Table 1 Characteristics of the postmenopausal women by fracture status

	Cases	Controls	*p* value
n	211	232	
Age (year)	68.4 ± 7.7	68.3 ± 6.7	0.937
Height (cm)	162.7 ± 6.1	161.2 ± 6.6	0.011
Weight (kg)	68.9 ± 10.5	70.0 ± 10.8	0.280
Body mass index (kg/m²)	26.0 ± 3.8	27.0 ± 4.3	0.015
Physical activity (hour/week)	2.6 ± 1.6	2.5 ± 1.7	0.421
Currently smoker, n (%)	29 (13.7)	24 (10.3)	0.257
Alcohol intake (drink/week)	3.2 ± 3.7	3.3 ± 3.5	0.407
Age at menopause (year)	49.1 ± 4.9	50.1 ± 4.2	0.021
History of previous fracture, n (%)	54 (25.6)	0	
Falls in last 12 months, n (%)	73 (34.6)	85 (36.6)	0.654
Self-reported good health, n (%)	147 (70.3)	165 (71.1)	0.860
Estimated GFR (ml/min/1.73m²)	77.4 ± 16.8	77.8 ± 14.9	0.823
Estimated GFR < 60 ml/min/1.73m²), n (%)	25 (11.9)	22 (9.5)	0.409
Diabetes mellitus type 2, n (%)	9 (4.3)	13 (5.6)	0.513
Hyperthyroidism, n (%)	8 (3.8)	6 (2.6)	0.468
Ulcerative colitis or Crohn's disease, n (%)	12 (5.7)	5 (2.2)	0.054
Rheumatoid arthritis, n (%)	11 (5.2)	8 (3.5)	0.407
Oral glucocorticoid use, n (%)	8 (3.8)	2 (0.9)	0.023
Take calcium supplements, n (%)	44 (20.9)	28 (12.1)	0.007
Take vitamin D supplements, n (%)	163 (77.3)	166 (71.6)	0.278
Serum 25(OH)D (nmol/L)	76.4 ±22.5	82.9 ± 26.1	0.031[a]
Serum 25(OH)D <50 nmol/L, n (%)	23 (10.9)	27 (11.6)	0.807
Serum PTH (pmol/L)	4.58 ± 2.40	4.13 ± 1.82	0.010[a]
Serum PTH >6.8 pmol/L	29 (13.7)	23 (9.9)	0.211
Corrected serum calcium (mmol/L)	2.43 ± 0.07	2.45 ± 0.06	< 0.001
Serum PINP (ng/mL)	49.7 ± 18.2	43.5 ± 14.1	< 0.001
Serum CTX (ng/mL)	0.49 ± 0.18	0.44 ± 0.17	0.014
DXA parameters of the hip			
Femoral neck (FN) aBMD (mg/cm²)	794 ± 100	860 ± 110	< 0.001
Total hip aBMD (mg/cm²)	853 ± 113	931 ± 115	< 0.001
CT parameters of the femoral subtrochanteric site			
Total bone vBMD (mg HA/cm³)	684 ± 113	750 ± 90.0	< 0.001
Cortical vBMD (mg HA/cm³)	1025 ± 72.6	1059 ± 56.6	< 0.001
Cortical thickness (mm)	4.06 ± 0.58	4.36 ± 0.54	< 0.001
Total cortical porosity (%)	43.8 ± 4.35	41.7 ± 3.39	< 0.001
Compact cortex porosity (%)	35.3 ± 3.10	34.3 ± 2.67	< 0.001
Outer transitional zone porosity (%)	45.6 ± 2.41	45.3 ± 2.18	0.227
Inner transitional zone porosity (%)	84.1 ± 1.57	84.2 ± 1.43	0.621
Trabecular BV/TV (%)	0.266 ± 0.241	0.272 ± 0.314	0.806

Values are mean ± standard deviation, or number (%).
Cases and controls were compared using analysis of variance adjusted for age.
[a]Additionally adjusted for season of blood sampling (winter vs. summer).
25(OH)D 25-hydroxyvitamin D, *PTH* parathyroid hormone, *PINP* procollagen type I N-terminal propeptide, *CTX* C-terminal cross-linking telopeptide of type I collagen, *GFR* glomerular filtration rate, *DXA* dual-energy x-ray absorptiometry, *aBMD* areal bone mineral density, *vBMD* volumetric bone mineral density, *HA* hydroxyapatite, *BV/TV* bone volume/tissue volume.
Reference range 25(OH)D <50 nmol/L, PTH 1.3-6.8 pmol/L, and corrected calcium 2.20-2.55 pmol/L

Table 2 Characteristics of women in quartiles of serum levels of vitamin 25-hydroxyvitamin D (25(OH)D) and characteristics of women in quartiles of serum levels of parathyroid hormone (PTH)

By quartiles of serum 25(OH)D	Q1	Q2	Q3	Q4 (reference)
n	112	110	110	111
Serum 25(OH)D, range (nmol/L)	16-63	64-78	79-94	96-191
Serum 25(OH)D (nmol/L)	50.0 ± 9.8	71.7 ± 4.2	86.3 ± 4.5	112 ± 16.8
Serum PTH (pmol/L)	5.18 ± 2.40[c]	4.39 ± 1.94[a]	4.07 ± 2.25	3.73 ± 1.57
Corrected serum calcium (mmol/L)	2.43 ± 0.07	2.45 ± 0.06	2.44 ± 0.07	2.44 ± 0.07
Age (year)	68.5 ± 7.8	68.2 ± 7.3	68.0 ± 6.6	68.8 ± 7.1
Body mass index (kg/m²)	27.3 ± 4.1[b]	26.5 ± 3.8	26.5 ± 3.9	25.8 ± 4.4
Prevalent fracture, n (%)	62 (55.4)[b]	55 (50.0)	50 (45.5)	44 (39.6)
Self-reported good health, n (%)	70 (62.5)[a]	78 (72.2)	77 (70.0)	87 (78.4)
Estimated GFR (ml/min/1.73m²)	80.4 ± 15.1[b]	76.5 ± 16.2	78.5 ± 16.2	75.0 ± 15.5
Take calcium supplements, n (%)	11 (9.8)[c]	14 (12.7)[b]	18 (16.4)	29 (26.1)
Take vitamin D supplements, n (%)	68 (60.7)[c]	80 (72.7)	88 (80.0)	93 (83.8)
Serum PINP (ng/mL)	44.1 ± 13.0	50.9 ± 21.1[a]	45.9 ± 15.8	44.9 ± 14.2
Serum CTX (ng/mL)	0.44 ± 0.14	0.51 ± 0.20[a]	0.46 ± 0.17	0.46 ± 0.18
Femoral neck (FN) aBMD (mg/cm²)	834 ± 108	823 ± 115	838 ± 118	820 ± 103
Femoral subtrochanteric parameters				
Total bone vBMD (mg HA/cm³)	713 ± 107	707 ± 108	719 ± 108	736 ± 102
Cortical vBMD (mg HA/cm³)	1038 ± 66.0	1037 ± 71.4	1041 ± 68.6	1055 ± 60.6
Cortical thickness (mm)	4.17 ± 0.57	4.17 ± 0.60	4.25 ± 0.59	4.27 ± 0.55
Total cortical porosity (%)	43.0 ± 3.95	43.1 ± 4.28	42.8 ± 4.12	42.0 ± 3.63
Trabecular BV/TV (%)	0.301 ± 0.324	0.267 ± 0.285	0.285 ± 0.295	0.223 ± 0.205
By quartiles of serum PTH	Q1 (reference)	Q2	Q3	Q4
n	107	118	109	109
Serum PTH, range (pmol/L)	0.9-2.9	3.0-3.9	4.0-5.2	5.3-17.8
Serum PTH (pmol/L)	2.23 ± 0.45	3.44 ± 0.27	4.56 ± 0.37	7.19 ± 2.14
Serum 25(OH)D (nmol/L)	90.3 ± 24.5	80.4 ± 23.8[a]	77.5 ± 23.8[c]	71.1 ± 23.0[c]
Corrected serum calcium (mmol/L)	2.45 ± 0.06	2.44 ± 0.06	2.43 ± 0.07[a]	2.44 ± 0.08
Age (year)	67.5 ± 6.5	67.7 ± 6.9	67.9 ± 6.8	70.4 ± 8.3[b]
Body mass index (kg/m²)	25.6 ± 3.7	26.9 ± 4.3	26.9 ± 4.0	26.6 ± 4.1
Prevalent fracture, n (%)	44 (41.1)	56 (47.5)	53 (48.6)	58 (53.2)
Self-reported good health, n (%)	82 (77.4)	83 (70.9)	78 (71.6)	69 (63.3)
Estimated GFR (ml/min/1.73m²)	78.4 ± 15.0	79.5 ± 14.1	78.3 ± 14.8	74.1 ± 18.7
Take calcium supplements, n (%)	23 (21.5)	18 (15.3)	20 (18.3)	11 (10.1)[a]
Take vitamin D supplements, n (%)	84 (78.5)	88 (75.6)	83 (76.1)	74 (67.9)
Serum PINP (ng/mL)	45.4 ± 15.3	44.8 ± 15.0	45.8 ± 14.0	50.0 ± 20.6
Serum CTX (ng/mL)	0.46 ± 0.16	0.43 ± 0.16	0.46 ± 0.17	0.51 ± 0.2[a]
Femoral neck (FN) aBMD (mg/cm²)	839 ± 114	846 ± 115	821 ± 99.4	808 ± 112
Femoral subtrochanteric parameters				
Total bone vBMD (mg HA/cm³)	722 ± 106	722 ± 103	719 ± 94.7	710 ± 121
Cortical vBMD (mg HA/cm³)	1042 ± 68.5	1043 ± 64.3	1047 ± 63.0	1039 ± 72.5
Cortical thickness (mm)	4.21 ± 0.58	4.25 ± 0.62	4.26 ± 0.50	4.13 ± 0.60
Total cortical porosity (%)	42.8 ± 4.10	42.7 ± 3.85	42.5 ± 3.77	42.9 ± 4.34
Trabecular BV/TV (%)	0.256 ± 0.220	0.307 ± 0.302	0.276 ± 0.319	0.235 ± 0.270

Values are mean ± standard deviation, or number (%).
25(OH)D 25-hydroxyvitamin D, *PTH* parathyroid hormone, *GFR* glomerular filtration rate, *PINP* procollagen type I N-terminal propeptide, *CTX* C-terminal cross-linking telopeptide of type I collagen, *aBMD* areal bone mineral density; *vBMD* volumetric BMD, *HA* hydroxyapatite, *BV/TV* bone volume/tissue volume.
[a]$p < 0.10$, [b]$p < 0.05$, [c]$p < 0.01$, [d]$p < 0.001$, for difference between quartiles compared to the reference in analysis of variance, adjusted for age, height, weight, and fracture status, and also adjusted for multiple testing (ref 35).

Table 3 Associations of a 1 SD lower serum 25-hydroxyvitamin D and a 1 SD higher parathyroid hormone, with bone turnover markers, femoral neck and total hip areal bone mineral density (aBMD) and femoral subtrochanteric bone parameters in SD units

SD unit		25-hydroxyvitamin D - 24.7 nmol/L				Parathyroid hormone + 2.13 pmol/l			
		Unadjusted		Adjusted		Unadjusted		Adjusted	
	SD unit	STB	*p* value	STB	*p* value	STB	*p* value	STB	*p* value
Bone turnover markers									
Log PINP	0.145 ng/ml	0.03	0.529	0.01	0.830	0.10	0.031	0.10	0.046
Log CTX	0.166 ng/ml	0.004	0.925	0.01	0.906	0.14	0.004	0.14	0.003
DXA hip parameters									
Femoral neck aBMD	111 mg/cm²	-0.02	0.739	-0.01	0.870	-0.15	0.002	-0.09	0.032
Total hip aBMD	120 mg/cm²	-0.03	0.540	-0.05	0.283	-0.11	0.018	-0.08	0.050
CT femoral subtrochanteric parameters									
Total vBMD	106 mg HA/cm³	-0.09	0.056	-0.07	0.118	-0.04	0.378	-0.01	0.744
Cortical vBMD	66.9 mg HA/cm³	-0.09	0.063	-0.06	0.212	-0.01	0.815	0.01	0.854
Cortical thickness	0.58 mm	-0.07	0.143	-0.05	0.270	-0.06	0.204	-0.02	0.629
Total cortical porosity	4.01%	0.09	0.063	0.06	0.210	0.01	0.812	-0.01	0.858
Compact cortex porosity	2.92%	0.07	0.128	0.05	0.320	0.001	0.979	-0.01	0.904
Outer transitional zone porosity	2.29%	0.04	0.392	0.03	0.516	0.03	0.560	0.03	0.532
Inner transitional zone porosity	1.50%	-0.02	0.739	-0.004	0.936	0.08	0.084	0.10	0.054
Log trabecular BV/TV	0.44%	0.04	0.434	0.03	0.588	-0.11	0.027	-0.10	0.036

SD standard deviation, *STB* standardized coefficient in linear regression analysis adjusted for age, height, weight, fracture status, supplementation of calcium, corrected serum calcium, and season of blood sampling (winter vs. summer).
PINP procollagen type I N-terminal propeptide, *CTX* C-terminal cross-linking telopeptide of type I collagen, *DXA* dual-energy x-ray absorptiometry, *aBMD* areal bone mineral density; *vBMD* volumetric BMD, *HA* hydroxyapatite, *BV/TV* bone volume/tissue volume.

Table 4 Odds ratio (OR) and 95% confidence interval (CI) for non-vertebral fracture for each of the many clinical risk factors and for the femoral subtrochanter parameters in univariate analysis

	SD unit	OR (95% CI)	*p* value
Age	+ 7.21 year	1.13 (0.92-1.39)	0.242
Height	+ 6.40 cm	1.39 (1.12-1.72)	0.003
Weight	– 10.7 kg	1.19 (0.98-1.46)	0.085
Body mass index	– 4.07 kg/m²	1.26 (1.04-1.53)	0.017
Currently smoker	yes vs. no	1.41 (0.78-2.56)	0.261
Oral glucocorticoid use	yes vs. no	5.08 (1.03-25.2)	0.047
Rheumatoid arthritis	yes vs. no	1.95 (0.75-5.06)	0.170
Hyperthyroidism	yes vs. no	1.63 (0.55-4.85)	0.383
Ulcerative colitis/Crohn's disease	yes vs. no	2.81 (0.96-1.04)	0.060
Falls in the last 12 months	≥ 1 vs. 0	0.92 (0.62-1.36)	0.675
Estimated GFR	– 10.7 ml/min/1.73m²	0.98 (0.81-1.18)	0.812
Estimated GFR < 60 ml/min/1.73m²	yes vs. no	1.28 (0.70-2.35)	0.420
Serum PINP	+ 16.5 ng/ml	1.49 (1.20-1.85)	< 0.001
Serum CTX	+ 0.18 ng/ml	1.22 (1.00-1.49)	0.047
Femoral neck (FN) aBMD	– 0.111 mg/cm²	2.11 (1.66-2.68)	< 0.001
Femoral subtrochanter Cortical porosity	+ 4.01%	1.71 (1.38-2.11)	< 0.001
Femoral subtrochanter Cortical thickness	– 0.58 mm	1.79 (1.44-2.23)	< 0.001

SD standard deviation, *aBMD* areal bone mineral density, *GFR* glomerular filtration rate, *PINP* procollagen type I N-terminal propeptide, *CTX* C-terminal cross-linking telopeptide of type I collagen.

Table 5 Odds ratio (OR) and 95% confidence interval (CI) for non-vertebral fracture, per standard deviation (SD) change in 25-hydroxyvitamin D (25(OH)D) and parathyroid hormone (PTH)

	25-hydroxyvitamin D		Parathyroid hormone	
SD units	- 24.7 nmol/L		+ 2.13 pmol/l	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Univariate analysis	1.31 (1.08-1.59)	0.006	1.24 (1.02-1.51)	0.030
Model 1	1.41 (1.13-1.76)	0.002	1.37 (1.11-1.71)	0.004
Model 2	1.32 (1.05-1.65)	0.019	1.27 (1.02-1.60)	0.037
Model 3	1.28 (1.01-1.62)	0.038	1.30 (1.02-1.64)	0.033
Model 4	1.28 (1.01-1.62)	0.040	1.27 (1.00-1.60)	0.046
Model 5	1.27 (1.00-1.61)	0.047	1.29 (1.01-1.63)	0.047
Model 6	1.33 (1.05-1.69)	0.018	1.19 (0.94-1.51)	0.153
Model 7	1.30 (1.02-1.65)	0.035	1.23 (0.96-1.56)	0.104

Model 1: Adjusted for age, height, weight, supplementation of calcium, corrected serum calcium, oral glucocorticoid use, ulcerative colitis or Crohn's disease, and season of blood sampling.
Model 2: Additionally and mutually adjusted for 25(OH)D and PTH in the same model.
Model 3: Model 2 + adjusted for cortical porosity.
Model 4: Model 2 + adjusted for cortical thickness.
Model 5: Model 2 + adjusted for cortical porosity and cortical thickness.
Model 6: Model 2 + adjusted for femoral neck areal bone mineral density (FN aBMD).
Model 7: Model 2 + adjusted for cortical porosity and cortical thickness, and FN aBMD.

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 from John Wiley and Sons (Ref [33] Zebaze et al (2016) J Bone Miner Res 31:1827–1834).