BONE MINERAL DENSITY IN STATINS USERS: ANALYSIS OF A POPULATION- BASED COHORT FROM SPAIN

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OBJECTIVE

To analyze the effects of statins on bone mineral density (BMD), in participants from a large population-based cohort

PATIENTS

- 2315 subjects (1422 postmenopausal women and 893 men)

- Patients previously treated for osteoporosis as well as those with other bone diseases or receiving glucocorticoids or other drugs affecting bone or lipid metabolism (apart from statins) were excluded

METHODS

- We also studied the effect on BMD of:
  - Type of statin
  - Dose
  - Pharmacokinetic properties
  - Length of treatment

- BMD: DXA. Hologic, 4500

RESULTS

Table 1. Baseline characteristics

	Statin users n= 478	Non users n= 1837	p
Age (years)	65.9±9.1	62.8±9.6	<0.0001
Sex (females)	53.6	63.5	<0.0001
BMI (Kg/m^2)	29.7±4.1	28.7±4.6	<0.0001
Waist perimeter (cm)	101.6±11.3	97.2±12.3	<0.0001
Dairy calcium intake (mg/d)	550 [400-800]	600 [400-800]	0.4
Education level (years)	8 [8-8]	8 [8-10]	0.045
Years since menopause	16 [9-24]	10 [4-21]	<0.0001
Previous fracture	16.7	14.4	0.2
Family history of hip fracture	12.8	15.9	0.1
Smoking	15.1	15.6	0.8
Alcohol intake	32.0	25.5	0.005
Physical activity (moderate or vigorous)	97.7	98.4	0.3
Falls in the previous year	21.5	21.9	0.9
Hypertension	64.4	40.3	<0.0001
Type 2 diabetes	33.1	9.7	<0.0001
Coronary heart disease	19.0	2.6	<0.0001
COPD	10.6	7.6	0.2
Cerebrovascular disease	6.7	1.9	<0.0001
Dementia	1.0	0.9	0.8
Prevalent vertebral fracture	20.0	17.9	0.3
Glucose (mg/dl)	97 [88-114]	92 [85-101]	<0.0001
Total cholesterol (mg/dl)	202.2±41.1	223.6±37.0	<0.0001
LDL cholesterol (mg/dl)	122.1±35.1	143.3±31.5	<0.0001
HDL cholesterol (mg/dl)	53 [45-63]	56 [47-68]	<0.0001
Triglycerides (mg/dl)	107 [78-150]	97 [72-131]	<0.0001
CRP (mg/dl)	0.2 [0.1-0.5]	0.2 [0.1-0.5]	0.8
GFR (ml/min/1.73 m^2)	70 [60-81]	71 [61-84]	0.007
Corrected calcium (mg/dl)	9.2 [9.0-9.4]	9.2 [9.0-9.4]	0.3
Phosphate (mg/dl)	3.3 [2.9-3.7]	3.3 [3.0-3.6]	0.9
Alkaline phosphatase (U/l)	69 [57-83]	68 [57-82]	0.9

Table 2. Baseline bone metabolism parameters according to sex and statin use

	Statin users n=478		Non-statin users n=1837			
	Women (256)	Men (222)	Women (1166)	Men (671)	p	p'
PTH (pg/ml)	52.2 [39.9-66.9]	52.1 [39.2-66.8]	50.8 [40.8-64.2]	51.7 [40.7-63.2]	0.3	0.7
25OHD (ng/ml)	21.5±8.3	22.5±8.3	21.9±8.1	22.9±8.0	0.5	0.4
PINP (ng/ml)	41.2 [31.4-52.9]	31.9 [25.1-42.9]	47.1 [35.9-62.0]	35.1 [26.7-44.9]	<0.0001	0.006
CTX (ng/ml)	0.330 [0.224-0.464]	0.234 [0.153-0.377]	0.387 [0.267-0.525]	0.274 [0.187-0.379]	<0.0001	0.013

Data are expressed as: mean±standard deviation or median [interquartile range] as appropriate.

p indicates differences between women on statins vs. non-statin users.

p' indicates differences between men on statins vs. non-statin users

Table 3. General linear model in women

	Statin users n= 256 mean (SE)	Non-statin users n= 1166 mean (SE)	p
Lumbar BMD			
Unadjusted	0.938 (0.009)	0.923 (0.004)	0.11
Age	0.943 (0.009)	0.922 (0.004)	0.024
Age + BMI	0.936 (0.009)	0.923 (0.004)	0.13
Model 1	0.936 (0.009)	0.919 (0.004)	0.065
Model 2	0.933 (0.009)	0.921 (0.004)	0.21
Femoral neck BMD			
Unadjusted	0.741 (0.007)	0.726 (0.003)	0.035
Age	0.754 (0.007)	0.723 (0.003)	<0.0001
Age + BMI	0.746 (0.007)	0.724 (0.003)	0.001
Model 1	0.744 (0.007)	0.719 (0.003)	<0.0001
Model 2	0.742 (0.007)	0.720 (0.003)	0.002
Total hip BMD			
Unadjusted	0.864 (0.008)	0.851 (0.004)	0.11
Age	0.876 (0.008)	0.848 (0.004)	0.001
Age + BMI	0.866 (0.007)	0.850 (0.003)	0.031
Model 1	0.864 (0.007)	0.843 (0.003)	0.021
Model 2	0.86 (0.007)	0.846 (0.003)	0.049

- Model 1: Age, BMI, calcium intake, years since menopause, exercise, smoking, alcohol intake, family history of hip fracture, GFR (MDRD-4 formula). Model 2: Model 1 plus LDL-cholesterol, diabetes and history of coronary heart disease and/or cerebrovascular disease.

Table 4. General linear model in men

	Statin users n= 222 mean (SE)	Non-statin users n= 671 mean (SE)	p
Lumbar BMD			
Unadjusted	1.044 (0.011)	1.016 (0.006)	0.024
Age	1.042 (0.011)	1.017 (0.006)	0.037
Age + BMI	1.039 (0.011)	1.018 (0.006)	0.07
Model 1	1.038 (0.011)	1.018 (0.006)	0.1
Model 2	1.029 (0.011)	1.021 (0.006)	0.51
Femoral neck BMD			
Unadjusted	0.838 (0.008)	0.815 (0.005)	0.02
Age	0.840 (0.008)	0.815 (0.005)	0.008
Age + BMI	0.836 (0.008)	0.816 (0.005)	0.027
Model 1	0.836 (0.008)	0.816 (0.005)	0.031
Model 2	0.832 (0.008)	0.818 (0.005)	0.21
Total hip BMD			
Unadjusted	0.998 (0.009)	0.973 (0.005)	0.013
Age	1.000 (0.009)	0.972 (0.005)	0.007
Age + BMI	0.995 (0.008)	0.974 (0.005)	0.024
Model 1	0.995 (0.008)	0.975 (0.005)	0.045
Model 2	0.992 (0.008)	0.976 (0.005)	0.14

- Model 1: Age, BMI, calcium intake, smoking, alcohol intake, exercise, family history of hip fracture, GFR (MDRD-4 formula). Model 2: Model 1 plus LDL-cholesterol, diabetes, history of coronary heart disease and/or cerebrovascular disease.

Figure 1. Mean femoral neck BMD according to the statin polarity

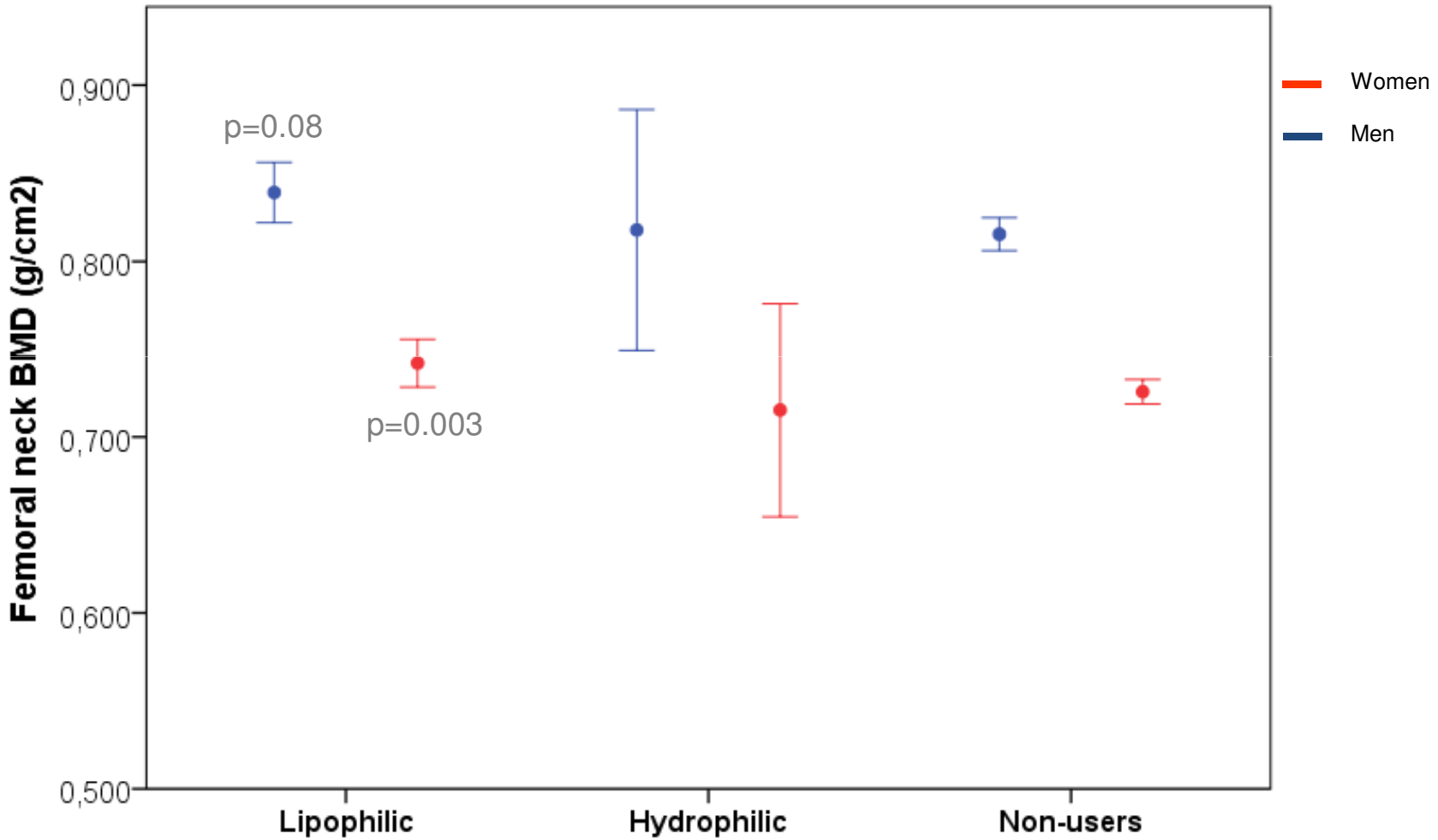
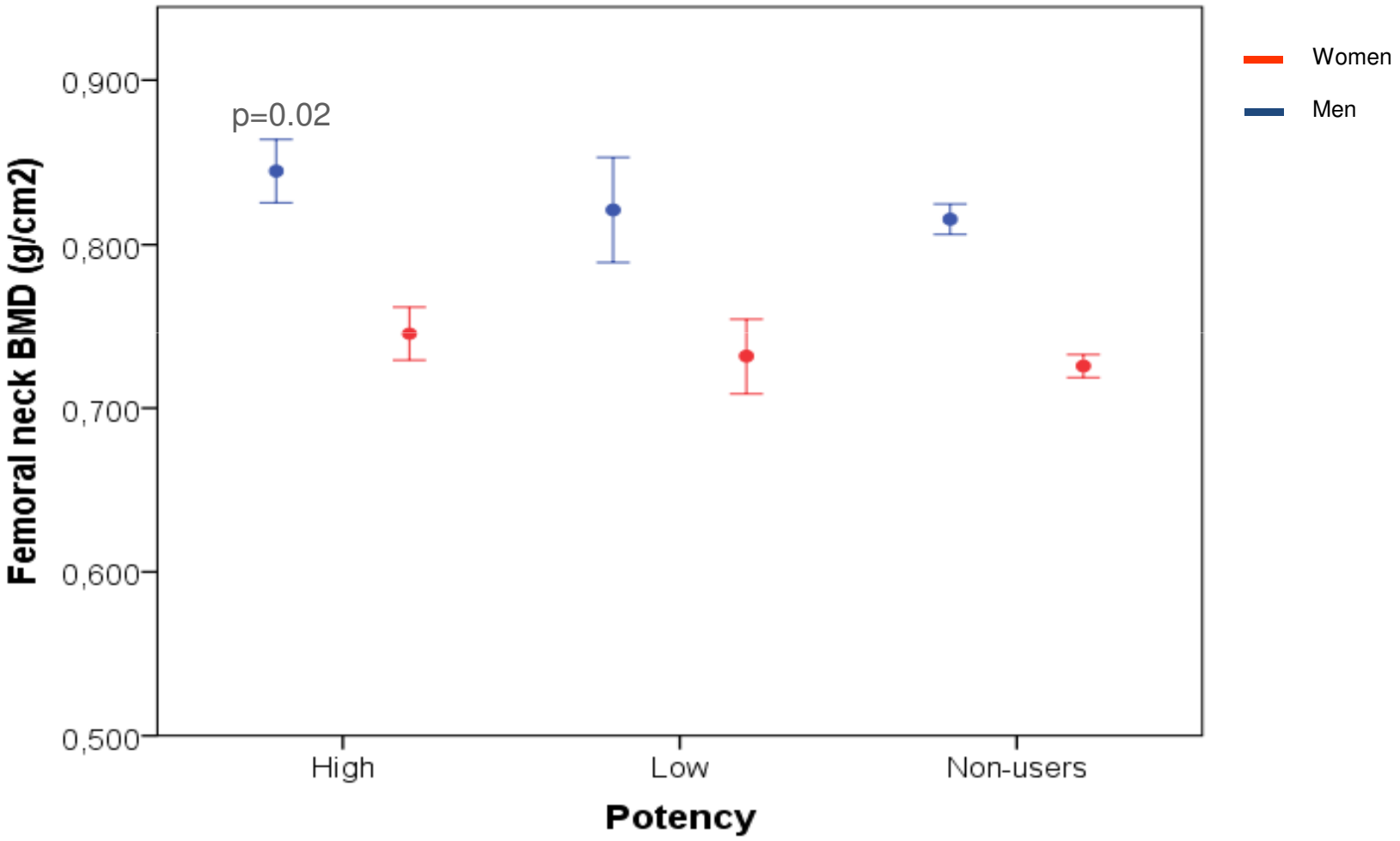


Figure 2. Mean femoral neck BMD according to the statin potency



CONCLUSIONS

- In a large population-based cohort, women on statins had higher BMD at the hip than non-users

- Overall, this increase in BMD was more evident in subjects on lipophilic or high-potency statins