INFLUENCE OF SEX STEROIDS ON SCLEROSTIN LEVELS IN PATIENTS WITH PROSTATE CANCER

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BACKGROUND AND OBJECTIVES: There is increasing evidence for the key role of osteocytes in the regulation of bone remodeling. One of the main products of these cells, sclerostin, inhibits bone formation and may also stimulate bone resorption. To our knowledge, there are few data in prostate cancer (PC) patients especially in patients with hypogonadism related to androgen deprivation therapy (ADT).

DESIGN, SETTING AND PATIENTS: Cross-sectional study including 25 patients with PCa treated with androgen deprivation therapy (ADT), 34 patients with untreated PCa, and 22 healthy controls.

• Serum total testosterone (T) and estradiol (E2) were measured by ECLIA. Free testosterone, bioavailable testosterone, free estradiol and bioavailable estradiol were calculated.

• Markers of bone turnover were determined as follows: total osteocalcin (OC), serum carboxyterminal cross-linked telopeptide of type I collagen (CTX) , and tartrate-resistant acid phosphatase 5b (TRAP5b)

• Lumbar spine and femoral bone mineral density (BMD) were measured by dual X-Ray absorptiometry (Hologic QDR 4500). World Health Organization criteria for osteoporosis were used.

• Serum sclerostin was measured using quantitative sandwich enzyme-linked immunosorbent assay (ELISA) developed by Biomedica (Austria).

Intra e inter-assay variability by our laboratory were and 4% and 3%, respectively. Sclerostin measurements are reported throughout in picomoles per liter (pmol/L) and lower limit of detection was <10 pmol/L.

RESULTS:

Table 1. Clinical, anthropometric and biochemical parameters of study subjects according to group and ADT treatment.

Group	Control (n=22)	non ADT (n=34)	ADT (n=25)	Reference range
Age (years)	70 ± 5	67 ± 6	73 ± 6	-
BMI (Kg//cm^2)	27.2 ± 3.3	28.4 ± 3.9	29.7 ± 4.8	-
Physical activity (h/week)	7.2 ± 3.1	4.9 ± 2.9	6.2 ± 3.2	-
Osteoporosis (%)	18	18	28**	-
Morphometric VF (%)	6	15	25**	-
Serum parameters:				
Calcium (mg/dL)	9.3 ± 0.4	9.34 ± 0.36	9.24 ± 0.38	8.6 - 10.2
Phosphorus (mg/dL)	3.3 ± 0.4	3.11 ± 0.37	3.49 ± 0.44	3.6 - 6
PTH (pg/mL)	47.82 ± 18.23	53.7 ± 20.0	58.8 ± 22.5	15 - 65
25(OH)D (ng/mL)	19.1 ± 8.7	21.6 ± 9.6	24.6 ± 11.9	15 - 74
BSAP (µg/L)	10.85 ± 2.88	14.33 ± 6.10*	18.93 ± 6.67*	7.43 - 31.37
CTX (ng/mL)	0.34 ± 0.12	0.36 ± 0.19	0.49 ± 0.21*	0.15 - 0.44
TRAP5b (UI/L)	1.8 ± 0.6	2.08 ± 0.87	2.44 ± 1.18	1.3 - 4.82
Sclerostin (pmol/L)	38.48 ± 9.19	48.24 ± 15.93*	64.52 ± 27.21 *	-
DXA parameters:				
BMD LS (g/cm^2)	1.002 ± 0.173	0.942 ± 0.156	0.880 ± 0.199 *	-
BMD FN (g/cm^2)	0.820 ± 0.110	0.758 ± 0.172	0.720 ± 0.156 *	-
BMD TH (g/cm^2)	0.931 ± 0.131	0.898 ± 0.197	0.858 ± 0.178	-

BMI: body mass index; 25(OH)D: 25-hidroxyvitamin D; iPTH: intact parathormone; CTX: carboxiterminal cross-linked telopeptide of type I collagen; TRAP5b: tartrate-resistant acid phosphatase 5b; BSAP: Alkaline phosphatase bone isoenzime; BMD: bone mineral density; LS: lumbar spine; FN: femoral neck; TH: total hip; VF: vertebral fractures.
Data for continuous variables are presented as mean ± SD. Data for categorical variables are presented as percentages.
ANOVA model or Mann-Whitney test: *: p<0.05; for control *vs* ADT/non ADT group.
X^2 for comparisons of categorical variables: **: p<0.05 for control *vs* ADT/non ADT group.

Table 2. Correlation coefficients between sex esteroids levels and serum esclerostin levels.

	ADT (n=25)	non ADT (n=34)	p value
Total T (ng/mL)	0.098 ± 0.076	4.491 ± 1.432	< 0.001
Free T (ng/mL)	0.0013 ± 0.008	0.075 ± 0.021	< 0.001
Bioavailable T (ng/mL)	0.030 ± 0.020	1.838 ± 0.556	< 0.001
Total E2 (pg/mL)	9.501 ± 4.291	30.809 ± 8.066	< 0.001
Free E2 (pg/mL)	0.166 ± 0.108	0.790 ± 0.359	< 0.001
Bioavailable E2 (pg/mL)	4.026 ± 2.729	19.351 ± 8.920	< 0.001

PC: prostate carcinoma. ; T: testoterone; E2: estradiol.
Data are presented as mean ± SD. Unpaired *t* test or Mann-Whitney test for ADT *vs* non ADT patients.

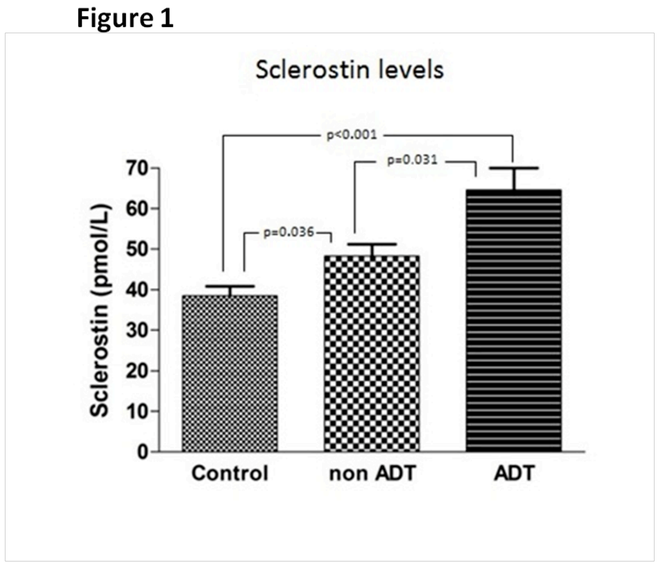
Table 3. Correlation coefficients between biochemical variables and DXA parameters with serum esclerostin levels.

PC patients	correlation coefficient (r)	p value
Total T (ng/mL)	-0.309	0.029
Free T (ng/mL)	-0.299	0.035
Bioavailable T (pg/mL)	-0.280	0.049
Total E2 (pg/mL)	-0.140	0.331
Free E2 (pg/mL)	-0.040	0.784
Bioavailable E2 (ng/mL)	-0.022	0.878
Ratio Total (E2/T)	0.470	0.000
Ratio Bioavailable (E2/T)	0.524	0.000
Ratio Free (E2/T)	0.523	0.000

PC: prostate carcinoma. ; T: testoterone; E2: estradiol.

Figure 1. Serum sclerostin levels in control group, PCa patients without ADT and PCa patients with TDA.

Figure 1



CONCLUSIONS:

1) Circulating sclerostin levels are significantly increased in patients with prostate cancer and particularly in those with androgen-deprivation therapy.
2) The inverse relationship between sclerostin and testosterone in these patients suggests that androgens are key regulators of bone metabolism in this population.

Conflicts of interest: none.