RESEARCH COMMUNICATION

Effect of Body Mass Index on Serum Prostate-specific Antigen Levels among Patients Presenting with Lower Urinary Tract Symptoms

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Abstract

Purpose: Studies among asymptomatic male subjects have suggested that a higher body mass index (BMI) is associated with lower serum prostate-specific antigen (PSA) levels. We aimed to investigate whether a similar effect also occurs in patients presenting with lower urinary tract symptoms (LUTS) to a urological unit and its potential implications. Methods: A retrospective review was carried out at our centre between 2005 and 2009. The serum PSA and BMI of the patients were retrieved from a prospectively collected database. The BMI was divided into normal (<23kg/m^2), overweight (23-27kg/m^2), and obese (>27kg/m^2) categories according to WHO recommendation for analysis of the association with PSA level. Results: A total of 1,612 patients with a mean age of 64.6 were included. The mean PSA levels for the normal, overweight, and obese patients were 4.84, 4.54, and 3.95 ng/ml, respectively, with a significant negative correlation (Spearman's coefficient= -0.05, p=0.03). A significant negative association between PSA and BMI among the normal, overweight, and obese groups was also demonstrated by analysis of variance (p=0.01). After adjusting for age differences, there was a significant difference between PSA level for obese patients with a BMI>27 (3.95ng/ml) and non-obese patients with a BMI<27 (4.67ng/ml) with analysis of covariance (p=0.02). Conclusion: In symptomatic male patients, a higher BMI was significantly associated with lower PSA levels. BMI should be considered in the interpretation of serum PSA levels in overweight and obese patients presenting with LUTS.

Keywords: Body mass index - lower urinary tract symptoms - obesity - prostate cancer - PSA

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Introduction

The incidence and mortality of prostate cancer have both increased rapidly in the past two decades in Asian countries. The age-adjusted incidences of prostate cancer in Chinese populations have increased by 38-118%, and the age-adjusted mortality has increased by 70-170% (Sim and Cheng, 2005). The prostate-specific antigen (PSA) is widely used for prostate cancer screening, diagnosis, and monitoring of treatment response, and prostate biopsy is generally recommended for men with a PSA value ≥ 4ng/mL.

Obesity has been shown to be associated with a higher Gleason grade (Freedland et al., 2004), higher biochemical failure rates after radical prostatectomy and radiation therapy (Freedland et al., 2004; Strom et al., 2006), and higher mortality (Andersson, 1997). The results obtained from different prostate cancer screened populations show that obese patients have lower serum PSA levels. However, as the mean serum PSA values from these studies only ranged from 0.7-1.5 ng/ml, the effect of obesity on the PSA values is of little clinical significance, as most asymptomatic men with a serum PSA in this range would not be offered a prostate biopsy.

However, in some parts of the world, prostate cancer screening is still not a general practice and the majority of patients will only have their serum PSA checked when they present to clinicians with lower urinary tract symptoms. The serum PSA level of these symptomatic patients may not be in the same range as that of asymptomatic subjects. As a result, whether the same inverse association between BMI and serum PSA exists in symptomatic patients is still unknown.

In this study, the association between BMI and serum PSA in patients with lower urinary tract symptoms and its possible clinical implications is investigated.

Materials and Methods

This was a retrospective study of male patients presenting at our unit with lower urinary tract symptoms (LUTS) from 2005 to 2009. For all male patients presenting

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at our centre with LUTS, a comprehensive assessment, including history, physical examination, and basic blood tests, was performed during the initial consultation. The information obtained was then prospectively collected in a computer database. In this review, the age, weight, height (for the calculation of the BMI), and serum PSA level of the patients were retrieved for analysis. The patients were divided into three groups: normal (BMI < 23kg/m2), overweight (BMI 23-27 kg/m2), and obese (BMI > 27kg/m2), in accordance with the World Health Organization expert consultation on the appropriate BMI for the Hong Kong Chinese population (WHO, 2004). This study protocol was approved by our local clinical research ethics committee.

As according to the Kolmogorov-Smirnov statistic the PSA levels were not normally distributed, the PSA values were logarithmically transformed to attain a normal distribution before analysis. Non-parametric tests were used for the original PSA values otherwise. The relationship between serum PSA and BMI was assessed with Spearman's correlation. Analysis of variance (ANOVA) was used to test for the mean differences between the three BMI groups. The relationship between serum PSA and age was assessed with Pearson's correlation, and analysis of covariance (ANCOVA) was used to adjust for the effect of age on PSA levels among the different BMI groups.

Results

During the study period, 1630 subjects presented with LUTS at our centre and 1612 men had both BMI and PSA information available for our analysis. All of them were ethnic Chinese, and the majority were in the age range of 60-69 years old (35.9%). The mean age was 64.64 (range 29-97). The majority (45.3%) of the patients was in the overweight group with a BMI of 23-27, and 16.9% were in the obese group with a BMI of > 27. Most patients (71.2%) had a serum PSA level of < 4 ng/ml, and 21.2% had a PSA level of 4-10 ng/ml (Table 1).

BMI was negatively correlated with serum PSA levels according to Spearman's correlation (coefficient -0.05, p = 0.03). The number of patients in the normal, overweight, and obese groups according to the definition of the World Health Organization expert consultation was 609, 731, and 272, respectively. Although the mean PSA levels of the normal (4.84 ng/ml) and overweight patients (4.54 ng/ml) were above the usual cut off level of 4 ng/ml, the mean serum PSA level for the obese patients (3.95 ng/ml) was lower than 4 ng/ml. The mean serum PSA level decreased progressively with increasing BMI level across the three BMI groups. Both the mean and geometric means of the serum PSA level were significantly and negatively associated with BMI according to a Kruskal Wallis analysis (p = 0.003) and analysis of variance (ANOVA) (p = 0.01), respectively. The mean serum PSA of the obese patients was 18.4% lower than that of the normal patients. By dividing patients into obese (BMI > 27) and non-obese (BMI < 27) groups, a significant negative association was also seen in both the mean (p = 0.001) and geometric mean (p = 0.003) of the serum PSA level (Table 2).

Table 1. Characteristics of the 1612 Chinese Men and the Relationship between BMI and PSA

Parameters		n (%)	PSA (ng/ml) Mean	Geometric mean
Age	< 50	111 (6.9%)	1.21	
	50-59	406 (25.2%)	2.34	
	60-69	579 (35.9%)	3.35	
	70-79	411 (25.5%)	4.55	
	> 80	105 (6.5%)	11.73	
	Total	1612	p < 0.001*	
BMI †	<23	609 (37.8%)	4.84	2.22
	23-7	731 (45.3%)	4.54	2.14
	>27	272 (16.9%)	3.95	1.76
			p = 0.003**	P = 0.01***
PSA ‡ (ng/ml)	< 1	447 (27.7%)		
	1-1.99	393 (24.4%)		
	2-2.99	193 (12.0%)		
	3-3.99	115 (7.1%)		
	4-9.99	342 (21.2%)		
	10-19.9	85 (5.3%)		
	> 20	37 (2.3%)		

†Body mass index; ‡Prostate-Specific Antigen; *Pearson's correlation between PSA and Age (Pearson's coefficient 0.167); **Kruskal-Wallis test; ***ANOVA of logarithmically transformed PSA

Table 2. Relationship between PSA and Obesity

BMI†	Non-obese<27	Obese>27	p-value
Sample size	1340	272	
PSA‡ Mean (ng/ml)	4.67	3.95	p = 0.001*
PSA Geometric mean	2.18	1.76	p = 0.003**
	adjusted for age		p = 0.02***

†Body mass index; ‡prostate-specific antigen; *Mann Whitney U test; **T-test of logarithmically transformed PSA; ***ANCOVA

Age was also positively correlated with serum PSA level (Table 1), with a Pearson's coefficient of 0.167 (p < 0.001). However, after adjusting for age, analysis of covariance (ANCOVA) showed that BMI was still negatively associated with serum PSA level (p = 0.02) (Table 2).When, as suggested by Chia et al (2009), patients with a serum PSA level of > 20 were excluded (n = 36), obese patients (mean PSA 2.73 ng/ml) still had significantly lower serum PSA levels than non-obese patients (mean PSA 3.28 ng/ml) (p = 0.01).

Discussion

In this study, we confirmed that the observation of a negative correlation between serum PSA level and BMI in asymptomatic male patients was also present in male patients presenting with LUTS. Moreover, the serum PSA levels of these symptomatic patients were higher than those observed in asymptomatic populations in the literature. As mentioned, although the mean PSA level of normal and overweight patients was above the recommended level for transrectal ultrasound guided biopsy of 4 ng/ml, the mean serum PSA level for obese patients was lower than 4 ng/ml. This observation of a lower PSA level in an obese population with LUTS may have potential implications for the diagnosis and prognosis of prostate cancer in these patients.

In the literature, there are many studies that suggest

Table 3. Summary of Published Papers (with a sample size > 1,000) on the Relationship between BMI and PSA in Asymptomatic M en

Reference	Ethnicity	Sample size	Mean Age	Mean PSA	BMI/PSA Relationship
Ku et al. 2003	Korean	6,005	47	0.9	NS†
Kim et al. 2007	Korean	8,640	52.8	1.1	Inverse‡
Ando et al. 2008	Japanese	5,246	46	0.8	Inverse
Chia et al. 2009	Chinese	2,410	59.1	1.5	Inverse
Wang et al. 2009	Chinese	1,573	64	1	Inverse
Ohwaki et al. 2009	Japanese	19,367	50	0.7	Inverse
Thompson et al. 2004	White (85%)	1,565	/	/	NS
Baillargeon et al. 2005	White (87%)	2,770	56.8	1.3	Inverse
Barqawi et al. 2005	White	4,458	60	1.1	Inverse
Kristal et al. 2006	White (94%)	3,341	62.4	1.3	Inverse
Werny et al. 2007	All	2,396	51	0.9	
	White	1,476		0.9	Inverse
	Mexican American	485		0.9	NS
	Black	435		0.9	NS
Rundle et al. 2008	White (82%)	3,152	50	0.9	Inverse
Grubb et al. 2009	White (90%)	28,380	62.3	1.2	Inverse
Culp et al. 2009	All	3,152	56.6	1.3	
	White non-Hispanic	1,,686		1.3	Inverse
	Hispanic	743		1.2	NS
	African-American	625		1.4	NS

†Not significant; ‡Significant inverse association

that there is an inverse association between BMI and PSA levels in asymptomatic men under prostate cancer screening. A summary of the results of such studies with a sample size of greater than 1,000 is given in Table 3. A consistent inverse association between BMI and PSA levels in asymptomatic men has been shown in 12 out of 14 studies involving both Caucasian and Asian populations. The underlying reason for the relationship between BMI and serum PSA is still unknown. Ohwaki et al. (2010) and Grubb et al. (2009) suggested that the inverse association can be explained by hemodilution due to higher plasma volumes in obese men. An alternative explanation is that obese men have a lower androgen level. Androgen plays an important role in the growth and differentiation of the normal prostate, and thus a lower androgen level may lead to a lower PSA mass. However, Banez et al. (2007) found that PSA mass in obese patients was similar or even higher than that in normal populations, making the androgenic explanation less plausible.

Our study is the first to make a similar observation in a male population presenting with LUTS. The potential clinical implications of the relationship may be different between our symptomatic population and previously reported asymptomatic samples. The mean PSA in the published studies ranged from 0.7-1.5ng/mL, far less than the recognized cutoff value of 4 ng/ml for prostatic biopsy. However, in our study, the obese population had a mean serum PSA level below the common cutoff point (4 ng/ml) for prostatic biopsy, whereas the other two groups had serum PSA levels of more than 4. As a result, prostatic biopsy may be offered less frequently to obese patients, which may lead to delay in cancer diagnosis. Prostate cancers in obese patients may need to grow to a greater size or a higher grade, hence producing more PSA, before the serum level rises above the cutoff point for biopsy. As a result, tumors in obese patients may be diagnosed at a more advance stage compared with patients with a lower BMI. This may partly explain the relatively poorer outcome of prostate cancer in obese patients. This problem is expected to become more important in Asia in the future, as the obese population is increasing.

In many of the studies of PSA level in screened populations, patients with a PSA level of > 10 or > 20 or patients who were subsequently diagnosed with CA prostate were excluded from the analysis. We did not exclude any of these patients, as we sought to analyze the trend in PSA levels in all patients presenting with lower urinary tract symptoms rather than in a selected group of patients. Nevertheless, even when the analysis was restricted to patients with a PSA level of < 20, the same inverse relationship was still observed.

The main strengths of this study include the prospective collection of the data, direct measurement (rather than self-reporting) of height and weight on the same day of PSA blood sampling, and analyses of all patients without exclusion. This study has potential implications for the interpretation of PSA levels in considering prostate biopsy in obese men with lower urinary tract symptoms, especially as the numbers of these patients is increasing. Different PSA cutoffs could be used in eligible obese patients with or without lower urinary tract symptoms. Although new PSA cutoff values have been proposed for asymptomatic obese patients, larger scale studies are needed to find the right cutoff for symptomatic obese men.

In conclusion, a higher BMI in symptomatic male patients was significantly associated with lower PSA levels. BMI should be considered in the interpretation of serum PSA levels in overweight and obese patients presenting with lower urinary tract symptoms.

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