Prostate Cancer in Elderly Croatian Men: 5-HT Genetic Polymorphisms and the Influence of Androgen Deprivation Therapy on Osteopenia—A Pilot Study

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Background: The aim of this study was to determine the relationship between body mass index, biochemical parameters, and 5-hydroxytryptamine (5-HT) genetic polymorphisms and prostate dysfunction in an elderly general male population. **Results:** One hundred and seventeen elderly male subjects [60 men without symptoms of prostate hyperplasia, 42 men with untreated benign prostatic hyperplasia (BPH), and 15 men with prostate cancer (PCa)] treated with finasteride or flutamide were included. Multiple comparisons showed significant difference in age, T-score, concentration of phosphorus, calcium, C-reactive protein, and prostate-specific antigen (PSA) between the groups. T-score was the lowest and phosphorus concentration was the highest in the PCa group. Highest PSA, proteins, calcium, and Hekal's formula score were found in the BPH group. Patients with PCa were more frequent GG+GA carriers of 5-HT1B 1997A/G gene polymorphism ($p=0.035$). Univariate regression analysis showed association of PCa-treated subjects with age ($p=0.010$) and 5-HT1B genetic polymorphism ($p=0.018$). Antiandrogen therapy affects T-score ($p=0.017$), serum phosphorus ($p=0.008$), glucose ($p=0.036$), and total proteins ($p=0.050$). Multivariate-stepwise logistic regression analysis showed the significant association of treated PCa with age ($p=0.028$) and inorganic phosphorus ($p=0.005$), and a marginal association with ultrasonographic T-score ($p=0.052$). **Conclusions:** Antiandrogen therapy might induce bone mineral loss in elderly PCa patients. Preliminary data imply that the genetic variants of the 5-HT1B receptor might be associated with PCa.

Introduction

PROSTATE CANCER (PCa) is one of the most common cancers in aged men. Literature data suggest that combination of several anthropometric, biochemical, clinical, and genetic factors could contribute to its development (Frydenberg *et al.*, 1997). Screening for PCa usually includes determination of prostate-specific antigen (PSA) levels combined with digital rectal and/or abdominal or rectal ultrasonography of the prostate (Rundle *et al.*, 2009). Primary treatment of locally advanced and metastatic PCa often involves androgen deprivation therapy (ADT), using both steroidal or nonsteroidal antiandrogens. This therapy alters a man's hormone production to shrink, manage, or even cure the cancer (Taylor

et al., 2009; Suzuki *et al.*, 2010). One of the steroidal antiandrogens available and often used in Croatia is finasteride, a 4-aza analog of testosterone and a competitive inhibitor of both tissue and hepatic 5- α reductase. Treatment with finasteride inhibits testosterone conversion to dihydrotestosterone (DHT) (Rittmaster *et al.*, 1989; Geller, 1990; Stoner, 1990), which is associated with the development of benign prostatic hyperplasia (BPH) and possibly PCa (Tenover *et al.*, 1997; Matsumoto *et al.*, 2002). Flutamide (prostandril) is a nonsteroidal antiandrogen drug that competes with testosterone and its powerful metabolite DHT for binding to androgen receptors in the prostate gland (Neri, 1989). Although ADT provides beneficial effects such as reduction in DHT and PSA concentration, stabilizing the disease, and prolonging survival (Suzuki *et al.*,

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2010), it can also change bone metabolism (resulting in loss of mineral density and higher risk of fracture) and increase the risk of cardiovascular mortality and diabetes (Suzuki *et al.*, 2010; Serpa Neto *et al.*, 2010). This is because antihormonal therapy changes relevant blood concentrations of estrogens and androgens responsible for the suppression of bone resorption and promotion of bone formation (Nishiyama *et al.*, 2005). Osteopenia is a very common co-morbidity in men with treated PCa (Ziara *et al.*, 2009).

Some studies have indicated that obesity is associated with lower risk of nonaggressive type of the disease, but also with a higher risk of the aggressive type, and that metabolic syndrome has been implicated in PCa mortality (Buschemeyer and Freedland, 2007). However, the association between obesity, metabolic syndrome, and PCa is not clear (Buschemeyer and Freedland, 2007; Rundle *et al.*, 2009). Lower PSA levels and larger-sized prostates in men with higher body mass index (BMI) make biopsy of prostate less accurate for finding an existing cancer (Buschemeyer and Freedland, 2007). Recent data suggest that obesity might be associated with increased risk of malignancy (Hekal and Ibrahim, 2010) and that it is less common in benign prostate disease. Many reports have shown an inverse relationship between PSA and BMI; Hekal and Ibrahim (2010) designed an inverse PSA-BMI equation to enhance the sensitivity of PSA marker in obese patients.

Serotonin [5-hydroxytryptamine (5-HT)] is a brain neurotransmitter and/or a peripheral hormone (Berger *et al.*, 2009) that is released by prostate neuroendocrine cells too (Jungwirth *et al.*, 2008). It has an important role in tumor growth, differentiation, and gene expression. Serotonin stimulates cellular mechanisms and regulates cell proliferation and tumor growth throughout its receptors (Siddiqui *et al.*, 2005). In this respect the polymorphisms of serotonergic receptor genes have an important place in the regulation of serotonergic function. In addition, polymorphisms of the serotonergic type 1B (5-HT1B), type 2A (5-HT2A), and type C2 (5-HT2C) receptor gene were associated with different complex disease traits (Liolitsa *et al.*, 2001).

The aim of this study was to determine the relationship between various anthropometric, biochemical, and genetic factors and various degrees of prostate dysfunction in an elderly, mobile, general population with the hypothesis that biochemical variables are associated with the etiology and treatment of PCa.

Materials and Methods

The study was a part of a large national multicenter epidemiological study of chronic diseases in the Croatian population. It started in 1969, with follow-ups in 1972, 1982, and 2006/2007 when male patients were over 70 years old. Data on bone stiffness were collected during the latest follow-up in 2006 and 2007. The study was approved by the local Research and Ethics Committee. Study procedures have been reported earlier (Pizent *et al.*, 2010; Pašalić *et al.*, 2011).

Subjects

The participants were randomly selected from the electoral roll and included the population from inland Croatia (city of Zagreb and district of Virovitica) and coastal Croatia (city of Split and district of Omiš). The 2006/2007 follow-up recruited

144 men. However, 27 of them were not included in the study due to the following reasons: no urine sample ($n=10$), technical difficulties with serum sampling ($n=10$), and poor cooperation during check-up and/or incomplete records ($n=7$). The study sample consisted finally of 117 men: 60 men with not declared symptoms of prostate hyperplasia (nBPH group); 42 with untreated, but verified BPH (BPH group); and 15 with treated PCa (PCa group). Participants with diagnosed PCa had been receiving antiandrogen therapy with finasteride (13 subjects) or flutamide (2 subjects) after radical prostatectomy. Presence of anuria, oliguria, and blood in urine was also recorded.

All participants were able to take care of themselves and perform everyday activities. Their age ranged between 70 and 94 years. All were taken anthropometric measurements, blood pressure, spirometry, electrocardiography, ultrasound bone densitometry, and blood tests. Trained medical doctors performed physical examination and the interview, while nurses conducted all technical support and blood sampling.

Ultrasound bone densitometry

Quantitative ultrasound (QUS) measurements of the heel (nondominant side) were performed using a "Sahara" sonometer ("Hologic"). The primary parameters measured with ultrasound were broadband ultrasound attenuation (BUA; dB/MHz) and speed of sound (SOS; m/s). These two parameters were combined to form a new parameter, the quantitative ultrasound index (QUI), referred to as ultrasound stiffness, which was used to evaluate bone status (Galić and Šimunović, 2008). QUI can range from 0 to 170, with higher values associated with greater bone mass. T-scores for QUI were calculated using Croatian QUS normative data (Krieg *et al.*, 2008; Kaštelan *et al.*, 2006) according to the formula: $(P-YA)/SD_Y$ (where P is the participant result, YA young adult mean value, and SD_Y standard deviation from YA). The instrumental quality control was performed daily by scanning the manufacturer-provided, temperature-sensitive phantom. To examine short-term precision *in vivo*, 10 participants had two repositioned measurements. The coefficient of variation percent (CV%) was 4.1%, 0.6%, and 4.9% for BUA, SOS, and QUI, respectively.

Biochemical analyses

Blood samples were taken from an antecubital vein after an overnight fast. After centrifugation, sera were divided into 1 mL aliquots and stored at -20°C . Serum glucose, creatinine, urea, proteins, calcium, phosphorus, C-reactive protein (CRP), and alkaline phosphatase (ALP) were determined with an Olympus AU400 selective autoanalyzer using reagents from the same manufacturer (Olympus). Cholesterol, high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) levels were determined enzymatically by a Roche COBAS MIRA autoanalyzer using reagents from Boehringer-Mannheim Diagnostics and Hoffman-La Roche (Roche Diagnostics). Low-density lipoprotein cholesterol (LDL-C) was calculated according to the Friedewald formula $[\text{LDL-C}] = [\text{total cholesterol}] - [\text{HDL-C}] - [\text{TG}/5]$.

PSA was determined by PSA enzyme-linked immunosorbent assay-kit (DRG Diagnostics). The relationship between PSA and obesity was calculated according to PSA-BMI adjusted formula or Hekal's equation $[(\text{measured PSA } (\mu\text{g/L})) * [\text{age (years)}]/[\text{BMI}]]$ (Hekal and Ibrahim, 2010).

Genetic analysis

DNA was extracted from whole blood with a Biosprint DNA-isolation kit (Qiagen) on a KingFisher automatic system (Thermo Labsystems). *5-HT1B* 1997A/G (*rs13212041*), *5-HT2A* 102T/C (*rs6313*), and *5-HT2C*–759C/T (*rs13212041*) polymorphisms were genotyped with a reverse transcriptase–polymerase chain reaction-based TaqMan allelic discrimination assay by using commercial kits (Applied Biosystems) and an ABI Prism 7000 Sequencing Detection System apparatus.

Statistical analysis

Group frequencies were calculated by counting. Categorical variables were compared using Pearson's chi-square test or Fisher's exact test. Continuous variables were expressed as means $\pm$ standard deviation (SD) and 95% confidence interval for mean (95% CI). Group comparisons of continuous variables were performed by analysis of variance, including multiple comparisons and *t*-test or Kruskal-Wallis and Mann-Whitney test if variables were not

TABLE 1. MEAN AND STANDARD DEVIATION OR MEDIAN AND RANGE VALUES OF RELEVANT BIOCHEMICAL PARAMETERS IN ELDERLY MEN, AND THE DIFFERENCE BETWEEN APPARENTLY HEALTHY MEN (WITHOUT SIGNS OF PROSTATE HYPERPLASIA) (NONBENIGN PROSTATIC HYPERPLASIA; *N*=60), MEN WITH SIGNS OF PROSTATE HYPERPLASIA (BENIGN PROSTATIC HYPERPLASIA; *N*=42), AND MEN WITH TREATED PROSTATE CANCER (PROSTATE CANCER; *N*=15)

	Group	Mean	SD	ANOVA	Multiple comparisons	
				p		p
Age (years)	non-BPH	77.6	4.63	0.021	non-BPH & BPH	0.813
	BPH	77.8	3.67		non-BPH & PCa	0.007
	PCa	81.1	4.98		BPH & PCa	0.014
T-score	non-BPH	0.17	1.68	0.063	non-BPH & BPH	0.870
	BPH	0.23	1.19		non-BPH & PCa	0.029
	PCa	−1.01	1.30		BPH & PCa	0.027
Alkaline phosphatase (U/L)	non-BPH	46.0	15.2	0.146	non-BPH & BPH	0.835
	BPH	45.4	12.9		non-BPH & PCa	0.070
	PCa	53.9	19.1		BPH & PCa	0.061
Phosphorous (mmol/L)	non-BPH	0.90	0.17	0.021	non-BPH & BPH	0.866
	BPH	0.91	0.17		non-BPH & PCa	0.007
	PCa	1.04	0.17		BPH & PCa	0.013
Calcium (mmol/L)	non-BPH	2.30	0.15	0.006	non-BPH & BPH	0.002
	BPH	2.41	0.19		non-BPH & PCa	0.079
	PCa	2.40	0.17		BPH & PCa	0.709
Proteins (g/L)	non-BPH	70.5	5.19	0.004	non-BPH & BPH	0.007
	BPH	73.2	4.67		non-BPH & PCa	0.006
	PCa	74.5	5.53		BPH & PCa	0.403
Hekal score	non-BPH	3.44	2.13	<0.001	non-BPH & BPH	<0.000
	BPH	14.5	17.7		non-BPH & PCa	0.447
	PCa	5.97	10.2		BPH & PCa	0.015
Mann-Whitney test						
		Median	Range	Kruskal-Wallis		p
CRP (μg/L)	non-BPH	2.21	0.00–14.70	0.077	non-BPH & BPH	0.137
	BPH	2.82	0.34–41.46		non-BPH & PCa	0.206
	PCa	1.72	0.36–48.79		BPH & PCa	0.036
PSA (μg/L)	non-BPH	1.17	0.17–3.83	<0.001	non-BPH & BPH	<0.001
	BPH	2.58	0.42–26.60		non-BPH & PCa	0.327
	PCa	0.86	0–14.70		BPH & PCa	0.003
Glucose (mmol/L)	non-BPH	5.40	4.0–13.6	0.558	non-BPH & BPH	0.490
	BPH	5.60	3.6–13.8		non-BPH & PCa	0.330
	PCa	5.60	4.7–16.5		BPH & PCa	0.593

SD, standard deviation; BPH, benign prostatic hyperplasia; PCa, prostate cancer; CRP, C-reactive protein; PSA, prostate-specific antigen; ANOVA, analysis of variance.

normally distributed. Univariate and multivariate-stepwise logistic regression analyses were used to assess possible risk factors associated with antiandrogen therapy in patients treated for PCa. The level of significance was set at 0.05. Statistical analyses were performed with STATISTICA 7 for Windows (StatSoft, Inc.; 2003) and the SAS 8.2 software package (SAS Institute, Inc.; SAS Online Doc; 1999 <http://v8doc.sas.com/sashtml/>).

Results

Among 117 subjects enrolled in the current study, the prevalence of verified BPH and PCa was 35.9% and 12.8%, respectively. Table 1 shows the characteristics and differences in relevant parameters between the three groups of participants. Multiple comparisons show a statistically significant difference in age, T-score, and serum phosphorus and CRP between men with PCa on antiandrogen therapy (PCa group) and the other two (nBPH and BPH) groups. A statistically significant difference in serum calcium was found between the nBPH and BPH groups, whereas significant difference in PSA was found between the BPH group and the other two groups. Ultrasonographic T-score was the lowest and phos-

phorus concentration was the highest in the PCa group. The highest values of PSA, proteins, calcium, and Hekal's formula score were found in the BPH group. Although significant, the difference in protein and calcium concentrations between the groups was clinically irrelevant. There were no significant differences in TG, cholesterol, HDL-C, LDL-C, urea, and creatinine between the groups (data not shown).

Table 2 shows characteristics of the relevant parameters after pooling nBPH and BPH groups (non-PCa group) and the difference between non-PCa and PCa groups. The PCa group had significantly higher concentrations of glucose, phosphorus, and proteins, and ALP activity than the non-PCa group. Ultrasound densitometry variables (T-score, SOS, BUA, QUI, and bone mineral density) were significantly lower in the PCa than in the non-PCa group. There was no statistically significant difference in biochemical variables, including lipid profiles, urea, and creatinine concentrations.

Allele and genotype frequencies of the 5-HT1B 1997A/G, 5-HT2A 102T/C, and 5-HT2C-759C/T polymorphisms in non-PCa and PCa groups are shown in Table 3. The frequency of AA homozygotes of the 5-HT1B 1997A/G polymorphism was significantly lower in the PCa than in the non-PCa group. There was no significant difference in allele and genotype

TABLE 2. ANTHROPOMETRIC AND BIOCHEMICAL PARAMETERS IN ELDERLY MEN AND THE DIFFERENCE BETWEEN MEN WITHOUT CANCER (WITH AND WITHOUT SIGNS OF PROSTATE HYPERPLASIA) (NON-PCa) AND MEN WITH TREATED PROSTATE CANCER (PCa)

	non-PCa (n=102)				PCa (n=15)				t-Test	
	Mean	SD	95% CI of mean		Mean	SD	95% CI of mean			p
			Lower	Upper			Lower	Upper		
Age (years)	77.7	4.2	76.7	78.5	81.1	5.0	78.3	83.8	0.006	
BMI (kg/m ²)	28.1	3.2	27.5	28.8	27.8	3.6	25.9	29.9	0.761	
SOS	1560	41	1549	1570	1532	37	1505	1558	0.047	
BUA	87	23	81	92	71	18	57	84	0.038	
QUI	104	26	98	111	86	22	70	102	0.041	
BMD	0.73	1.13	0.45	1.02	0.47	0.14	0.37	0.57	0.461	
T-score	0.19	1.48	-0.18	0.57	-1.0	1.3	-1.94	-0.08	0.019	
ALP (U/L)	45.7	14.2	42.9	48.5	53.9	19.1	43.3	64.5	0.050	
Phosphorous (mmol/L)	0.90	0.17	0.87	0.94	1.04	0.17	0.94	1.13	0.005	
Calcium (mmol/L)	2.34	0.18	2.31	2.38	2.40	0.17	2.30	2.48	0.383	
Cholesterol (mmol/L)	5.08	1.04	4.88	5.28	5.30	1.23	4.62	5.98	0.461	
HDL-C (mmol/L)	1.15	0.40	1.07	1.23	0.99	0.20	0.88	1.10	0.141	
LDL-C (mmol/L)	3.18	0.97	2.99	3.38	3.51	1.03	2.94	4.08	0.232	
TG (mmol/L)	1.65	1.02	1.46	1.85	1.76	0.97	1.22	2.30	0.707	
Creatinine (μmol/L)	104	34.8	97	111	106	21.8	94	118	0.786	
Urea (mmol/L)	7.21	2.67	6.69	7.73	6.93	1.58	6.06	7.81	0.699	
Proteins (g/L)	71.6	5.15	70.6	72.6	74.5	5.53	71.4	77.6	0.046	
Hekal score	8.09	12.7	5.49	10.7	5.97	10.2	0.34	11.6	0.541	
Glucose (mmol/L)	6.21	2.06	5.80	6.60	7.68	3.93	5.51	9.85	0.026	
			</							

PCa, prostate cancer; BMI, body mass index; SOS, speed of sound; BUA, broadband ultrasound attenuation; QUI, quantitative ultrasound index; BMD, bone mineral density; ALP, alkaline phosphatase; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride.

TABLE 3. 5-HT1B, 5-HT2A, AND 5-HT2C RECEPTOR GENOTYPE AND ALLELE COUNT AND FREQUENCIES (PERCENTAGES) IN GROUPS OF ELDERLY MEN WITHOUT CANCER (WITH AND WITHOUT SIGNS OF PROSTATE HYPERPLASIA) (NON-PCa) AND WITH TREATED PROSTATE CANCER (PCa)

Subjects	5-HT1B 1997A/G polymorphism			
	Allele		Homozygotes	Carriers
	A n (%)	G n (%)	AA n (%)	GG + GA n (%)
non-PCa (n = 101)	97 (75.8)	31 (24.2)	66 (68)	31 (32)
PCa (n = 15)	14 (58.3)	10 (41.7)	6 (40)	9 (60)
Pearson's χ^2 -test	$\chi^2 = 3.124$; df = 1; $p = 0.077$		$\chi^2 = 4.49$; df = 1; $p = 0.035$	
Subjects	5-HT2A 102T/C polymorphism			
	Allele		Homozygotes	Carriers
	C n (%)	T n (%)	CC n (%)	TT + CT n (%)
non-PCa (N = 97)	125 (61.9)	77 (38.1)	41 (40.6)	60 (59.4)
PCa (n = 15)	20 (66.7)	10 (33.3)	7 (46.7)	8 (53.3)
Pearson's χ^2 -test	$\chi^2 = 0.225$; df = 1; $p = 0.614$		$\chi^2 = 0.199$; df = 1; $p = 0.656$	
Subjects	5-HT2C – 759C/T polymorphism			
	Allele			
	C n (%)		T n (%)	
non-PCa (n = 99)	76 (76.8)		23.2 (23.2)	
PCa (n = 15)	14 (93.3)		1 (6.7)	
Pearson's χ^2 -test	$\chi^2 = 2.151$; df = 1; $p = 0.142$			
Fisher's exact test	$p = 0.188$			

TABLE 4. UNIVARIATE AND MULTIVARIATE-STEPWISE LOGISTIC REGRESSION ANALYSIS OF ELDERLY MEN WITHOUT CANCER (WITH AND WITHOUT SIGNS OF PROSTATE HYPERPLASIA) (NONPROSTATE CANCER; $N=15$) AND WITH TREATED PROSTATE CANCER ($N=102$)

Variable	Univariate				Multivariate-stepwise			
	OR	95% CI limits		p	OR	95% CI limits		p
		Lower	Upper			Lower	Upper	
Age	1.171	1.038	1.320	0.010	1.289	1.027	1.617	0.028
Phosphorous	98.979	3.287	> 1000	0.008	> 1000	10.257	> 1000	0.005
T-score	0.440	0.224	0.865	0.017				0.052
PSA	0.936	0.770	1.137	0.504				
Cholesterol	1.234	0.743	2.051	0.417				
TG	1.093	0.667	1.790	0.724				
HDL-C	0.229	0.031	1.674	0.147				
CRP	0.854	0.648	1.125	0.262				
MS-IDF	1.091	0.346	3.438	0.882				
BMI	0.973	0.820	1.155	0.759				
Glucose	1.216	1.013	1.460	0.036				
ALP	1.002	0.991	1.013	0.687				
Calcium	3.696	0.199	68.502	0.380				
Proteins	1.121	1.000	1.256	0.050				
Hekal score	1.020	0.947	1.099	0.606				
5-HT1B	3.596	1.248	10.366	0.018				
5-HT2A	0.714	0.134	3.813	0.694				
5-HT2C	0.236	0.029	1.892	0.174				

OR, odds ratio; CI, confidence interval; MS-IDF, metabolic syndrome according International Diabetes Federation criteria.

cannot be the main reason for significant bone mineral loss. ADT has great impact in it, as supported by numerous literature data.

In this study, we have also investigated the association between BMI and lipid levels in subjects with PCa. We did not find any relationship between PSA levels and BMI, or between BMI and lipid levels in any of the groups. This is in agreement with earlier experimental data that showed that finasteride had no clinically significant effects on serum lipid profile including total cholesterol, LDL-C, HDL-C, and TG (Geller, 1990; Rittmaster and Finasteride, 1994), but in contrast to those data that showed high incidence of obesity and metabolic syndrome in patients with PCa (Buschemeyer and Freedland, 2007; Hekal and Ibrahim, 2010).

Genetic polymorphisms might be associated with different diseases including PCa. Clinical characterizations of polymorphisms within particular genes might be useful for screening for early onset PCa (Hughes and Giri, 2009). Some polymorphisms of insulin receptor genes on men from Croatian descent were recently investigated (Saracevic *et al.*, 2011) and the study showed the possible association of *INSR H1085H C>T* polymorphism with PCa risk. Serotonin and its receptors are abundantly present in normal and/or neoplastic prostate tissue (Abrahamsson, 1999). They have an important role in tumor growth, differentiation, and gene expression (Siddiqui *et al.*, 2005). In PC3 PCa cell line, 5-HT1A receptor antagonists and to a greater extent 5-HT1B receptor antagonists significantly inhibit cell growth and induce apoptosis (Siddiqui *et al.*, 2006). The identification of 5-HT receptors as a novel target in castration-resistant PCa (Dizeyi *et al.*, 2011) pointed toward neuroendocrine factors facilitating progression and migration of PCa cells in an androgen-deficient environment. These findings might be useful for future investigations of 5-HT receptors as potential targets of anticancer therapy.

We studied the frequency of 5-HT receptor gene polymorphisms in elderly men treated for PCa (PCa group) and in nontreated (both non-BPH and BPH) subjects. To the best of our knowledge, this is the first study that shows different frequencies of 5-HT1B variants between these groups. This difference was due to the significantly higher frequency of G (GG+GA) carriers versus homozygous AA genotype in the PCa group. Although this group included in our study was small, our results indicate that 5-HT1B variants might be used as a genetic risk marker for the growth of PCa and also that 5-HT1B receptors might be an important target for the development of anticancer therapy.

A limitation of the study was the small number of participants, including those with PCa and age-matched healthy controls. The association between PCa and single nucleotide polymorphism (SNP) in 5-HT1B gene should be confirmed by epidemiological studies that would involve a larger number of subjects in clinically controlled urological studies. The advantage of the study was in the determination of the relationship between large number of biochemical and clinical variables and prostate dysfunction in elderly general population.

Conclusions

Our study has shown a significant bone mineral loss in men who had been receiving ADT for PCa and also implicated that some genetic variants of 5-HT1B receptor might be involved in the predisposition for PCa. The results of the current study did not confirm the associations between PCa, obesity, and lipid profile.

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Disclosure Statement

No competing financial interests exist.

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