19747573]
35. Yamamoto M, Yamaguchi T, Yamauchi M, et al. Low serum level of the endogenous secretory receptor for advanced glycation end products (esRAGE) is a risk factor for prevalent vertebral fractures independent of bone mineral density in patients with type 2 diabetes. *Diabetes Care.* 2009; 32(12):2263–2268. [PubMed: 19752174]

Figure 1.

A, B, C: Comparison of the ratios of bone measurements to total lean body mass. The ratios in non-diabetic women were normalized to 1 and those in diabetic women were expressed relative to non-diabetic women. * $P < 0.05$. ** $P < 0.01$ compared with Non-diabetes.

Table 1

The characteristics of the women in the BMD OS cohort by diabetes cohort

	No diabetes (n=5497)	Diabetes, without insulin use (n=299)	Diabetes, with Insulin use (n=128)
Age	63.7 ± 7.4	64.6 ± 7.2 *	64.2 ± 7.3
Height (cm)	161.6 ± 6.5	160.1 ± 6.6 **	161.8 ± 6.6
Weight (kg)	71.9 ± 16.4	80.3 ± 18.9 **	83.5 ± 17.8 **
Body Mass index (kg/m ²)	27.4 ± 5.8	31.2 ± 7.0 **	31.9 ± 6.8 **
Whole body soft lean mass (kg)	37.10 ± 5.11	39.92 ± 6.09 **	43.51 ± 6.22 **
Whole body fat mass (kg)	31.10 ± 11.31	36.51 ± 12.5 **	37.02 ± 12.72 **
Whole body % lean mass (%)	53.95 ± 7.22	51.85 ± 6.49 **	53.77 ± 7.37
Ethnicity		**	**
Non-Hispanic White	4391 (79.9%)	169 (56.5%)	55 (43.0%)
Black	647 (11.8%)	74 (24.7%)	59 (46.1%)
Hispanic	396 (7.2%)	36 (12%)	6 (4.7%)
American Indian	63 (1.1%)	20 (6.7%)	8 (6.3%)
Smoking			
Never smoked	2927 (54%)	170 (58.8%)	66 (52.4%)
Past smoker	2092 (38.6%)	92 (31.8%)	47 (37.3%)
Current smoker	401 (7.4%)	27 (9.3%)	13 (10.3%)
Alcohol intake		**	**
Non drinker	958 (17.6%)	88 (29.9%)	35 (27.6%)
Past drinker	1117 (20.5%)	105 (35.7%)	57 (44.9%)
<1 drink per month	677 (12.4%)	35 (11.9%)	10 (7.9%)
<1 drink per week	1036 (19%)	35 (11.9%)	14 (11%)
1 - <7 drinks per week	1163 (21.3%)	22 (7.5%)	11 (8.7%)
Fracture history			
No	3282 (61.8%)	191 (66.6%)	74 (59.7%)
Yes	2025 (38.2%)	96 (33.4%)	50 (40.3%)
History of fracture on/after age			
55			
No	3424 (82%)	206 (85.8%)	87 (82.9%)
Yes	750 (18%)	34 (14.2%)	18 (17.1%)
Age first told had diabetes less than 21	NA	6 (2.1%)	6 (4.7%)
21–29	NA	6 (2.1%)	6 (4.7%)
30–39	NA	20 (6.8%)	16 (12.6%)
40–49	NA	45 (15.4%)	37 (29.1%)
50–59	NA	102 (34.9%)	38 (29.9%)
60–69	NA	92 (31.5%)	22 (17.3%)
70 or older	NA	21 (7.2%)	2 (1.6%)
Total Calcium intake (mg)	1126.5 ± 718.2	963.1 ± 621.9 **	824.4 ± 559.5 **

	No diabetes (n=5497)	Diabetes, without insulin use (n=299)	Diabetes, with Insulin use (n=128)
Calcium supplements intake		**	**
No	2676 (48.7%)	196 (65.6%)	89 (69.5%)
Yes	2821 (51.3%)	103 (34.4%)	39 (30.5%)
Total Vitamin D intake (mcg)	9.5 ± 7.0	8.6 ± 6.9 **	7.7 ± 6.9 **
Vitamin D supplements intake		**	**
No	3094 (56.3%)	207 (69.2%)	93 (72.7%)
Yes	2403 (43.7%)	92 (30.8%)	35 (27.3%)
History of falls in the last 12 months			
No	3624 (67.8%)	191 (65.6%)	78 (61.9%)
Yes	1719 (32.2%)	100 (34.4%)	48 (38.1%)
Number of falls in last 12 months			**
None	3624 (67.8%)	191 (65.6%)	78 (61.9%)
1 time	1081 (20.2%)	54 (18.6%)	24 (19%)
2 times	423 (7.9%)	30 (10.3%)	7 (5.6%)
3 or more times	215 (4%)	16 (5.5%)	17 (13.5%)
Hormone use status		**	**
Never used	2396 (43.6%)	167 (50.0%)	82 (64.57%)
Past user	796 (14.5%)	48 (16.1%)	16 (12.6%)
Current User	2304 (41.9%)	83 (27.9%)	29 (22.8%)

*
P<0.05.

**
P<0.01 compared with Non-diabetes

Table 2

The DXA measurements (mean $\pm$ SD) by diabetes status, unadjusted followed by adjusted values where applicable. Adjusted values were based on the linear regression model for: age, ethnicity, height, weight, neck-shaft angle, neck length, total expenditure from physical activity and hormone use.

	No diabetes (n=5497)	Diabetes, without insulin use (n=299)	Diabetes, with Insulin use (n=128)
Spine BMD (g/cm ²)	0.973 $\pm$ 0.17	1.034 $\pm$ 0.190 **	1.045 $\pm$ 0.172 **
	0.976 $\pm$ 0.152	1.018 $\pm$ 0.152 **	1.001 $\pm$ 0.153
Hip BMD (g/cm ²)	0.840 $\pm$ 0.136	0.886 $\pm$ 0.163 **	0.912 $\pm$ 0.170 **
	0.842 $\pm$ 0.109	0.864 $\pm$ 0.110	0.850 $\pm$ 0.110
Spine T-score	-0.906 $\pm$ 1.046	-0.610 $\pm$ 1.215 **	-0.534 $\pm$ 1.212 *
	-1.075 $\pm$ 1.377	-0.671 $\pm$ 1.380 **	-0.855 $\pm$ 1.383
Hip T-score	-1.084 $\pm$ 1.505	-0.618 $\pm$ 1.713 **	-0.759 $\pm$ 1.560 **
	-0.893 $\pm$ 0.863	-0.724 $\pm$ 0.865 **	-0.860 $\pm$ 0.868
Femoral narrow neck			
BMD (g/cm ²)	0.708 $\pm$ 0.129	0.744 $\pm$ 0.152 **	0.764 $\pm$ 0.161 **
	0.710 $\pm$ 0.109	0.729 $\pm$ 0.109 **	0.716 $\pm$ 0.109
Cross-sectional area (cm ²)	2.025 $\pm$ 0.365	2.126 $\pm$ 0.440 **	2.197 $\pm$ 0.508 **
	2.031 $\pm$ 0.296	2.085 $\pm$ 0.296 **	2.052 $\pm$ 0.297
Outer diameter (cm)	3.013 $\pm$ 0.215	3.005 $\pm$ 0.212	3.030 $\pm$ 0.297
	3.014 $\pm$ 0.197	3.013 $\pm$ 0.197	3.021 $\pm$ 0.198
Section Modulus (cm ³)	0.906 $\pm$ 0.197	0.95 $\pm$ 0.231 **	1.005 $\pm$ 0.340 **£
	0.909 $\pm$ 0.162	0.926 $\pm$ 0.163	0.929 $\pm$ 0.163
Intertrochanter			
BMD (g/cm ²)	0.710 $\pm$ 0.134	0.749 $\pm$ 0.157 **	0.783 $\pm$ 0.168 **£
	0.712 $\pm$ 0.111	0.730 $\pm$ 0.112 **	0.727 $\pm$ 0.112
Cross-sectional area (cm ²)	3.433 $\pm$ 0.651	3.659 $\pm$ 0.791 **	3.808 $\pm$ 0.776 **
	3.441 $\pm$ 0.518	3.561 $\pm$ 0.519 **	3.526 $\pm$ 0.520
Outer diameter (cm)	5.088 $\pm$ 0.338	5.131 $\pm$ 0.349	5.136 $\pm$ 0.404
	5.090 $\pm$ 0.299	5.126 $\pm$ 0.299	5.122 $\pm$ 0.300
Section Modulus (cm ³)	2.841 $\pm$ 0.599	3.041 $\pm$ 0.726 **	3.110 $\pm$ 0.675 **
	2.846 $\pm$ 0.485	2.982 $\pm$ 0.485 **	2.917 $\pm$ 0.487
Shaft			
BMD (g/cm ²)	1.135 $\pm$ 0.184	1.192 $\pm$ 0.214 **	1.218 $\pm$ 0.201 **
	1.138 $\pm$ 0.158	1.172 $\pm$ 0.159 **	1.159 $\pm$ 0.159
Cross-sectional area (cm ²)	3.064 $\pm$ 0.502	3.253 $\pm$ 0.607 **	3.355 $\pm$ 0.564 **
	3.073 $\pm$ 0.399	3.189 $\pm$ 0.400 **	3.165 $\pm$ 0.401 *
Outer diameter (cm)	2.840 $\pm$ 0.187	2.869 $\pm$ 0.193 *	2.898 $\pm$ 0.198 **
	2.842 $\pm$ 0.164	2.861 $\pm$ 0.164	2.872 $\pm$ 0.165

	No diabetes (n=5497)	Diabetes, without insulin use (n=299)	Diabetes, with Insulin use (n=128)
Section Modulus (cm ³)	1.599 ± 0.294	1.707 ± 0.348 **	1.771 ± 0.332 **£
	1.604 ± 0.228	1.671 ± 0.228 **	1.667 ± 0.229 **

* P<0.05.

** P<0.01 compared with Non-diabetes

£ P<0.05 compared with diabetes without insulin use