

Sex Hormone Binding Globulin is associated with markers of Vertebral Fracture and Vertebral Fracture Risk

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AIM

To determine whether sex hormone binding globulin (SHBG) levels are associated with skeletal parameters constituting markers of vertebral fractures, including a) bone mineral density (BMD) b) trabecular bone score (TBS) and also c) prevalent vertebral fractures (VFs)

CONCLUSION

This study suggests that SHBG concentrations affect vertebral fracture risk through BMD and not through micro-architecture parameters (LS-TBS). Since the effect of SHBG on BMD was independent of sex steroids, further studies are needed to explore the mechanisms through which SHBG affects BMD.

BACKGROUND

- High levels of SHBG have been associated to increased fracture risk.
- It remains unclear whether this association is independent of sex steroids (estradiol and testosterone) and bone strength markers (LS-BMD, LS-TBS).

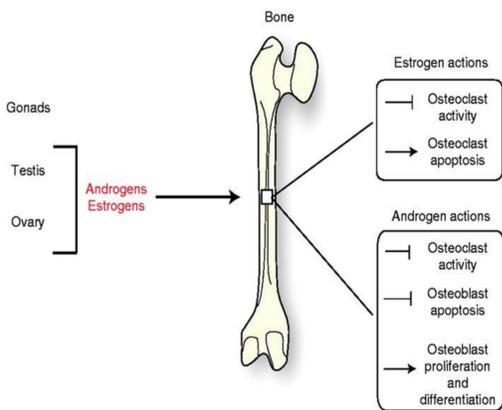
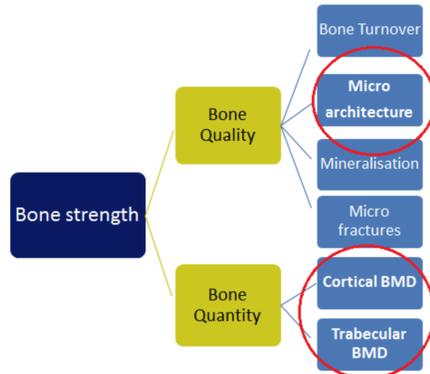


Fig.1 The effects of sex steroids on bone

Fig.2 Bone strength components; highlighted in red are the components we have measured in this study through LS-TBS and LS-BMD



METHODS

- We assessed X-Ray measurements of 6224 men and women participants of Rotterdam Study. VFs were scored with quantitative morphometric (QM) and algorithm based qualitative (ABQ) method.
- Serum SHBG and prevalent VFs were assessed at baseline whereas LS-BMD and LS-TBS were assessed 4 years later.
- To determine the associations linear and logistic regression models were performed:

LS-BMD (or LS-TBS) ~ Age+sex+height+BMI+ Bone treatment+Smoking+HRT+PA+Glucose+calcium+cholesterol+ phosphates +insulin+ estradiol+testosteron + SHBG (tertiles)

Model1: VFs~ Age+sex+height+BMI+ Sex + Bone treatment+smoking+HRT+PA+Glucose+calcium+cholesterol+p hosphates +insulin+ estradiol+testosteron +SHBG(tertiles)

Model2: Model1 + LS-TBS

Model3: Model2 + LS-BMD

RESULTS

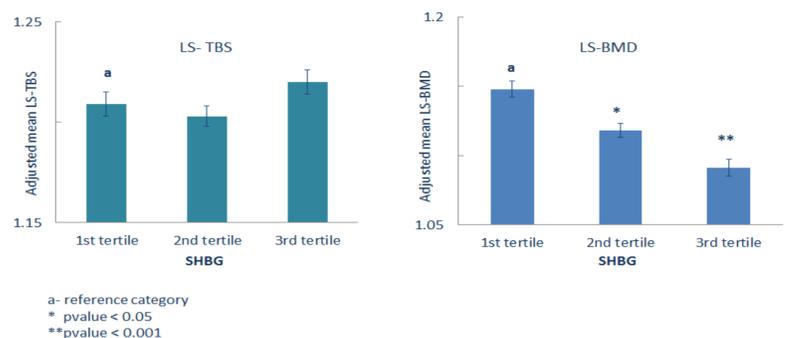
Table1. Baseline characteristics of the study population

	VFs ABQ			VFs QM		
	Controls (4355)	Cases (176)	p-value	Controls (4273)	Cases (854)	p-value
Age (years)	64.8 (6.8)	69.2 (7.3)	<0.001	64.5 (6.8)	67.6 (7.8)	<0.001
Sex (female)	2448 (56.2)	126 (71.6)	<0.001	2421 (56.7)	481 (56.3)	0.8
Height (cm)	167.2 (9.1)	163.3 (9.3)	<0.001	167.3 (9.1)	166.5 (9.7)	0.02
Weight (kg)	75.8 (12.8)	69.6 (12.6)	<0.001	75.6 (12.7)	74.7 (13.3)	0.06
BMI (kg/m ²)	27.0 (3.9)	26.0 (3.8)	0.001	27.0 (3.9)	26.9 (3.9)	0.4
LS- BMD (g/cm ²)	1.128 (0.2)	0.927 (0.1)	<0.001	1.126 (0.2)	1.087 (0.2)	0.001
LS- TBS	1.212 (0.1)	1.157 (0.1)	<0.001	1.215 (0.1)	1.184 (0.1)	<0.001
SHBG (nmol/l)	58.6 (28.7)	77.5 (36.8)	<0.001	58.7 (28.7)	64.6 (32.3)	<0.001
Estradiol (pmol/l)	74.19 (64.5)	52.61 (40.1)	<0.001	74.48 (55.6)	72.78 (50.5)	0.6
Testosterone (nmol/l)	8.02 (8.9)	5.8 (8.6)	<0.001	7.95 (8.9)	8.05 (9.0)	0.8
Sex Hormone Therapy (yes)	131 (3.0)	2 (1.2)	0.1	129 (3.2)	21 (2.6)	0.3
Bone treatment (yes)	46 (1.1)	15 (9.2)	<0.001	44 (1.1)	31 (3.8)	<0.001
Smoking (yes)	725 (16.8)	38 (21.6)	0.09	723 (17.0)	150 (17.6)	0.6
Systolic Blood Pressure (mm Hg)	143.5 (21.3)	143.4 (19.0)	0.9	143.3 (21.4)	143.8 (20.6)	0.5
Diastolic Blood Pressure (mm Hg)	76.7 (11.0)	75.0 (11.1)	0.047	77.0 (11.2)	76.0 (11.4)	0.01
Physical Activity (MET hours)	84.0 (44.0)	77.0 (44.0)	0.044	84.2 (44.5)	77.6 (41.6)	<0.001
Glucose (serum) (mmol/l)	6.02 (1.6)	5.68 (1.1)	0.006	6.00 (1.6)	5.92 (1.7)	0.2
Calcium (serum) (mmol/l)	2.42 (0.09)	2.41 (0.1)	0.5	2.41 (0.09)	2.41 (0.09)	0.4
Cholesterol (serum) (mmol/l)	5.82 (1.0)	5.9 (1.0)	0.07	5.8 (1.0)	5.8 (1.0)	0.5
Phosphate (serum) (mmol/l)	1.09 (0.1)	1.15 (0.1)	<0.001	1.1 (0.1)	1.1 (0.1)	0.6
Insulin (serum) (pmol/l)	90.0 (130.5)	72.2 (60.0)	<0.001	88.5 (92.0)	92.4 (247.5)	0.6

MET- metabolic equivalent of tasks in hour

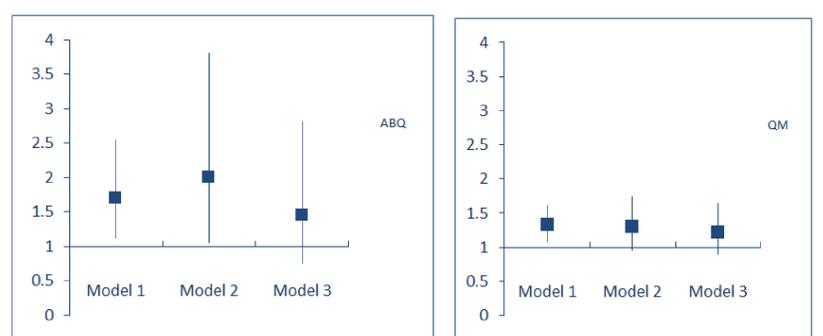
Cases were significantly older, shorter, lighter, with lower LS-BMD and LS-TBS, lower DBP according to ABQ and QM, whereas cases had lower BMI, lower estradiol and testosterone levels, lower insulin and glucose levels and more females fractured only according to ABQ.

Fig.3 Adjusted mean LS-TBS and LS-BMD through SHBG tertiles



There was no significant difference in LS- TBS between SHBG tertiles whereas there was significant difference in LS-BMD between SHBG tertiles.

Fig.4 The Association between SHBG and VFs (ABQ and QM)



SHBG was significantly associated with VFs (both ABQ & QM) despite sex steroids levels but the association was not independent of LS-BMD.