Characteristics of lifetime factors, bone metabolism, and bone mineral density in patients with hip fracture

Juha Partanen[1], Jorma Heikkinen[2], Timo Jämsä[3], and Pekka Jalovaara[1]

[1] Department of Orthopaedic and Trauma Surgery, University of Oulu, P.O. Box 5000, FIN-90014 Oulu, Finland
[2] Deaconess Institute of Oulu, Oulu, Finland
[3] Department of Medical Technology, University of Oulu, Oulu, Finland

Abstract Seventy-four postmenopausal women with non-pathological hip fracture were recruited to a study in which they were compared for lifetime factors, some biochemical measurements of bone metabolism, and bone mineral density (BMD), with 40 age-adjusted controls without fracture. The fracture patients were less independent; their walking ability was weaker; their vision was poorer; they had more general diseases (strokes, diabetes, malignant diseases, heart and vascular diseases); more of them had had deliveries; and they were using significantly more loop diuretics, and antidepressant, neuroleptic, and diabetes drugs than the controls. Thirty-seven patients and 19 controls were excluded from the statistical comparison of BMD and the biochemical measurements of bone metabolism because they had had treatments with calcium, vitamin D, bisphosphonates, estrogens, calcitonin, or corticosteroids, and one fracture patient was excluded for primary hyperparathyroidism. The BMD of the upper femur was significantly lower in the fracture group compared with the control group. Serum total calcium (S-Ca) and serum vitamin D (S-25-(OH)-D) were significantly lower and the levels of calcitonin (S-CT) significantly higher in the fracture group than in the control group, but none of the bone formation markers showed significant differences between the study groups. A comparison of patients with cervical and trochanteric fractures showed BMD to be significantly lower in the upper femur in the trochanteric fracture group. There were no significant differences in the biochemical measurements (with the exception that S-CT was higher in the cervical fracture group), nor in the lifetime factors between the fracture types. In conclusion, some lifetime factors and low S-Ca, low S-25-(OH)-D, high S-CT, and low BMD of the upper femur seem to be related to the risk of hip fracture, and low BMD and low S-CT seem to be related to the trochanteric fracture type in postmenopausal women.

Key words hip fracture · bone mineral density (BMD) · biochemical markers · lifetime factors

Introduction

Hip fractures in the elderly have become a major problem in many developed countries, and they generate enormous medical and social costs, because they commonly result in permanent disability, admission into institutional care, or death [1]. The increasing burden of fractures requires vigorous prevention of osteoporosis in the elderly [1]. Special predictors of osteoporotic fractures, and especially hip fractures, are being investigated extensively [2–5]. Falling mechanics, low bone mineral density (BMD), and impairment in mobility have all been established as independent risk factors for hip fracture [6]. A combination of biochemical markers and BMD may help to improve hip fracture risk assessment in the elderly [1]. It has been suggested that there are etiologic differences between cervical and trochanteric fractures [7–9], and knowledge of such differences would also clarify the etiology of these fractures and facilitate effective targeting of preventive efforts [8].

The aim of this study was to compare hip fracture patients with controls and to compare cervical with trochanteric hip fracture patients in terms of lifetime factors, some biochemical measurements of bone metabolism, and bone mineral density.

Subjects and methods

Study subjects

The study subjects consisted of 102 consecutive postmenopausal women with nonpathological cervical or trochanteric hip fractures in 1998 without previous hip fracture or surgery, and 40 age-adjusted controls (mean age, 73.7 years; range, 63–84 years) drawn from women coming from the same geographical area, who had had bone densitometry in a private clinic during the years 1998–1999. Twenty-eight patients aged over 84 years

were excluded because of failure to find suitable controls with regard to age. Thus, 74 patients (fracture group; mean age, 74.2 years; range, 53–84 years) constituted the study group. Forty-nine had a cervical fracture (cervical group; mean age, 73.1 years; range, 53–84 years) and 25 a trochanteric fracture (trochanteric group; mean age, 76.3 years; range, 61–84 years). There was no significant difference in age between the cervical and trochanteric fracture patients. The exclusion criteria for the controls were as follows: past history of hip fracture; any metabolic bone disease; or treatment with sex hormones, calcitonin, or bisphosphonates.

Thirty-seven patients and 19 controls were excluded from the statistical comparison of BMD and the biochemical measurements of bone metabolism because they had had treatments with calcium, vitamin D, bisphosphonates, estrogens, calcitonin, or corticosteroids, and one fracture patient was excluded for primary hyperparathyroidism (Table 3).

Written informed consent was obtained from all the patients and controls, and the study protocol was approved by the institutional ethics committee.

Bone densitometric measurement

BMD of the upper femur was measured by two different equally tested and calibrated scanners (Lunar DPX; Lunar Radiation, Madison, WI, USA), using equal measurement routines. Before the measurements, a control phantom was scanned daily, and the same measurement program was used in both similar Lunar DPX densitometries. The coefficient of variation (CV) of the femoral neck in vivo reported by the manufacturer was 0.6%–1.7%. The measurement of the patients was performed 2–4 days after the fracture.

Three parts of the hip (nonfracture side of the fracture patients and left side of the controls) were measured at the sites of the femoral neck (FEBMD), Ward's triangle (WABMD), and trochanter (TRBMD).

Biochemical measurements

Blood samples for measurements of bone metabolism were obtained from the patients (on the first or second postoperative day) and from controls in the morning after an overnight fast. Serum was separated and the samples were analyzed immediately, with the exception of the samples for serum calcitonin (S-CT) and serum osteocalcin (S-OC), which were stored at $-20°C$ for 1–2 months until assayed. All assays were performed in a clinical laboratory according to good clinical practice.

Serum intact N-terminal of procollagen type 1 (S-PINP) was measured using a radioimmunoassay test kit (ISO9001; Orion Diagnostica, Espoo, Finland; sensitivity, 3.0μg/l; intra-assay CV, 5.5%; interassay CV, 5.6%)

[10]. Serum 25-hydroxyvitamin D (S-25-(OH)-D) was measured using a commercial radioimmunoassay test kit (25-hydroxyvitamin D H^3 RIA; Catalog no. 68100E; DiaSorin, Stillwater, MN, USA; sensitivity, 4.0nmol/l, intra-assay CV, 8.8%) [11]. Serum parathyroid hormone (S-PTH) was assayed using a commercial radioimmunoassay (Intact PTH Parathyroid Hormone 100T Kit; catalog no. 40-2170; Nichols Institute Diagnostics, San Juan Capistrano, CA, USA; sensitivity, 7.5ng/l; intra-assay CV, 2.6%; interassay CV, 5.9%) according to the manufacturer's instructions [12]. Serum alkaline phosphatase (S-ALP) was analyzed by the method recommended by the Committee on Enzymes of the Scandinavian Society for Clinical Chemistry and Clinical Physiology (Reagents, Oy Reagena, Finland; Analyzer, BM/Hitachi 911 Automatic Analyzer; Hitachi, Tokyo, Japan; sensitivity, $3.7 \cdot 10^{-4} \Delta A/min$ per U/l; intra-assay CV, 0.8%; interassay CV, 2.9%). Serum bone-specific alkaline phosphatase isoenzyme (S-BAP) was measured by the REP Electrophoresis kit (Helena Bio-Sciences, Cat. no. 3200; Tyne and Wear, Sunderland, UK). Total serum calcium (S-Ca) was analyzed by flame photometry (Eppendorf AFIX 5055; Eppendorf-Netheler-Hinz, Hamburg, Germany; sensitivity, $2.4 \cdot 10^{-1} \Delta A$ per mmol/l; intra-assay CV, 0.7%; interassay CV, 3.3%) [13]. Serum calcitonin (S-CT) was assayed by a radioimmunoassay test kit (Calcitonin, catalog no. DSL-1200; Diagnostic System Laboratories, Webster, TX, USA; sensitivity, 4.0pmol/l; intra-assay CV, 5.0%; interassay CV, 12.4%) [14]. Serum osteocalcin (S-OC) was measured by an immunoradiometric assay test kit (Human Osteocalcin Kit, immunoradiometric assay (IRMA), 40-2248; Nichols Institute Diagnostics; sensitivity, 4.0μg/l; intra-assay CV, 5.2%; interassay CV, 8.3%).

Lifetime factors

The data were recorded on a special form by the same interviewer, a trained nurse, who interviewed both the fracture patients at admission and the controls. The following data were recorded: body weight, height, body mass index (BMI), menarcheal age, age at menopause, parity, ovarian surgery, independence, walking ability (which was assessed by means of a walking score on a five-point scale; see Table 5), use of walking aids, femoral muscle strength (assessed on a three-point scale; see Table 5), vision, diet, use of alcohol and coffee, smoking, current medication, and concurrent diseases (see Tables 5 and 6).

Statistical analyses

The data organization and statistical analyses were performed by a statistician, using the SPSS statistical soft-

ware (version 9.0; SPSS, Chicago, IL, USA). Student's t-test and the Mann-Whitney U-test were used to compare the differences for significance. The χ^2 and Fischer's exact test (2×2 table) were used to compare the dichotomous variables, and the χ^2 and exact tests were used in the analysis of multiple categorical variables. $P < 0.05$ was considered significant.

Results

Weight and BMI

Body weight and BMI were significantly lower ($P = 0.001$; $P = 0.004$, respectively) in the fracture group compared with the control group (Table 1).

Body weight and BMI were higher in the cervical hip fracture patients compared with the trochanteric fracture patients ($P = 0.005$; $P = 0.021$, respectively; Table 1).

BMD

All the BMD values were significantly lower in the fracture group than in the control group (FEBMD; WABMD; TRBMD; $P < 0.001$; $P = 0.002$; $P < 0.001$, respectively; Table 1).

BMD in the trochanteric group was significantly lower than in the cervical group (FEBMD; WABMD; TRBMD; $P = 0.011$; $P = 0.003$; $P = 0.022$, respectively; Table 1).

When the fracture group was examined without exclusions, 7.2% of the patients had BMD of the upper femur greater than -1 SD of that of young adults, 24.6% had BMD between -1 SD and -2.5 SD, and 68.2% of the patients had BMD below -2.5 SD of that of young adults.

Biochemical measurements

The S-Ca and S-25-(OH)-D levels in the fracture group were significantly lower than in the control group ($P < 0.001$). The level of S-CT was significantly ($P = 0.002$) higher in the fracture group than in the control group (Table 2).

There were no significant differences between the trochanteric and cervical groups in any biochemical measurements except for S-CT, which was higher ($P = 0.044$) in the cervical group than in the trochanteric group (Table 2).

Lifetime factors

The fracture group included significantly more users of loop diuretics, i.e., furosemide ($P < 0.001$), insulin, oral

Table 1. Weight, height, body mass index (BMI), and bone mineral density (BMD) measured at femoral neck (FEBMD), Ward's triangle (WABMD), and trochanter region (TRBMD) in postmenopausal hip fracture patients and controls

Group		n	Weight (kg)	P	n	Height (cm)	P	n	BMI (kg/m²)	P	n	FEBMD (g/cm²)	P	n	WABMD (g/cm²)	P	n	TRBMD (g/cm²)	P
Fracture	Mean	74	60.9	0.001	74	159.0	NS	74	24.1	0.004	36	0.676	<0.001	36	0.561	0.002	36	0.624	<0.001
	SD		12.9			5.9			5.2			0.132			0.16			0.15	
Controls	Mean	40	68.2		40	159.7		40	26.9		21	0.833		21	0.679		21	0.783	
	SD		8.5			5.9			3.9			0.088			0.102			0.09	
Cervical fracture	Mean	49	63.9	0.005	49	159.8	NS	49	25.1	0.021	24	0.725	0.011	24	0.621	0.003	24	0.671	0.022
	SD		13.0			5.8			5.4			0.116			0.151			0.143	
Trochanteric fracture	Mean	25	55.1		25	157.6		25	22.2		12	0.61		12	0.46		12	0.553	
	SD		10.7			6.0			4.1			0.123			0.117			0.127	

NS, Not significant

antidiabetics ($P = 0.029$), neuroleptics ($P = 0.049$), and antidepressants ($P = 0.005$) than the control group. Asthma drugs (inhaled cortisone, inhaled decongestants) and thyroid hormone were significantly ($P = 0.032$ and $P < 0.021$, respectively) more often used in the control group (Table 3).

Heart diseases (coronary disease, hypertension, heart failure, valvular diseases) and strokes (ischemic brain disorders) were significantly more frequent in the fracture group compared with the control group ($P = 0.011$ and $P = 0.002$, respectively). Type I and type II diabetes mellitus, and malignant diseases, were also significantly ($P = 0.002$ and $P = 0.031$, respectively) more common in the fracture group than in the control group (Table 3).

Use of alcohol was significantly ($P = 0.006$) more frequent in the control group than in the fracture group (Table 4). The fracture group was less active physically compared with the controls ($P < 0.001$; Table 4). More of the controls lived independently ($P < 0.001$), their walking ability was better ($P < 0.001$), and they used walking aids less often ($P = 0.002$) than the fracture patients. Femoral muscle strength and vision were also better in the control group than in the fracture group ($P < 0.001$) (Table 5).

The fracture group included significantly ($P = 0.036$) more women who had had one or more deliveries (Table 6).

No significant differences were seen in any lifetime factor between the cervical and trochanteric groups (Tables 5 and 6).

Discussion

Although our control group was not randomly drawn from the average population, it can be considered adequate because it was selected by age adjustment from an extensive database of postmenopausal women who had had a BMD measurement, because of the suspicion of osteoporosis, in an outpatient clinic and came from the same geographical area as the fracture patients.

There were some limitations of our study: the study was cross-sectional, and the group sizes, especially the size of the trochanteric fracture group, were relatively small, and we did not measure bone resorption markers.

The body weight of the controls was higher than that of the fracture patients, which difference is in line with previous reports [15]. We also found the body weight of the women with cervical fractures to be higher than that of the women with trochanteric fractures, which is also in accordance with the previous reports [15]. This difference may be related to the lower BMD observed in patients with the trochanteric hip fracture compared with patients with the cervical hip fracture.

Our fracture patients were less healthy than the controls, as they had had more heart diseases, strokes, diabetes, and malignant diseases. Diabetes has been reported to be associated with osteopenic and/or osteoporotic syndrome(s) [16] and hip fractures [17,18], and heart diseases with occurrence of hip fractures [18]. Whether the increased risk should be attributed to a reduced bone mass or to factors associated with falling has not yet been determined [17]. According to Ramnemark et al. [19] and Lau et al. [18], history of stroke is a major risk factor for hip fracture, as was also true in our study. Hip fractures might be caused by the high incidence of accidental falls in stroke patients, and another contributing risk factor may be the development of disuse osteoporosis on the paretic side [19]. On the other hand, Schürch et al. [20] did not find any differences between their fracture and control groups in associated diseases, with the exception of the extrapyramidal syndrome.

It is generally known that hip fracture patients have lower BMD than non-fracture controls or the average population [1,21,22], which was also shown in our study.

Table 2. Biochemical measurements associated with bone and calcium metabolism in postmenopausal hip fracture patients and controls

Group	n		S-ALP (U/l)	S-Ca (mmol/l)	S-CT (pmol/l)	S-25-(OH)-D (nmol/l)	S-PTH (ng/l)	S-PINP (μg/l)	S-BAP (U/l)	S-OC (μg/l)
Fracture	36	Mean	160.63	2.14[3*]	7.37[2*]	24.73[3*]	54.66	49.06	61.42	26.98
		SD	60.79	0.15	5.21	12.93	33.01	38.95	27.68	25.98
Controls	21	Mean	148.50	2.32	4.92	56.90	41.42	38.86	64.56	24.22
		SD	50.14	0.16	2.27	27.06	14.31	19.98	37.04	8.56
Cervical fracture	24	Mean	162.42	2.13	8.31[1*]	25.98	56.99	48.54	58.14	27.93
		SD	61.55	0.11	5.89	13.92	36.50	39.27	25.80	30.40
Trochanteric fracture	12	Mean	156.73	2.17	5.36	22.00	49.78	50.18	68.28	24.92
		SD	61.85	0.22	2.46	10.53	25.05	40.11	31.38	12.71

S-ALP, Serum alkaline phosphatase; S-Ca, serum total calcium; S-CT, serum calcitonin; S-25-(OH)-D, serum vitamin D; S-PTH, serum parathyroid hormone; S-PINP, serum intact N-terminal of procollagen type 1; S-BAP, serum bone-specific alkaline phosphatase isoenzyme; S-OC, serum osteocalcin
[1*] $P = 0.044$; [2*] $P = 0.002$; [3*] $P < 0.001$

Table 3. The use of drugs, and affecting diseases, in postmenopausal hip fracture patients and controls

Group	n	Calcium products	Vitamin D	Epilepsy drugs	Loop diuretics	Thyroid drugs	Rheumatoid drugs	Diabetes drugs	Asthma drugs	Peroral corticosteroids	Biphosphonates	Peroral estrogens	Calcitonin	Neuroleptics	Antidepressants	Anxiety drugs	Hypnotic drugs	Psychotropic drugs	Other drugs
Fracture	74	15	16	4	26[2*]	2[*]	5	16[2*]	3[*]	13	2	8	4	8[*]	20[6*]	24	9	27	55
Controls	40	14	15	0	2	6	2	2	7	5	0	0	0	0	2	0	6	7	33
Cervical fracture	49	11	13	4	16	1	4	12	0[7*]	6	2	6	3	4	14	2	5	18	34
Trochanteric fracture	25	4	3	0	10	1	1	4	3	7	0	2	1	4	6	2	4	9	21

[1*] $P = 0.049$; [2*] $P = 0.021$; [3*] $P = 0.035$; [4*] $P = 0.032$; [5*] $P = 0.029$; [6*] $P = 0.005$; [7*] $P < 0.001$

Group	n	Heart diseases	Stroke	Respiratory diseases	Urinary diseases	Diabetes	Rheumatic diseases	Parkinson disease	Malignant disease
Fracture	74	56[2*]	14[3*]	8	7	24[3*]	9	2	12[1*]
Controls	40	21	0	7	7	3	4	1	1
Cervical fracture	49	38	8	3	6	18	7	2	7
Trochanteric fracture	25	18	6	5	1	6	2	0	5

[1*] $P = 0.031$; [2*] $P = 0.011$; [3*] $P = 0.002$

But then, one third of our fracture patients did not fully meet the criteria of osteoporosis as defined by the WHO (<-2.5 SD) [23], and a minor part of them even had almost normal bone density. The important roles of the falling mechanism and bone geometry in the pathogenesis of hip fractures might explain the occurrence of hip fractures among these patients [24,25]. In agreement with our findings, several authors have also reported that individuals with trochanteric hip fractures are more osteoporotic than cervical hip fracture patients [21,26].

Serum vitamin D and calcium levels have been reported to be lower in hip fracture patients than in controls [27]. In our study, the patients with hip fracture had lower levels of total calcium and lower levels of 25-(OH)-D in serum than the controls, and the correlation between S-25-(OH)-D and S-PTH was inversely significant. This might imply subsequent secondary hyperparathyroidism, which is postulated to be largely responsible for the excessive cortical bone loss [16] that exposes the patients to a higher risk of hip fracture.

According to Garnero et al. [28], an elevated level of bone resorption—but not of bone formation—was associated with an increased risk of hip fracture, which is in agreement with our results concerning bone formation markers.

We observed higher levels of S-CT in our fracture patients than in the controls. This finding is in agreement with the studies by Dubin et al. [29] and Prince et al. [30], but contrary to those of Boonen et al. [31] and Reginster et al. [32]. The increased S-CT might be the result of a feedback mechanism in osteoporotics, with increased bone resorption tending to increase the S-Ca level. Calcitonin antagonizes this mechanism. This mechanism might be more involved in patients with cervical fracture than in those with trochanteric fracture with lower BMD.

The use of loop diuretics has been suggested to be a risk factor for low BMD [33] and a predictor of osteoporotic fractures [1]. Bone loss is probably produced by the calciuric effect of loop diuretics [33,34], and focuses on cortical bone loss [34]. Our results confirm the earlier reports. Because there were more patients with diabetes in the fracture group, antidiabetic drugs were also more commonly used but the role of antidiabetic drugs in the risk of hip fracture is unknown. Antidepressant and neuroleptic drugs were shown to be significantly more used in the fracture group, which finding has been established before [35]. It is postulated that the sedative and autonomic effects of psychotropic drugs increase the risk of falling and, thus, fracture risk, in elderly persons [35].

The functional ability of the fracture patients was poor when evaluated in terms of independence, walking ability, physical activity, use of walking aids, vision, and

Table 4. Lifetime factors concerning diet, use of alcohol, use of coffee, smoking, and physical activity in postmenopausal hip fracture patients and controls

Variable	Fracture patients	Percentage	Controls	Percentage	P value	Cervical fr. patients	Percentage	Trochanteric fr. patients	Percentage	P value
Diet					NS					NS
Normal	63	85.0	33	82.5		40	81.6	23	92.0	
Vegetarian	2	2.7	2	5.0		2	4.1	0		
Normal diet, but no use of milk products	8	10.8	3	7.5		6	12.2	2	8.0	
Protein-rich diet	1	1.4	2	5.0		1	2.0	0		
Total	74	100.0	40	100.0		49	100.0	25	100.0	
Use of alcohol					$P = 0.006$					NS
Daily	0		0			0		0		
Weekly or monthly	16	21.6	19	47.5		11	22.5	5	20.0	
Never	58	78.4	21	52.5		38	77.5	20	80.0	
Total	74	100.0	40	100.0		49	100.0	25	100.0	
Use of coffee					NS					NS
5–10 Cups of coffee/day	9	13.4	1	2.5		30	66.6	16	72.7	
1–5 Cups of coffee/day	57	85.1	38	95.0		15	33.3	5	22.7	
No use of coffee	1	1.5	1	2.5		0		1	4.5	
Total	67	100.0	40	100.0		45	100.0	22	100.0	
Smoking					NS					NS
Yes	14	19.2	4	10.0		8	16.7	6	24.0	
No	59	80.8	36	90.0		40	83.3	19	76.0	
Total	73	100.0	40	100.0		48	100.0	25	100.0	
Physical activity					$P < 0.001$					NS
Daily	24	35.9	27	67.5		15	34.1	9	37.5	
Once or more/week	22	32.3	13	32.5		16	36.4	6	25.0	
Not at all	8	11.8	0			4	9.1	4	16.7	
Previously regular	14	20.6	0			9	20.5	5	20.8	
Total	68	100.0	40	100.0		44	100.0	24	100.0	

fr., Fracture

Table 5. Lifetime factors concerning independence, walking ability, use of walking aids, femoral muscle strength, and vision

Variable	Fracture patients	Percentage	Controls	Percentage	P value	Cervical fr. patients	Percentage	Trochanteric fr. patients	Percentage	P value
Independence					$P < 0.001$					NS
Living alone	31	41.9	38	95.0		22	44.9	16	64.0	
Living with other person(s)	21	28.4	2	5.0		16	32.7	5	20.0	
Living in institution	21	28.4	0	0.0		10	20.4	11	44.0	
Living in other place of living	1	1.4	0	0.0		1	2.0	0	0.0	
Total	74	100.0	40	100.0		49	100.0	25	100.0	
Walking ability					$P < 0.001$					NS
Walk alone outdoors	49	66.2	39	97.5		33	67.3	16	64.0	
Walk alone outdoors supported by other person	4	5.4	0	0.0		3	6.1	1	4.0	
Walk alone indoors	15	20.3	1	2.5		10	20.4	5	20.0	
Walk alone indoors supported by other person	5	6.8	0	0.0		2	4.1	3	12.0	
Unable to walk	1	1.4	0	0.0		1	2.0	0	0.0	
Total	74	100.0	40	100.0		49	100.0	25	100.0	
Femoral muscle strength					$P < 0.001$					NS
Can rise up from the chair without supporting with the hands	20	27.0	35	92.1		15	30.6	5	20.0	
Can rise up from the chair with support with the hands	49	66.2	3	7.9		31	63.3	18	72.0	
Can rise up from the chair supported by other person	5	6.8	0	0.0		3	6.1	2	8.0	
Total	74	100.0	38	100.0		49	100.0	25	100.0	
Use of walking aids					$P = 0.002$					NS
No use of walking aids	43	58.1	36	90.0		26	53.1	17	68.0	
One or two sticks or tripod	6	8.1	3	7.5		2	4.1	4	16.0	
Use of walking frame or rollator	23	31.1	1	2.5		19	38.8	4	16.0	
Wheelchair or bedbound	2	2.7	0	0.0		2	4.1	0	0.0	
Total	74	100.0	40	100.0		49	100.0	25	100.0	
Vision					$P < 0.001$					NS
Good	34	46.6	35	87.5		21	43.8	13	52.0	
Poor (unable to see near and/or far)	39	53.4	5	12.5		27	56.2	12	48.0	
Total	73	100.0	40	100.0		48	100.0	25	100.0	

Table 6. Lifetime factors concerning menarcheal age, parity, ovary surgery, and age at menopause in postmenopausal hip fracture patients and controls

Variable	Fracture patients	Percentage	P value	Controls	Percentage	P value	Cervical fr. patients	Percentage	Trochanteric fr. patients	Percentage	P value
Menarcheal age (years)			NS			NS					NS
Mean	15.6			14.1			15.1		16.4		
Deliveries			NS			$P = 0.036$					NS
No childbirths	12	16.7		14	35.0		5	10.6	7	28.0	
1 Childbirth or more than 1 childbirth	60	83.3		26	65.0		42	89.4	18	72.0	
Total	72	100.0		40	100.0		47	100.0	25	100.0	
Ovarian surgery			NS			NS					NS
No ovarian surgery or one ovary removed	59	81.9		33	84.6		38	80.9	21	84.0	
One or both ovaries removed	13	18.1		6	15.4		9	19.1	4	16.0	
Total	72	100.0		39	100.0		47	100.0	25	100.0	
Age at menopause (years)			NS			NS					NS
Mean	50.1			48.5			49.9		50.5		

femoral muscle strength. Similar findings have been reported by other authors [1,36]. The lesser mobility of the elderly leads to higher bone resorption [37] and may explain the lower BMD values in the fracture group, especially in the patients with trochanteric fracture.

There were no differences in the gynegological lifetime factors between the controls and the fracture patients, except that deliveries were more frequent among the hip fracture patients, which is in agreement with a recent study [38], although nulliparity has also been linked with osteoporosis and osteopenia [16]. Reproduction may predispose the proximal femur to permanent bone loss in a considerable proportion of postpartum women [39]. BMD is generally lost during lactation and recovered after weaning [40]. However, the possible long-term relationships between osteoporosis and parity or lactation are, so far, unknown.

We found no significant differences in the lifetime factors between the cervical and trochanteric fracture groups, although the groups were quite small in size. This is in agreement with the study of Sernbo and Johnell [7] and that by Michaëlsson et al. [8], who found differences in several lifetime factors, but these were age-dependent and not real risk factors after age adjustment.

In conclusion, impaired functional ability; the use of loop diuretics and antidiabetic, antidepressant, and neuroleptic drugs; some concurrent diseases, such as strokes, diabetes, malignant diseases, and heart and vascular diseases; low BMD of the upper femur; low S-Ca; low S-25-(OH)-D; and high S-CT seem to be related to the risk of hip fracture, while low BMD and low S-CT seem to be related to the trochanteric fracture type in postmenopausal women.

References

1. Tromp AM, Ooms ME, Popp-Snijders C, Roos JC, Lips P (2000) Predictors of fractures in elderly women. Osteoporos Int 11:134–140
2. Cummings SR, Nevitt MC, Browner WS, Stone K, Fox KM, Ensrud KE, Cauley J, Black D, Vogt TM (1995) Risk factors for hip fracture in white women. Study of Osteoporotic Fractures Research Group. N Engl J Med 332:767–773
3. Dargent-Molina P, Favier F, Grandjean H, Baudoin C, Schott AM, Hausherr E, Meunier PJ, Breart G (1996) Fall-related factors and risk of hip fracture: the EPIDOS prospective study. Lancet 348:145–149
4. Huopio J, Kröger H, Honkanen R, Saarikoski S, Alhava E (2000) Risk factors for perimenopausal fractures: a prospective study. Osteoporos Int 11:219–227

5. Willig R, Jalovaara P (2000) Effect of age on some blood variables relating to bone metabolism in women. Int J Surg Invest 1:495–502

6. Greenspan SL, Myers ER, Kiel DP, Parker RA, Hayes WC, Resnick NM (1998) Fall direction, bone mineral density, and function: risk factors for hip fracture in frail nursing home elderly. Am J Med 104:539–545

7. Sernbo I, Johnell O (1987) Background factors in patients with hip fractures—differences between cervical and trochanteric fractures. Compr Gerontol [A] 1:109–111

8. Michaëlsson K, Weiderpass E, Farahmand BY, Baron JA, Persson PG, Ziden L, Zetterberg C, Ljunghall S (1999) Differences in risk factor patterns between cervical and trochanteric hip fractures. Swedish Hip Fracture Study Group. Osteoporos Int 10:487–494

9. Mautalen CA, Vega EM, Einhorn TA (1996) Are the etiologies of cervical and trochanteric hip fractures different? Bone 18:133S–137S

10. Tähtelä R, Turpeinen M, Sorva R, Karonen SL (1997) The aminoterminal propeptide of type I procollagen: evaluation of a commercial radioimmunoassay kit and values in healthy subjects. Clin Biochem 30:35–40

11. Hollis BW, Kamerud JQ, Selvaag SR, Lorenz JD, Napoli JL (1993) Determination of vitamin D status by radioimmunoassay with an 125I-labeled tracer. Clin Chem 39:529–533

12. Berson SA, Yalow RS, Aurbach GD, Potts JT Jr (1963) Immunoassay of bovine and human parathyroid hormone. Proc Natl Acad Sci USA 49:613–617

13. Robertson WG, Marshall RW (1979) Calcium measurements in serum and plasma—total and ionized. CRC Crit Rev Clin Lab Sci 11:271–304

14. Erdogan MF, Güllü S, Baskal N, Uysal AR, Kamel N, Erdogan G (1997) Omeprazole: calcitonin stimulation test for the diagnosis, follow-up and family screening in medullary thyroid carcinoma. J Clin Endocrinol Metab 82:897–899

15. Eriksson SA, Widhe TL (1988) Bone mass in women with hip fracture. Acta Orthop Scand 59:19–23

16. Kleerekoper M, Avioli L (1997) Evaluation and treatment of postmenopausal osteoporosis. In: Favus MJ (ed) Osteoporosis: Fundamentals of Clinical Practice. Lippincott-Raven, Philadelphia, pp 89–96

17. Forsen L, Meyer HE, Midthjell K, Edna TH (1999) Diabetes mellitus and the incidence of hip fracture: results from the Nord-Trondelag Health Survey. Diabetologia 42:920–925

18. Lau EM, Suriwongpaisal P, Lee JK, Das DS, Festin MR, Saw SM, Khir A, Torralba T, Sham A, Sambrook P (2001) Risk factors for hip fracture in Asian men and women: the Asian osteoporosis study. J Bone Miner Res 16:572–580

19. Ramnemark A, Nyberg L, Borssén B, Olsson T, Gustafson Y (1998) Fractures after stroke. Osteoporos Int 8:92–95

20. Schürch MA, Rizzoli R, Mermillod B, Vasey H, Michel JP, Bonjour JP (1996) A prospective study on socioeconomic aspects of fracture of the proximal femur. J Bone Miner Res 11:1935–1942

21. Nakamura N, Kyou T, Takaoka K, Ohzono K, Ono K (1992) Bone mineral density in the proximal femur and hip fracture type in the elderly. J Bone Miner Res 7:755–759

22. Sugimoto T, Kanbara Y, Shiraishi H, Kawakatsu M, Negishi H, Fukase M, Fujita T, Chihara K, Tsutsumi M (1994) Femoral and spinal bone mineral density in Japanese osteoporotics with hip fracture. Osteoporos Int 4:144–148

23. WHO Study Group (1994) Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. WHO, Geneva

24. Hayes WC, Myers ER, Morris JN, Gerhart TN, Yett HS, Lipsitz LA (1993) Impact near the hip dominates fracture risk in elderly nursing home residents who fall. Calcif Tissue Int 52:192–198

25. Partanen J, Jämsä T, Jalovaara P (2001) Influence of the upper femur and pelvic geometry on the risk and type of hip fractures. J Bone Miner Res 16:1540–1546

26. Karlsson MK, Johnell O, Nilsson BE, Sernbo I, Obrant KJ (1993) Bone mineral mass in hip fracture patients. Bone 14:161–165

27. Benhamou CL, Tourliere D, Gauvain JB, Picaper G, Audran M, Jallet P (1995) Calciotropic hormones in elderly people with and without hip fracture. Osteoporos Int 5:103–107

28. Garnero P, Hausherr E, Chapuy MC, Marcelli C, Grandjean H, Muller C, Cormier C, Bréart G, Meunier PJ, Delmas PD (1996) Markers of bone resorption predict hip fracture in elderly women: the EPIDOS Prospective Study. J Bone Miner Res 11:1531–1538

29. Dubin NH, Monahan LK, Yu-Yahiro JA, Michael RH, Zimmerman SI, Hawkes W, Hebel JR, Fox KM, Magaziner J (1999) Serum concentrations of steroids, parathyroid hormone, and calcitonin in postmenopausal women during the year following hip fracture: effect of location of fracture and age. J Gerontol A Biol Sci Med Sci 54:M467–M473

30. Prince RL, Dick IM, Price RI (1989) Plasma calcitonin levels are not lower than normal in osteoporotic women. J Clin Endocrinol Metab 68:684–687

31. Boonen S, Broos P, Verbeke G, Aerssens J, Van Herck E, Jans I, Dequeker J, Bouillon R (1997) Calciotropic hormones and markers of bone remodeling in age-related (type II) femoral neck osteoporosis: alterations consistent with secondary hyper-parathyroidism-induced bone resorption. J Gerontol A Biol Sci Med Sci 52:M286–M293

32. Reginster JY, Deroisy R, Bruwier M, Franchimont P (1992) Calcitonin metabolism in senile (type II) osteoporosis. Osteoporos Int 2:141–145

33. Ooms ME, Lips P, Van Lingen A, Valkenburg HA (1993) Determinants of bone mineral density and risk factors for osteoporosis in healthy elderly women. J Bone Miner Res 8:669–675

34. Adland-Davenport P, McKenzie MW, Notelovitz M, McKenzie LC, Pendergast JF (1985) Thiazide diuretics and bone mineral content in postmenopausal women. Am J Obstet Gynecol 152:630–634

35. Ray WA, Griffin MR, Schaffner W, Baugh DK, Melton LJ, III (1987) Psychotropic drug use and the risk of hip fracture. N Engl J Med 316:363–369

36. Boonyaratavej N, Suriyawongpaisal P, Takkinsatien A, Wanvarie S, Rajatanavin R, Apiyasawat P (2001) Physical activity and risk factors for hip fractures in Thai women. Osteoporos Int 12:244–248

37. Lips P, van Ginkel FC, Netelenbos JC, Wiersinga A, van der Vijgh WJ (1990) Lower mobility and markers of bone resorption in the elderly. Bone Miner 9:49–57

38. Fujiwara S, Kasagi F, Yamada M, Kodama K (1997) Risk factors for hip fracture in a Japanese cohort. J Bone Miner Res 12:998–1004

39. Holmberg-Marttila D, Sievänen H (1999) Prevalence of bone mineral changes during postpartum amenorrhea and after resumption of menstruation. Am J Obstet Gynecol 180:537–538

40. Sowers M (1996) Pregnancy and lactation as risk factors for subsequent bone loss and osteoporosis. J Bone Miner Res 11:1052–1060