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Stroke is a Risk Factor for Fracture-A 17-Year Follow-Up Study in Men and Women

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Abstract

Objective: The aim was to study risk factors for osteoporotic fractures and cerebro-cardiovascular disease (CVD) during 17 years of follow-up.

Design: A prospective study was performed on a random population sample (n = 1616) in Gothenburg, Sweden; 746 men and 870 women, aged 25-64 years in 1995, from the WHO MONICA Project. Fractures were verified by X-ray, CVD events by medical records and lifestyle factors and medical treatment via a questionnaire. Quantitative Calcaneal Ultrasound (QUS) examinations were performed. Fasting blood samples were taken, and in fertile women on cycle day 7-9.

Results: Since 1995, 13% of the subjects had suffered fractures, (women 15%, and men 10%). Stroke (p = 0.0144), female sex (p = 0.0006) and low leisure time physical activity (p = 0.0025) before 1995 predicted a future fracture, independently of age, body weight or previous fracture. More CVD, mainly stroke, higher cholesterol levels but less lipid-lowering treatment, higher blood pressure and fibrinogen, lower QUS, lower physical activity during leisure time, more use of tranquilisers, and, in women, low estradiol, were found among subjects with fractures, compared with non-fractured subjects.

Conclusions: Stroke and a sedentary lifestyle predicted future fractures. Stroke is a risk factor for fracture and must be considered in the care of patients suffering from cerebrovascular events.

Keywords

Predictors, Fractures, Cardiovascular disease, Stroke, Tranquilisers

Introduction

Fractures and cerebro-cardiovascular disease (CVD) are major problems in society, both for the individual and for the health service, given the ageing population. The skeletal metabolism is governed by hormones, growth, and nutritional and lifestyle factors, which are all affected by increasing age. Moreover, the skeletal tissue becomes more osteopenic in both sexes with increasing age [1-3].

Stroke and dementia predicted hip fractures in 7495 men at 30 years of follow-up [4], and the importance of elevated serum cholesterol for fractures increased with time in a 20-year follow-up study of men and women [5]. These results indicate that studies on risk factors for fractures need much longer follow-up periods than those commonly used today. A review collected evidence of an association between CVD and bone loss [6]. An association was seen between low bone mineral density, measured with Dual energy X-ray Absorptiometry (DXA), and stroke in elderly women during two years of follow-up [7], but very few studies have found an association between fractures and stroke. However, the majority of the studies referred to were cross-sectional. Among the prospective studies, only four of 18 had longer follow-up periods than ten years and fracture as an outcome was rare [6].

The aim of this longitudinal study was to investigate possible risk factors for osteoporotic fractures and associations between fractures and CVD during 17 years of follow-up in a random population sample of men and women.

Material and Methods

Subjects

A randomly selected population sample from the city census, including 746 men and 870 women aged 25-64 years, which comprised the third population screening in 1995 in the World Health Organisation (WHO) study Monitoring of trends and determinants for cardiovascular disease (MONICA), Gothenburg, Sweden [8]. In total, 1200 men and 1200 women were invited to this worldwide project in 38 countries. The participation rate varied from 52% (young men) to 82% (older women). The predictive value of the data in 1995 for future fracture until January 1, 2013 was calculated.

The study was approved by the Ethics Committee at the University of Gothenburg, the National Data Inspection Board and complies with the ethical standards of the Helsinki declaration. All participants provided written informed consent.

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Methods

Study design: This is a prospective longitudinal follow-up study over 17 years. Data obtained in 1995 were analyzed as possible predictors of fractures sustained after 1995 until January 1, 2013 in all 1616 subjects. We were able to retrieve data on fractures and CVD events from all 1616 subjects for the entire follow-up time.

Anthropometry: Body weight was measured to the nearest 0.1 kg in the fasting state with the subject in underwear and without shoes. Body height was measured barefoot and to the nearest 1.0 cm. Body mass index (BMI) was calculated as body weight divided by height squared (kg/m^2). Waist circumference was measured with a soft measuring tape midway between the lowest rib margin and the iliac crest in the standing position. The hip circumference was measured over the widest part of the gluteal region and the waist/hip circumference ratio (WHR) was calculated.

CVD events and lifestyle factors: A medical history was obtained from each subject. Myocardial infarction before 1995 was verified through medical records and classified according to the International Classification of Diseases (ICD) 10 with code I21 and ischemic and hemorrhagic stroke with codes I61, I63 and I64.

Smoking habits, coffee consumption, medication, and physical activity during work and leisure time were assessed with a questionnaire. Smoking habits were coded as: 1, current smoker; 2, ex-smoker, and 3, never smoked. A non-smoker was a person who had never smoked or occasionally smoked less than one cigarette per day. Ex-smokers were former regular smokers (> 1 month) who were not current smokers. Smokers were asked not to smoke during the morning of their examination.

Physical activity at work was graded from 1 to 4. Grade 1 was defined as mainly sedentary, grade 2 as predominantly walking on one level but no heavy lifting, grade 3 as mainly walking including climbing stairs, or walking uphill or lifting heavy objects, and grade 4 as heavy physical labour. Physical activity during leisure time was graded from 1 to 4. Grade 1 was defined as mainly sedentary, such as reading or watching television. Grade 2 was defined as moderate activity comprising walking, riding a bicycle, and/or light garden work at least 4 h per week. Grade 3 included regular exercise such as running, swimming, tennis, or heavy gardening at least 2-3 h per week. Grade 4 was defined as athletic training or participation in competitive sports regularly and several times per week. This activity questionnaire is based on a physiological assessment of expenditure for various types of activity, and low activity was shown to predict an increased risk of myocardial infarction [9,10].

Pharmacological treatment: Inquiries were made about ongoing pharmacological treatment in 1995 and was coded according to the Anatomical Therapeutic Chemical (ATC) Classification System. N-class agents comprised tranquilizers, sedatives, antidepressants, and CNS-acting analgesics. In this study, the N group is stated as tranquilizers.

Quantitative ultrasound measurements (QUS)

QUS (LUNAR Achilles, Madison, WI, USA) was performed once in all subjects at the screening in 1995 using water-based devices on the right os calcaneus, with the subject in the sitting position. The ultrasound uses high-frequency sound waves to measure the heel bone, using the velocity of the ultrasound signal (Speed of Sound = SOS) and the frequency attenuation (Broadband Ultrasound Attenuation = BUA). SOS and BUA are combined by the manufacturer to form an index called stiffness, which is expressed as a percentage of the result from young adults (peak bone mass), according to the manufacturer. The same operator performed the ultrasound measurements with the same machine throughout the study. The procedure took 20 minutes for each subject. The standard error of a single determination was assessed according to the formula: $\sqrt{[(\sum d\ )]/n}$, where $\sum d_i^2$ is the sum of individual differences squared and n is the number of observations. The SOS varied between 1441 and 1584 m/s, and the standard error was 3.71 (0.25%). The standard error calculation was based on the QUS measurements in 36 subjects aged 34-66 years who were examined twice with an interval of 1 h and with the subjects walking around between the examinations with the same QUS device as in the present study [3]. In these subjects, the BUA varied between 80 and 138 db/MHz; standard error 2.20 (2.18%), and the stiffness varied between 84% and 142%; standard error 1.85 (2.77%). The sensitivity of the QUS versus the DXA ranged from 76% to 84% and the specificity from 36% to 57% [11](fd 7).

Blood samples: Venous blood samples from an antecubital vein were drawn between 8 and 10 am after an overnight fast. Samples in menstruating women were collected on cycle day 7-9. After centrifugation, serum and plasma aliquots were frozen in 1 ml glass ampoules and stored at -70˚C until analysis, which took place within one year for all variables.

Serum total cholesterol, high-density lipoprotein cholesterol (HDL), and triglycerides were determined enzymatically (Boehringer, Mannheim, Germany).

Blood samples for hormone analyses were randomly drawn from every fourth participant. Serum testosterone was determined by radioimmunoassay (RIA) (Radioassay System Laboratories IT: ICN Biochemicals Inc. Diagnostics Division, Costa Mesa, CA, USA). Serum estradiol was determined by RIA (Clinical Assays™ Estradiol-2, DiaSorin, Saluggia, Italien). Serum intact PTH and insulin-like growth factor 1 (IGF-1) were determined by immunoradiometric assay (Nichols Institute Diagnostics, San Capistrano, CA, USA).

Osteocalcin was determined using a double antibody radioimmunoassay method (International CIS, Gif-sur-Yvette, France). Fibrinogen was analysed according to a polymerisation method described by von Clauss [12].

Fractures

Records of X-ray-verified fractures deemed to be of osteoporotic origin (upper arm, wrist, ankle, leg, hip, pelvis, rib, vertebra and foot, according to ICD 10 codes S22 (rib), S32 (pelvis), S42 (humerus), S52 (forearm), S62 (wrist), S72 (hip), S82 (tibia), S92 (foot), T08 (vertebrae), T10 (upper arm), T12 (leg), T14 (osteoporotic fracture) during 17 years (1995-2012) were retrieved from the Gothenburg hospital registers via the National Board of Health and Welfare, Stockholm, Sweden. How they occurred was also assessed. Low-energy fractures were regarded as possible osteoporotic fractures, whereas fractures related to multitrauma accidents were not included. This evaluation was performed without knowledge of the ultrasound results.

Statistical methods

In the performed analyses we included only the first event of either fracture or CVD that occurred before and/or after 1995. Means and standard deviations (SD) are shown for continuous variables. Correlations with age were calculated using the Spearman rank correlation. Partial correlations with adjustment for age and BMI were calculated. The odds ratio (OR) with a 95% confidence intervall (CI) was calculated. Multiple, logistic regression models were used to test the interaction between factors. Variables were entered in a forward manner. Fisher's Exact test was used for dichotomous variables, and Mantel- Haenszel's Chi Square test for ordered categorical variables. Poisson regression analyses were performed in order to study the interaction between stroke and time after stroke on the hazard function of fracture. A p value of < 0.05 (two-sided test) was considered statistically significant.

Results

Fractures: Among the 1616 men and women, 210 subjects (13%) suffered at least one fracture after 1995; 132 out of 870 women (15%) and 78 out of 746 men (10%).

In total, 321 fractures occurred after 1995, corresponding to 1.53 fractures/subject. Eighty-one per cent of the subjects had fractured once, 12% had fractured twice, 3% three times and 4% four times.

Table 1: Fracture predictors at the examination in 1995 for fractures occurring thereafter and their age-adjusted Odds Ratios (OR), and mean ± SD for fractured vs. non-fractured individuals.

Variable, 1995, n (%)		No fracture after 1995 (n = 1406)	Fracture after 1995 (n = 210)	p value*	OR (95% CI)**
Age, years, n (%)		45.6 (11.2)	52.6 (9.4)	**0.0000**	1.06 (1.05-1.08)
Gender	Men (all), n (%)	668 (47.5)	78 (37.1)		
	Women (all), n (%)	738 (52.5)	132 (62.9)	**0.0070**	1.59 (1.17-2.16)
Women vs. men and age group***	25-34 years	310	14	0.0595	0.32 (0.01-1.04)
	35-44 years	377	30	0.7869	1.11 (0.52-2.35)
	45-54 years	362	73	**0.0063**	2.14 (1.24-3.71)
	55-64 years	357	93	**0.0061**	1.93 (1.21-3.09)
Height, cm		171.8 (9.5)	169.4 (9.1)	**0.0009**	0.98 (0.97-1.00)
Weight, kg		74.4 (14.2)	74.7 (14.8)	0.9249	1.00 (0.99-1.01)
Body mass index, kg/m^2		25.1 (4.0)	25.9 (4.3)	**0.0105**	1.01 (0.98-1.05)
Waist, cm		85.2 (12.6)	86.6 (12.6)	0.2861	1.00 (0.98-1.01)
Hip, cm		99.9 (8.6)	101.0 (8.4)	0.2092	1.00 (0.99-1.02)
Waist/hip ratio		0.851 (0.086)	0.855 (0.083)	0.8589	0.26 (0.05-1.53)
Systolic blood pressure, mmHg		127.9 (18.6)	133.3 (20.3)	**0.0001**	1.00 (0.99-1.01)
Diastolic blood pressure, mmHg		81.8 (10.5)	83.3 (10.4)	**0.0181**	0.99 (0.98-1.01)
SOS, m/s		1528 (31)	1517 (30)	**0.0001**	0.99 (0.99-1.00)
BUA, dB/Hz		109.5 (11.8)	106.0 (9.2)	**0.0002**	0.98 (0.97-1.00)
Stiffness, %		81.1 (14.6)	75.3 (13.3)	**0.0000**	0.98 (0.97-1.00)
Physical activity at work, 1-4, low-high, n (%)	1	466 (35.0)	61 (34.1)		
	2	494 (37.1)	59 (33.0)		
	3	318 (23.9)	52 (29.1)		
	4	55 (4.1)	7 (3.9)	0.4152	1.10 (0.92-1.33)
Physical activity at leisure, 1-4, low-high, n (%)	1	247 (18.5)	50 (26.0)		
	2	811 (60.7)	120 (62.5)		
	3	254 (19.0)	21 (10.9)		
	4	23 (1.7)	1 (0.5)	**0.0004**	0.67 (0.52-0.87)
Smokers, 1-3, current, ex, non, n (%)	1	356 (25.6)	56 (26.9)		
	2	326 (23.4)	44 (21.2)		
	3	711 (51.0)	108 (51.9)	0.9381	1.03 (0.86-1.23)
S-cholesterol, mmol/l		5.78 (1.22)	6.07 (1.10)	**0.0002**	0.99 (0.86-1.13)
S-triglycerides, mmol/l		1.57 (1.10)	1.65 (0.90)	**0.0199**	0.98 (0.85-1.12)
P-fibrinogen, g/l		2.76 (0.54)	2.90 (0.60)	**0.0024**	1.13 (0.84-1.53)
IGF-1, µg/l		166.4 (60.0)	144.9 (50.8)	**0.0049**	1.00 (0.99-1.00)
S-PTH, ng/l		37.1 (14.5)	40.6 (15.9)	0.0996	1.01 (0.99-1.03)
S-Osteocalcin, µg/l		9.24 (2.79)	9.09 (2.80)	0.5511	0.99 (0.90-1.09)
Previous fracture, n (%)		194 (13.8)	18 (8.6)	**0.0400**	0.50 (0.30-0.83)
HRT, women, n (%)		188 (25.5)	38 (28.8)	0.1003	1.21 (0.82-1.79)
Antihypertensives, n (%)		96 (6.8)	25 (11.9)	**0.0189**	1.11 (0.68-1.80)
Antidiabetics, n (%)		35 (2.5)	10 (4.8)	0.1106	1.27 (0.60-2.66)
Tranquilizers, n (%)		144 (10.2)	37 (17.6)	**0.0038**	1.52 (1.02-2.29)
Myocardial infarction before 1995, n (%)		20 (1.4)	6 (2.9)	0.2182	1.13 (0.44-2.89)
Stroke before 1995, n (%)		12 (0.9)	10 (4.8)	**0.0003**	3.44 (1.45-8.17)
Stroke or Myocardial infarction before 1995, n (%)		29 (2.1)	13 (6.2)	**0.0033**	1.78 (0.89-3.53)
Myocardial infarction after 1995, n (%)		31 (2.2)	12 (5.7)	**0.0100**	3.01 (2.37-4.83)
Stroke after 1995, n (%)		50 (3.6)	27 (12.9)	**0.0000**	3.49 (2.05-5.83)
Stroke or Myocardial infarction after 1995, n (%)		81 (5.8)	39 (18.6)	**0.0000**	3.23 (2.08-4.94)

*p value corresponds to the unadjusted analysis. **ORs correspond to the age-adjusted analysis. ***Fractures in the age strata are adjusted for sex.

SOS: Speed of Sound; BUA: Broadband ultrasound attenuation; IGF-1: Insulin-like growth factor-1; PTH: Parathyroid hormone; HRT: Estrogen hormone replacement therapy.

The fracture types were 31% radial, 15% knee, 14% vertebral, 14% rib, 14% ankle, 10% upper arm and 1% hip. The mean age of those who fractured was seven years higher than of those who did not, see table 1. Among the 1616 men and women, 212 subjects (13%), (10% women and 16% men) had at least one fracture before 1995; i.e., before the ages 25-64 years, see table 1. The dominating fracture types in this age span were ankle and wrist. Most fractures had occurred during high-energy sport activities (mainly football); hence, more men had fractured before 1995. A fracture before 1995 correlated positively with a higher degree of physical activity during leisure time, but no significant association was seen between QUS measurements and previous fracture.

Stroke, myocardial infarction and cardiovascular risk factors before 1995 in relation to fractures

There were 42 (3%) subjects with at least one myocardial infarction or stroke (n = 10 women, n = 32 men) before 1995 in the whole cohort of 1616 subjects. Nine of the 10 women (90%) had suffered a stroke compared with 4 of the 32 men (12%).

Of the 42 subjects with a CVD event before 1995, 13(31%) suffered a fracture after 1995 whereas 29 (69%) did not, see table 1.

Stroke, myocardial infarction and mortality after 1995 in relation to fractures

There were 120 subjects with at least one CVD event, myocardial infarction or stroke, after 1995, see table 1. Of those 120 subjects, 43 suffered a myocardial infarction (mean age 64 years) and 77 suffered a stroke (mean age 65 years).

Of the 43 subjects with a myocardial infarction after 1995, 12 (28%) also suffered a fracture after 1995, whereas 31 (72%) did not, see table 1. The mean age for those with a myocardial infarction and a fracture was 66 years, vs. 62 years for those with a myocardial infarction but without a fracture.

Table 2: Significant predictors for fracture after 1995, according to forward-stepwise, multivariate, logistic regression analysis with significant variables from table 1 as independent variables.

Variable at 1995	Odds Ratio	95% Confidence Interval	p value
Age, years	1.071	1.052-1.090	**< 0.0001**
Sex, woman	1.712	1.200-2.441	**0.0006**
Physical activity, leisure, 1-4 (low to high)	0.650	0.486-0.868	**0.0025**
Stroke before 1995	3.543	1.216-10.320	**0.0144**

Of the 77 subjects with a stroke after 1995, 27 (35%) also suffered a fracture after 1995, whereas 50 (65%) did not, table 1. The mean age for those with a stroke and a fracture was 67 years, vs. 63 years for those with a stroke but without a fracture.

After 1995 and until the end of study, 122 subjects died, 30 (25%) of whom had fractured after 1995.

The influence of time since stroke and fracture: Less than half of those with stroke and myocardial infarction, respectively, fractured after the vascular event. Of these, only one third had a vascular event within one month prior to the fracture. To study the influence of time since stroke on the risk of fracture, a Poisson regression analysis was performed. Immediately after a stroke, the hazard ratio was 2.21 (beta 0.7913, SE 0.5156, hazard ratio 2.21 (95% CI 0.80-6.06); p = 0.1249). After the stroke, the impact decreased by 11% per year. The time dependence was not significant.

Multivariable analysis: The risk of fracture after 1995 was increased by female sex and higher age, BMI, blood pressure, cholesterol, triglycerides, and fibrinogen, and by lower height, IGF-1, and QUS levels and less physical activity during leisure time, more use of antihypertensives and tranquilizers, and more myocardial infarction and stroke at the baseline examination in 1995, see table 1.

In a stepwise, logistic regression analysis including all the significant factors in table 1, higher age, female sex, lower degree of physical activity during leisure time and more stroke increased the risk of fractures, independently of other factors, see table 2.

Pharmacological treatment: In 1995, antihypertensive agents were used by 94 subjects (5.8%) and tranquilizers by 181 (11.2%) , while use of lipid lowering and anti-osteoporotic agents or minerals was very rare, < 1% each. Estrogen hormone replacement therapy (HRT) was used by 26% of the the whole cohort of 870 women. Corticosteroids were used by ten subjects. Antihypertensives and tranquilizers at the 1995 examination predicted future fractures, see table 1.

Discussion

The main finding of this 17-year prospective random population study was that stroke, independently of other known risk factors for fractures, predicted a future fracture. Besides, higher age, being a woman and having a sedentary lifestyle were independent risk factors for future fracture. Impaired body balance is common after a stroke and there is a considerable risk of falling, which may result in a fracture [13]. However, a direct time-related causal relationship between stroke and falling, with a resulting fracture, could not be seen. A greater risk of fractures has been shown in patients after hospitalization for stroke [14]. This was also verified in this random population sample of men and women, independently of other factors. Larger populations are, however, needed to see a direct influence of the time since the stroke on the fracture incidence.

The present results speak in favor of a fracture being a sign of frailty in general, especially at higher ages, and mortality is also increased after a fracture [15].

The fracture panorama is in agreement with the age span, 25-64 years, which is not in the “hip risk zone”. The number of hip fractures was very small, only two, which initially may seem peculiar, as the age span in the follow-up ranges from 40 to 79 years. It has been shown, however, that hip fractures in men increase after the age of 75 [4]. The pronounced majority of radial, knee and ankle fractures is explained by the well-preserved reflexes to avoid falling on the hip at a younger age.

A fracture before 1995 was not predictive of a future osteoporotic fracture in this young population sample. This is explained by the young men who had fracturedfairly frequently during sport activities being physically fitter, and probably more careful afterwards. They were unlikely to suffer an osteoporotic fracture later in life. They also had more favorable bone mass, according to their QUS levels.

The present study cohort was probably one of the last treatment-naïve populations with regard to anti-osteoporotic treatment and lipid-lowering agents at study start in 1995. The use of these agents had increased from 0% to 3% and from 0% to 15%, respectively, at a reinvestigation in 2008 [16]. The pharmacological treatment, both in 1995 and 2008, mirrors the underlying secular trends based on published results from large clinical trials regarding fracture prevention, CVD prevention, and the risk of cancer due to HRT [17,18]. In 1995, HRT was very frequent, 26%, and was used both for menopausal symptoms and as treatment of osteoporosis. HRT has now declined in the general population to 8% in women, leading to a decrease in serum estradiol [16]. Lower serum estradiol was also seen in women in 1995, who later fractured.

The number of fractures sustained in this study was 13%, which is higher than in a similar random population study from 1985 (10%), OR 1.31 (95% CI 1.04-1.64; p = 0.0192), during 20 years of follow-up of men and women up to 85 years of age at the end of that study [5]. This indicates a higher fracture incidence in society nowadays. Despite the fact that 13% had fractured, the prescription of anti-osteoporotics has not increased at the same rate, indicating undertreatment of osteoporosis [16].

The fractured subjects had higher blood lipid levels than the non-fractured subjects, which is in agreement with the results from a previous population sample [5]. It is of great interest to determine whether lower cholesterol per se, independently of lipid-lowering agents, could result in a lower fracture incidence in the future. It has been debated whether the possible beneficial effect of lower lipid levels on bone could be attributed to statins per se or to decreased cholesterol per se. However, large studies, like 4S, LIPID, HPS, etc., reviewed by Rizzo, et al. [19], have hitherto failed to show that statins prevent fractures. A case control study showed a synergistic effect of statins and HRT on fractures but not of statins alone [20].

The finding of more strokes and higher blood pressure, cholesterol, triglyceride and fibrinogen levels in fractured subjects could indicate a metabolic and/or vascular pathogenesis in the development of fractures. It is tempting to speculate that a microangiopathy process is present also in bone. This hypothesis might also explain why smoking is a strong risk factor for fractures [4,5]. However, smoking had decreased from 26% in 1995 to 11% in 2008 when studying secular trends in the population [16] and was no longer a risk factor for fracture in the present study.

The role of cholesterol as a risk factor for fractures has been discussed in many studies with ambiguous results [21]. A 20-year follow-up study has, however, identified high serum total cholesterol as an independent long-term cause of osteoporotic fracture [5]. One study showed an increased risk of osteoporotic fracture in women with CVD [22]. A retrospective cohort study showed that subjects who received bisphosphonate therapy had a lower risk of stroke during a two-year follow-up period [23]. Apart from all selection biases, the observation is of interest in the possible pathogenetic link between CVD and fracture.The present findings indicate a high risk of fracture after a stroke, independently of the FRAX tool [24]. Whether there is an underlying mechanism predisposing for bone fracture and CVD events is yet to be proved. There seems to be a common genetic

denominator between osteoporosis and CVD, as found by Saarinen, et al. [25].

A limitation of this study was that the population was small, and the follow-up time may not belong enough. The age span was young, with few end points, especially hip fractures; however, the age span was wide enough to raise issues about possible confounders that may interfere and affect the results, for instance, age-related osteoporosis. This was clearly seen in the age strata in table 1 for men and women separately. However, other metabolic changes arising from aging cannot be adjusted for. Nevertheless, CVD and fracture share common risk factors. Stroke could be regarded as an alarming event for upcoming metabolic changes that may later result in a bone fracture, irrespective of motor and balance issues. The strengths are that this was a random population sample and comprised both men and women. All CVD events were verified through hospital registers and were strictly validated according to the WHO MONICA protocol, and fractures were verified by X-ray. We have captured the ages where many individuals start to suffer fractures of osteoporotic origin and CVD events.

In conclusion, stroke and a sedentary leisure time predicted future fractures, independently of other factors. Fractured subjects had higher cholesterol levels but fewer lipid-lowering agents than subjects without fractures. The results point towards a link between metabolic bone disease and cerebrovascular disease. Stroke is a risk factor for fractures and this must be considered in the care of patients suffering from cerebrovascular events.

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Conflict of Interest Statement

None of the authors has any conflicts of interest to declare.

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