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The Effect of Body Mass Index and Waist Circumference on Prostate Specific Antigen in Patients with Benign Prostatic Hyperplasia (BPH)

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Abstract

Background Obesity may be associated with lower prostate specific antigen(PSA) values, If true, this would result in fewer obese men having an elevated PSA, fewer biopsies performed, and fewer cancers detected , consequently cancers may be missed or not detected until at a more advanced stage.

Objective We examined the influences of age, body mass index (BMI) and waist circumference (WC) on PSA before and after adjusting for prostate volume. We also examined associations among age, body mass index, waist circumference and prostate volume (PV).

Methods We analyzed 125 Iraqi men aged 40 to 84 years old who attained the urological outpatient clinic for BPH evaluation during 2009. Curent health status information including prostate related problems, medical interview, basic physical examination and anthropometric measurements including height, weight, BMI and waist circumference were taken for all patients. Blood tests including PSA concentration were performed after overnight fast. A radiologist performed transrectal prostate ultrasound. PSA measurements preceded routine digital examination and transrectal prostate ultrasound.

Results The median serum PSA was significantly lower among obese subjects compared to normal BMI subjects. BMI showed a statistically significant moderately strong negative linear correlation (r = -0.5) with serum PSA. Waist circumference showed a similar pattern with a statistically significant linear correlation with serum PSA (r = -0.43); the median serum PSA was significantly lower among subjects with highest waist circumference compared to subjects in the lowest quartile of waist circumference. The median PSA was significantly higher among subjects with large prostate size compared to those with lowest quartile prostate size. The anthropometric measures were tested for association with PSA density, to adjust for the effect of prostate size on serum PSA.

Conclusion The current data suggest that the PSA cut-points used to recommend biopsy need to be adjusted for the degree of obesity.

Keywords body mass index, waist circumference, prostate specific antigen.

Introduction

Many investigators evaluated the relationship between body habitus, body mass index (BMI), and obesity and lower urinary tract symptoms/benign prostate hyperplasia (LUTS/BPH). There are plausible biologic considerations: adipose tissue is the main source of aromatization of testosterone to estrogen, and men with lower BMI have higher serum testosterone levels [1]. Several caveats must be mentioned:

digital rectal examination (DRE) is less likely to yield a diagnosis of BPH and prostate enlargement in very obese patients because of anatomic obstacles and patients with high BMI may be biased against surgical interventions [1,2].

Recent studies [3-8] suggest obesity may be associated with lower prostate specific antigen (PSA) values, If true, this would result in fewer obese men having an elevated PSA, fewer biopsies performed, and fewer cancers detected, consequently cancers may be missed or not detected until at a more advanced stage.

In contrast, in a study of 68 men, the average prostate weight increased both with age and with increasing obesity together with an increase in serum estradiol levels [9].

Despite its wide spread use, the PSA test is limited by low specificity and reduce sensitivity beyond a specific cutoff value [10,11]. Another problem is that PSA is affected by many non cancer related factors, Understanding those factors and how they interrelate would increase test usefulness, PSA is known to increase with age and prostate volume, and investigators have suggested that age specific PSA and density might provide more accurate clinical assessments than a single reference range applied to men of all ages [12].

Waist circumference (WC), which represents central obesity, is an important clinical parameter that has greater impact than BMI on metabolic disease incidence and its related mortality [13].

To clarify the influence of obesity, defined by BMI or WC, on serum PSA, We examined the magnitude of the association among BMI, WC, prostate volume (PV), and PSA.

Methods

Eligible subjects were 125 men of 40 to 84 years old who attained the urological outpatient clinic for BPH evaluation during 2009. Current health status information including prostate related problems, medical interview and basic physical examination, and anthropometric measurements including height, weight, BMI, and WC were done for all patients.

BMI was calculated as weight in kilograms divided by the square of the height in meters (Kg/m^2) [12].

WC was measured at the part of the trunk located midway between the lower costal margin (bottom of lower rib) and the iliac crest (top of pelvic bone) while the person is standing, with feet about 25-30 cm apart (10-12 in). The measurer should stand beside the individual and fit the tape snugly, without compressing any underlying soft tissues. The circumference should be measured to the nearest 0.5 cm (1/4 in), at the end of a normal expiration.

Blood tests including PSA concentration were performed after subjects fasted overnight; the test was done in the same Lab. A radiologist performed transrectal prostate ultrasound and PSA measurements precede routine digital examination and transrectal prostate ultrasound. PSA density (adjusted PSA for prostate volume) was calculated as PSA divided by Prostate volume.

We exclude from the study men who had a history of prostate cancer, prostate surgery or prostatitis, and who were taking anti androgenic medication such as finasteride. We then exclude men whose serum PSA concentration was greater than 6.5 ng/ml because of the increase the probability of prostate related disease or data error [14]. Patients with PSA density more than 0.12 and those with abnormal DRE were excluded because of increased risk of malignancy, and those with neurological history for lower urinary tract like diabetes mellitus [14].

Results

The results presented in this study were based on the analysis of 125 males with symptoms of BPH. Their age ranged between 40 and 84 years with a mean of 62.7±8.9(SD) years. About one half of the samples were in the 6th decade of life, while those under 50 years of age constituted only 7.2% of the sample. About quarter of the sample were of normal BMI, while obese subjects constituted 39.2% of the sample (Table 1).

The median serum PSA showed week significant changes with age, however no obvious or statistically significant linear trend (r= -0.12, *p*= 0.2) was elucidated.

The median serum PSA was significantly lower among obese subjects (1.5) compared to normal BMI subjects (3.8). BMI showed a statistically significant moderately strong negative linear correlation (r= -0.5) with serum PSA.

Waist circumference showed a similar pattern with a statistically significant linear correlation with serum PSA (r= -0.43). Serum PSA was significantly lower among subjects with highest waist circumference (1.6) compared to subjects in the lowest quartile of waist circumference (3).

The median PSA was significantly higher among subjects with largest prostate size (4) compared to those with lowest quartile prostate size (2). The prostate size showed a statistically significant weak positive linear correlation (r= -0.24) with serum PSA (Table 2).

The anthropometric measures were tested for association with PSA density, to adjust for the effect of prostate size on serum PSA.

The median PSA density was significantly lower among obese subjects (0.024) compared to normal BMI subjects (0.051) and lowest quartile of waist circumference (0.05), both BMI and WC showed a similar pattern with statistically significant negative linear correlation with PSA density (r= -0.47) (r= -0.51) (Table 3).

A multiple linear regression model was used to study the net and independent effect of each anthropometric measure on serum PSA after adjusting for age and prostate size. Age had no important or statistically significant association with serum PSA after adjusting for other explanatory variables included in the model.

Prostate size and the anthropometric had a significant association with serum PSA. All these explanatory variables were of almost equal importance in predicting the magnitude of serum PSA.

For each one cm^3 increase in prostate size the serum PSA is expected to increase by mean of 0.017 after adjusting for the remaining explanatory variables included in the model.

For each one Kg/m^2 increase in BMI the serum PSA is expected to decrease by a mean of 0.102 after adjusting for the remaining explanatory variables included in the model.

For each one cm increase in waist circumference the serum PSA is expected to decrease by a mean of 0.041 after adjusting for the remaining explanatory variables included in the model (Table 4).

Table 1: Frequency distribution of the study sample by age and Body mass index.

Age group (years)	No (%)
<50	9(7.2%)
50-59	30(24%)
60-69	59(47.2%)
70+	27(21.6%)
BMI (Kg/m^2)-Categories [15,16]	
Normal (< 25)	30(24%)
Overweight (25-29.9)	46(36.8%)
Obese (30+)	49(39.2%)
Total	125(100%)

Table 2: The median serum PSA by age and selected anthropometric measures.

	PSA (prostate specific antigen)				
	Range	Median	Interquartile range	No.	*p*
Age group (years)					0.016
<50	(1.8-5.6)	2	(2-3.3)	9	
50-59	(0.1-6)	1.6	(1.5-2.1)	30	
60-69	(0.2-10)	3	(1.6-4)	59	
70+	(0.1-10)	2.2	(1.5-4.8)	27	
r= -0.12 *p*= 0.2[NS]					
BMI (Kg/m^2)-Categories					<0.001
Normal (< 25)	(1-10)	3.8	(2-5)	30	
Overweight (25-29.9)	(0.1-10)	3	(2-4.2)	46	
Obese (30+)	(0.1-8)	1.5	(1-2.1)	49	
r= -0.47 *p* < 0.001					
Waist circumference (cm)-Quartiles					< 0.001
First (lowest) quartile (≤ 86.4)	(1-10)	3	(2-5)	40	
Second quartile (86.5-94.0)	(1.2-5.6)	3.2	(1.7-4.8)	23	
Third quartile (94.1-109.2)	(0.1-7)	1.8	(1-3.4)	43	
Fourth (Highest) quartile (109.3+)	(0.1-3)	1.6	(1-2.5)	19	
r= -0.51 *p* < 0.001					
Prostate size (cm^2)-Quartiles					0.01
First (lowest) quartile (≤ 44)	(0.1-8)	2	(1.5-2.5)	32	
Second quartile (45-70)	(0.1-10)	2	(1.5-3)	35	
Third quartile (71-92)	(0.1-10)	2	(1.5-3)	29	
Fourth (Highest) quartile (93+)	(0.2-6)	4	(2.3-5)	29	
r= 0.24 *p* < 0.001					

Table 3: The median PSA density by age and selected anthropometric measures.

		PSA density				
		Range	Median	Interquartile range	No.	P
1.	Age group (years)					0.13[NS]
	<50	(0.022-0.071)	0.05	(0.034-0.063)	9	
	50-59	(0.002-0.182)	0.032	(0.015-0.05)	30	
	60-69	(0.001-0.182)	0.033	(0.024-0.05)	59	
	70+	(0.001-0.148)	0.05	(0.026-0.06)	27	
	r= -0.03 *p*= 0.71[NS]					
2.	BMI (Kg/m^2)-Categories					< 0.001
	Normal (< 25)	(0.011-0.133)	0.051	(0.029-0.063)	30	
	Overweight (25-29.9)	(0.002-0.182)	0.045	(0.033-0.059)	46	
	Obese (30+)	(0.001-0.182)	0.024	(0.015-0.041)	49	
	r= -0.47 *p* < 0.001					
3.	Waist circumference (cm)-Quartiles					< 0.001
	First (lowest) quartile (≤ 86.4)	(0.011-0.182)	0.05	(0.034-0.106)	40	
	Second quartile (86.5-94.0)	(0.015-0.148)	0.04	(0.03-0.05)	23	
	Third quartile (94.1-109.2)	(0.001-0.152)	0.029	(0.015-0.05)	43	
	Fourth (Highest) quartile (109.3+)	(0.001-0.06)	0.024	(0.011-0.035)	19	
	r= -0.51 *p* < 0.001					

Table 4: Multiple Linear regression model with serum PSA (prostate specific antigen) as the dependent (outcome) variable and age, prostate size in addition to selected anthropometric measures as the independent (explanatory) variables

	Unstandardized Regression coefficient	Standardized Regression coefficient	Sig.
(Constant)	-7.6		0.10[NS]
Age (years)	0.026	0.114	0.17[NS]
Waist circumference (cm)	-0.041	-0.288	0.002
Prostate size (cm^2)	0.017	0.297	< 0.001
BMI (Kg/m^2)	-0.102	-0.278	0.002

R^2=0.34
p (model) < 0.001

Discussion

When we evaluate obese men with prostate enlargement, it may be important to consider that the obesity my lower base line PSA and obese men with early prostate cancer disease are increased risk for having PSA lower than the screening cutoff value [10,11,17].

Thus, it is important to examine the influence of obesity and its related factors including PV on PSA in the general screening population.

In the present study BMI and WC were negatively associated with PSA and adjusted PSA for prostate volume (PSA density). Therefore, we concluded that PSA is negatively associated with obesity (measured by BMI or WC), positively associated with PV and weakly associated with age.

Our study demonstrated that although obese men generally have higher PV than non obese men, they have a lower PSA, but the reason for that is not well known. Previous investigators have suggested that the inverse link between obesity and PSA levels is explained either by endocrine disturbances associated with abdominal obesity, Obesity leads to greater aromatization of testosterone and may associated with lower PSA production [17-19].

The volume dilution theory appears to more closely predict the inverse association between prostate-specific antigen (PSA) levels and obesity than the hormone disturbance theory. A more recent suggestion is that lower PSA are largely due to haemodilution by a large plasma volume in obese men [20-23].

These data demonstrate that PSA concentrations in prostate-cancer-free men inversely correlate with BMI, due to a rise in plasma volume with increasing BMI. Studies confirmed that Higher BMI correlated with higher plasma volumes. Partially adjusted mean PSA levels, on the other hand, decreased with increasing BMI. This relationship between BMI and PSA did not exist when investigators controlled for plasma volume. These data demonstrate that PSA concentrations in prostate-cancer-free men inversely correlate with BMI, due to a rise in plasma volume with increasing BMI [20-23].

In one theory, fat mass, but not lean mass and abdominal fat will be inversely associated with PSA levels, while both lean and fat mass, independent of body fat distribution, will be inversely associated with PSA levels in the second theory [17-19].

In men undergoing radical prostatectomy, higher BMI was associated with higher plasma volume; haemodilution may therefore be responsible for the lower serum PSA concentrations among obese men with prostate cancer [24-26].

To investigate further, Be-Long Cho, from Seoul National University Hospital, and colleagues studied 3593 Korean men aged 30-79 years who received regular check-ups at a health examination center and for whom prostate volume data were available; Obesity had a negative association with prostate specific antigen regardless of prostate volume, and a positive association with prostate volume. Age was not associated with prostate specific antigen after prostate volume adjustment. Obese men, especially those with a small prostate volume, may have lower baseline prostate specific antigen and, thus, be at higher risk for having prostate cancer undetected in a prostate specific antigen screening test [12].

The current data suggest that the PSA cut-points used to recommend biopsy need to be adjusted for the degree of obesity [10,12,27]. Further studies to correlate these results in relation to different races, geographic distribution, and specific age group relation may be needed.

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