**Table 1.** Characteristics of women with type 2 diabetes mellitus and controls

| | Type 2 diabetes mellitus | Controls without diabetes | |
|---|---|---|---|
| | Mean ± SD | Mean ± SD | p |
| n | 22 | 421 | |
| Age (years) | 70.9 ± 7.2 | 68.2 ± 7.2 | 0.089 |
| Weight (kg) | 73.8 ± 12.1 | 69.2 ± 10.6 | 0.040 |
| Height (cm) | 159.5 ± 7.8 | 162.0 ± 6.3 | 0.232 |
| Body mass index (kg/m²) | 29.0 ± 4.8 | 26.4 ± 4.0 | 0.006 |
| Physical activity (hour/week) | 2.5 ± 1.7 | 2.5 ± 1.6 | 0.877 |
| Currently smoker, n (%) | 2 (9.1) | 51 (12.1) | 0.892 |
| Prevalent fracture, n (%) | 9 (40.9) | 202 (48.0) | 0.513 |
| Falls in last 12 months, n (%) | 7 (31.8) | 151 (35.9) | 0.651 |
| Self-reported good health, n (%) | 11 (50.0) | 301 (71.8) | 0.045 |
| Take calcium supplements, n (%) | 3 (13.6) | 69 (16.4) | 0.710 |
| Take vitamin D supplements, n (%) | 16 (72.7) | 313 (74.4) | 0.866 |
| Fasting serum glucose (mmol/L) | 7.23 ± 2.05 | 5.33 ± 0.49 | < 0.001 |
| Fasting serum insulin (pmol/L)[a] | 102 (27-1117) | 55 (12-397) | < 0.001 |
| HOMA-IR[a] | 5.3 (1.1-114) | 2.2 (0.4-21) | < 0.001 |
| Fasting serum PINP (ng/mL) | 40.4 ± 13.7 | 46.8 ± 16.6 | 0.100 |
| Fasting serum CTX (ng/mL) | 0.461 ± 0.264 | 0.464 ± 0.172 | 0.988 |
| Serum Vitamin D (nmol/L) | 67.6 ± 21.2 | 80.4 ± 24.7 | 0.012 |
| Serum PTH (pmol/L) | 4.98 ± 1.81 | 4.31 ± 2.14 | 0.206 |
| eGFR (ml/min) | 74.2 ± 21.3 | 77.8 ± 15.5 | 0.584 |
| Total hip T-score | 0.71 ± 1.04 | 0.89 ± 1.00 | 0.343 |
| Total hip aBMD (mg/cm²) | 915 ± 125 | 893 ± 120 | 0.343 |
| Femoral neck (FN) aBMD (mg/cm²) | 829 ± 104 | 829 ± 112 | 0.869 |
| Femoral subtrochanteric architecture[b] | | | |
| Total bone vBMD (mg HA/cm³) | 783 ± 110 | 715 ± 105 | 0.002 |
| Cortical vBMD (mg HA/cm³) | 1073 ± 77.3 | 1041 ± 66.3 | 0.029 |
| Cortical thickness (mm) | 4.25 ± 0.50 | 4.21 ± 0.58 | 0.716 |
| Total cortical porosity (%) | 40.9 ± 4.39 | 42.8 ± 3.97 | 0.029 |
| Compact cortical porosity (%) | 33.9 ± 3.49 | 34.8 ± 2.89 | 0.185 |
| Outer transitional zone porosity (%) | 45.6 ± 2.58 | 45.4 ± 2.28 | 0.630 |
| Inner transitional zone porosity (%) | 84.0 ± 1.56 | 84.1 ± 1.50 | 0.624 |
| Trabecular BV/TV (%)[a] | 0.13 (0.04-1.28) | 0.17(0.01-1.82) | 0.599 |

Women with type 2 diabetes mellitus were compared with controls (without diabetes) using ANCOVA, adjusted for age and fracture status.

[a]Median (range) are presented due to skewed distribution, otherwise numbers are mean ± SD

[b]Assessed using low-resolution clinical CT

SD, standard deviation; Prevalent fracture (≥1 vs 0); Falls in last 12 months (≥1 vs 0); HOMA-IR, homeostatic model assessment of Insulin Resistance; PINP, procollagen type I N-terminal propeptide; CTX, C-terminal cross-linking telopeptide of type I collagen; PTH, parathyroid hormone; eGFR, estimated glomerular filtration rate, aBMD, areal bone mineral density, vBMD, volumetric bone mineral density; BV/TV, bone volume/tissue volume.

**Table 2.** Associations of a 1 SD increment in body mass index (BMI), serum levels of glucose and insulin, and insulin resistance with bone turnover markers and femoral subtrochanteric architecture

| | BMI (kg/m$^2$) | | Glucose (mmol/L) | | Insulin (pmol/L) | | HOMA-IR | |
|---|---|---|---|---|---|---|---|---|
| | STB | p | STB | p | STB | p | STB | p |
| Bone turnover markers | | | | | | | | |
| PINP (ng/mL) | -0.10 | 0.040 | -0.12 | 0.012 | -0.02 | 0.658 | -0.03 | 0.546 |
| CTX (ng/mL) | -0.18 | < 0.001 | -0.10 | 0.030 | -0.10 | 0.042 | -0.10 | 0.039 |
| Femoral subtrochanteric architecture[a] | | | | | | | | |
| Total vBMD (mg HA/cm$^3$) | 0.19 | < 0.001 | 0.19 | < 0.001 | 0.12 | 0.007 | 0.12 | 0.007 |
| Cortical thickness (mm) | 0.19 | < 0.001 | 0.08 | 0.090 | 0.08 | 0.086 | 0.07 | 0.114 |
| Total cortical porosity (%) | -0.03 | 0.503 | -0.13 | 0.006 | -0.06 | 0.207 | -0.08 | 0.077 |
| Trabecular BV/TV[b] | 0.12 | 0.010 | 0.06 | 0.177 | 0.07 | 0.138 | 0.06 | 0.235 |

SD, standard deviation; HOMA-IR, homeostatic model assessment of Insulin Resistance; PINP, procollagen type I N-terminal propeptide; CTX, C-terminal cross-linking telopeptide of type I collagen; vBMD, volumetric bone mineral density; BV/TV, bone volume/tissue volume.

STB, standardized beta coefficients using linear regression analyses and adjusted for age and fracture status.

[a]Assessed using low-resolution clinical CT

[b]Analyzed using log-transformed variables

**Table 3.** Characteristics of women with type 2 diabetes mellitus and controls stratified by fracture status

| | Type 2 diabetes mellitus | | Controls | |
|---|---|---|---|---|
| | With Fracture | Without fracture | With Fracture | Without fracture |
| n | 9 | 13 | 202 | 219 |
| Age (years) | 69.2 ± 7.1 | 72.1 ± 7.3 | 68.4 ± 7.8 | 68.1 ± 6.7 |
| Weight (kg) | 74.1 ± 11.6 | 73.5 ± 12.9 | 68.6 ± 10.5 | 69.8 ± 10.7 |
| Height (cm) | 160.8 ± 10.9 | 158.7 ± 5.0 | 162.7 ± 5.8 | 161.4 ± 6.7[a] |
| Body mass index (BMI) (kg/cm²) | 28.8 ± 4.5 | 29.2 ± 5.1 | 25.9 ± 3.7 | 26.8 ± 4.2[a] |
| Physical activity (hours/week) | 2.8 ± 1.9 | 2.3 ± 1.6 | 2.6 ± 1.6 | 2.5 ± 1.7 |
| Fasting serum glucose (mmol/L) | 7.19 ± 2.91 | 7.27 ± 1.30 | 5.29 ± 0.47 | 5.38 ± 0.51 |
| Fasting serum insulin (pmol/L)[d] | 103 (32-1117) | 99 (27-160) | 53 (12-316) | 57 (14-397) |
| HOMA-IR[d] | 5.2 (1.1-114) | 5.4 (1.3-11.6) | 2.1 (0.4-15) | 2.2 (0.5-21) |
| Serum PINP (ng/ml) | 48.2 ± 9.26 | 35.0 ± 14.0[a] | 49.7 ± 18.5 | 44.0 ± 14.0[c] |
| Serum CTX (ng/ml) | 0.46 ± 0.18 | 0.47 ± 0.32 | 0.49 ± 0.19 | 0.44 ± 0.16[a] |
| Serum Vitamin D (nmol/L) | 61.2 ± 21.6 | 72.1 ± 20.6 | 77.1 ± 22.4 | 83.5 ± 26.3[b] |
| Serum PTH (pmol/L) | 4.76 ± 1.75 | 5.13 ± 1.90 | 4.57 ± 2.43 | 4.07 ± 1.80[a] |
| eGFR (ml/min) | 68.4 ± 15.3 | 78.3 ± 24.4 | 77.8 ± 16.8 | 77.8 ± 14.2 |
| Total hip aBMD (mg/cm²) | 864 ± 111 | 950 ± 126[a] | 853 ± 114 | 930 ± 115[c] |
| Femoral neck (FN) aBMD (mg/cm²) | 798 ± 73.6 | 851 ± 119[a] | 794 ± 101 | 861 ± 112[c] |
| Femoral subtrochanteric architecture[e] | | | | |
| Total bone vBMD (mg HA/cm³) | 758 ± 143 | 800 ± 83.4 | 681 ± 110 | 747 ± 89.7[c] |
| Cortical vBMD (mg HA/cm³) | 1050 ± 98.9 | 1088 ± 47.4 | 1024 ± 71.3 | 1057 ± 56.8[c] |
| Cortical thickness (mm) | 3.97 ± 0.41 | 4.44 ± 0.47[a] | 4.06 ± 0.58 | 4.35 ± 0.55[c] |
| Total cortical porosity (%) | 42.3 ± 5.92 | 40.0 ± 2.84 | 43.9 ± 4.27 | 41.8 ± 3.40[c] |

In women with type 2 diabetes mellitus, those with and without fracture were compared, and similarly in controls, women with and without fracture were compared using ANCOVA adjusted for age and BMI.

[a]$p < 0.05$, [b]$p < 0.01$, [c]$p < 0.001$

[d]Median (range) are presented due to skewed distribution, otherwise numbers are mean ± standard deviation.

[e]Using low-resolution clinical CT

HOMA-IR, homeostatic model assessment of Insulin Resistance; PINP, procollagen type I N-terminal propeptide; CTX, C-terminal cross-linking telopeptide of type I collagen; PTH, parathyroid hormone; eGFR, estimated glomerular filtration rate; aBMD, areal bone mineral density; vBMD, volumetric bone mineral density; BV/TV, bone volume/tissue volume.

**Fig. 1.** Cross-section image of proximal femur and its compartments. Segmented computed tomography image obtained at the proximal femur using StrAx1.0, a non-threshold-based segmentation algorithm, showing the total cortex (the area used for the cortical porosity measurements), consisting of the three cortical compartments: compact-appearing cortex, outer and inner (red) transitional zones, and trabecular bone area. Porosity was assessed from QCT slices distal to the lesser trochanter. (Reproduced with permission of John Wiley and Sons (Ref [32] Zebaze et al. J Bone Miner Res. 31 (2016) 1827–1834).

**Fig. 2a**. (A) Procollagen type I N-terminal propeptide (PINP), (B) C-terminal cross-linking telopeptide of type I collagen (CTX), and (C) femoral subtrochanteric porosity of the total cortex (compact-appearing cortex, inner and outer transitional zones) and (D) cortical thickness as a function of serum glucose. The standardized beta coefficients (STB) are estimated using linear regression analyses and adjusted for age and fracture status. Bone architecture was assessed using low-resolution clinical CT.

**Fig. 2b**. (A) Procollagen type I N-terminal propeptide (PINP), (B) C-terminal cross-linking telopeptide of type I collagen (CTX), and (C) femoral subtrochanteric porosity of the total cortex (compact-appearing cortex, inner and outer transitional zones) and (D) cortical thickness as a function of body mass index (BMI). The standardized beta coefficients (STB) are estimated using linear regression analyses and adjusted for age and fracture status. Bone architecture was assessed using low-resolution clinical CT.

**Fig. 3.** Femoral subtrochanteric porosity of the total cortex (compact-appearing cortex, inner and outer transitional zones) assessed using low-resolution clinical CT as a function of diabetes duration. The standardized beta coefficients (STB) are estimated using linear regression analyses and adjusted for age, body mass index and fracture status.

**Fig. 4.** Mean porosity with 95% confidence intervals (±1.96 standard errors of the mean) of the total cortex (compact-appearing cortex, inner and outer transitional zones) in women with type 2 diabetes mellitus (T2DM) (yellow, n = 22) and controls (without diabetes) (white, n = 421), in women with fracture (black, n = 211) and without fracture (blue, n = 232). Porosity in stratified analysis, in women with T2DM with fracture (n = 9), in those with T2DM without fracture (n = 13), in controls with fracture (n = 202) and controls without fracture (n = 219). All comparisons of groups were adjusted for age and body mass index. Porosity was assessed using low-resolution clinical CT.