

Body mass index in relation to prostate specific antigen-related parameters

Dandan Lin

the first affiliated hospital of army medical university

Ting Liu

the affiliated hospital of army medical university

Luling Chen

the first affiliated hospital of army medical university

Zongtao Chen (✉ lindandanliuting@126.com)

the first affiliated hospital of army medical university

Research article

Keywords: Body mass index, Prostate specific antigen, Prostate specific antigen density, Prostate specific antigen mass

Posted Date: February 14th, 2020

DOI: <https://doi.org/10.21203/rs.2.23581/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Version of Record: A version of this preprint was published at BMC Urology on September 16th, 2021. See the published version at <https://doi.org/10.1186/s12894-020-00746-8>.

Abstract

Purpose

Limit previous studies were conducted to assess the association between body mass index (BMI) and series of prostate-specific antigen (PSA)-related parameters, which taken prostate volume (PV) and blood volume (BV) into consideration. The objective of this study was to assess the relationship between BMI and parameters of PSA concentrations in Chinese men.

Methods

A total of 86,930 men who had undergone annual medical examinations at the First Affiliated Hospital of Army Medical University between 1 January 2011 and 31 December 2018 were included. Partial Spearman correlation rank test was used to assess the relationship between BMI, PV, BV and PSA, and then estimated the correlation between BMI and series of PSA-related parameters.

Results

After adjustment for age, PV (correlation coefficient = 0.227, P-value < 0.001) was positively associated with PSA levels, but BMI (correlation coefficient = -0.057, P-value < 0.001) and BV (correlation coefficient = -0.041, P-value < 0.001) inversely correlated to PSA concentrations. Moreover, present study also indicated that BMI positively associated with PV and BV. Furthermore, present study identified that PSA mass (correlation coefficient = 0.001, P-value = 0.763) was not affected by obesity after adjustment for age in Chinese general men.

Conclusion

The results of this large-sample, hospital-based study in China indicated that a higher BMI might have a bigger PV and larger BV. BMI was negatively associated with PSA and PAS density, and no significantly association was detect between BMI and PSA mass.

Background

Prostate cancer was a leading cause of death among men in the developed countries [1]. In 2012, 1.1 million men were diagnosed with prostate cancer worldwide, accounting for 15% of all cancer diagnosed in men according to the World Health Organization's International Agency for Research on Cancer [2]. However, screening for prostate cancer was one of the most hotly debated health care issues as its controversial, leading to overtreatment, psychological distress, and significant medical costs [3].

Prostate specific antigen (PSA) is the most commonly used indicator for early screening and diagnosis of prostate cancer [4]. A relationship between obesity and lower PSA levels has been identified in several studies [5–8]. Obesity plays a key role in developing abnormalities in sex hormone metabolism and insulin levels, as the excess accumulation of adipose tissue or body fat. However, the specificity of PSA is

limited and the false positive rate is relatively high, as most men referred for biopsy for elevated PSA levels are not diagnosed with prostate cancer [9]. The frequently cited hypothesis in this respect were the consideration that men with a higher BMI might have larger prostate volumes (PV) [10, 11] and blood volume (BV) [8, 12], which could underestimate or overestimate PSA serum concentrations.

However, limit large sample studies in China were conducted to assess the association between BMI and series screening and diagnosis parameters of prostate cancer, which take PV and BV into consideration. The aim of this study is to detect whether there is a relationship between BMI, PV, BV and PSA in Chinese general men, and whether there is a PSA-related parameter was not affected by BMI based on physical examination information checkup data in southwestern China men.

Methods

Overall Study Design

From 1 January 2011 and 31 December 2018, 86,930 consecutive ostensibly healthy Chinese men recruited for physical examination information checkup in the Health Management Department of the First Affiliated Hospital of Army Military Medical University. The criteria for inclusion in this study were: physical examination, PSA testing, and prostate ultrasound testing were performed; There were no obvious abnormalities in prostate ultrasound diagnosis; No history of prostate cancer and prostate surgery.

Clinical Variables

The physical examination information for the recruited subjects were collected including age (year), height (cm), weight (kg), PSA level (ng/ml) and prostate volume (ml). BMI (kg/m^2) was defined as weight (kg) divided by the square of height (m^2). According to WHO's BMI grading standards for the Asia-Pacific region, the recruited subjects were divided into: normal weight ($18.5 \text{ kg} / \text{m}^2 \sim 23.9 \text{ kg} / \text{m}^2$), overweight ($24 \text{ kg} / \text{m}^2 \sim 27.9 \text{ kg} / \text{m}^2$) and obese ($\text{BMI} > 28 \text{ kg} / \text{m}^2$). Body surface area (m^2) = weight $^{0.425} \times$ height $^{0.725} \times 0.2025$. BV (L) = body surface area $\times 1.67$. PV (ml) = left and right diameter \times front and back diameter \times up and down diameter $\times 0.52$. PSA density (μg) = PSA / PV. PSA mass = PSA \times BV. A blood sample was obtained for serum PSA. All anthropometric measurements were made by trained observers using standardized techniques. All participants signed informed consent documents approved by institutional review boards.

Statistical Analysis

Partial Spearman rank test was used to test the pairwise correlation among the variables. The SPSS 20.0 software (SPSS, Inc, Chicago, IL) was used for statistical analysis and $P < 0.05$ was considered significantly for all analysis.

Results

Baseline characteristics of participants

In this study, data from 86,930 men were analyzed. The mean age was 46.39 years, the mean BMI was 25.01 kg / m², the mean PSA level was 0.65 ng / mL, the mean PV was 18.43 mL, the mean PSA density level was 0.04 µg, the mean BV level was 2.97 L, the mean PSA mass level was 1.91 µg. The demographics of the study population are listed in Table 1.

Table 1
Characteristics of the study population

	Mean	SD
Age (years)	46.21	12.10
Height (cm)	166.69	6.29
Weight (kg)	69.57	9.72
BMI (kg / m ²)	25.01	3.00
PSA (ng / mL)	0.60	0.49
PV (mL)	18.43	6.73
PSA density (µg)	0.03	0.04
BV (L)	2.97	0.23
PSA mass (µg)	1.78	1.44

Notes

BMI, body mass index; PSA, prostate specific antigen; PV, prostate volume; BV, blood volume; SD, standard deviation.

Correlation among BMI, BV, PV and PSA levels

Spearman rank test results showed that BMI ($P < 0.001$) and BV ($P < 0.001$) were negatively associated with PSA, but PV ($P < 0.001$) was positively associated with PSA after adjustment for age (Table 2), indicating PSA levels was affected by BV, PV and BMI. Furthermore, BV ($P < 0.001$) and PV ($P < 0.001$) were positively associated with BMI after adjustment for age, indicating that a higher BMI might have larger PV and larger BV. Specifically, BV and PV showed the most positively associated with BMI and PSA respectively.

Table 2
Pairwise correlation among the
variables after adjustment for age

	BMI	BV	PV
BMI	-	-	-
BV	0.651 [□]	-	-
PV	0.061 [□]	0.115 [□]	-
PSA	-0.057 [□]	-0.041 [□]	0.227 [□]

Notes

BMI, body mass index; PV, prostate volume; BV, blood volume; PSA, prostate specific antigen; [□] means P < 0.05

Correlation among BMI and PSA-related parameters

Table 3 showed the relationship between BMI and PSA, PSA density and PSA mass in different BMI categories. BMI was negatively associated with PSA (all sample: correlation coefficient = -0.057, P-value < 0.001; Normal weight: correlation coefficient = -0.026, P-value < 0.001; Overweight: correlation coefficient = -0.031, P-value < 0.001; Obese: correlation coefficient = -0.057, P-value < 0.001) and PSA density (all sample: correlation coefficient = -0.095, P-value < 0.001; Normal weight: correlation coefficient = -0.019, P-value < 0.001; Overweight: correlation coefficient = -0.022, P-value < 0.001; Obese: correlation coefficient = -0.036, P-value < 0.001) in all categories (Table 3). However, no significant association between BMI and PSA mass was detected in all categories (all sample: correlation coefficient = 0.001, P-value = 0.763; Normal weight: correlation coefficient = 0.008, P-value = 0.145; Overweight: correlation coefficient = -0.003, P-value = 0.497; Obese: correlation coefficient = -0.005, P-value = 0.554) (Table 3).

Table 3
Partial Spearman correlation among the variables after adjustment for age

BMI category	PSA		PSA density		PSA mass	
	Coefficient	p	Coefficient	p	Coefficient	p
All sample (n = 86930)	-0.057	< 0.001	-0.060	< 0.001	0.001	0.763
Normal (n = 32321)	-0.026	< 0.001	-0.019	0.001	0.008	0.145
Overweight (n = 40779)	-0.024	< 0.001	-0.022	< 0.001	-0.003	0.497
Obese (n = 13830)	-0.031	< 0.001	-0.036	< 0.001	-0.005	0.554

Notes

BMI, body mass index; PSA, prostate specific antigen;

Discussion

In present study, our results demonstrated that PV was positively associated with serum PSA concentrations, but BMI and BV inversely related to PSA levels, indicating BMI, BV and PV should be taken into account when referring men to a prostate biopsy based on serum PSA concentrations. Furthermore, this present study demonstrated that a higher BMI might have a higher PV and BV. In addition, we introduced new serum PSA-related parameters (PSA density and PSA mass) to associate with BMI in different categories, demonstrated that PSA mass was not related to BMI in Chinese general men.

Our results showed that serum PSA concentrations decreased with increasing BMI among Chinese general men with no previous prostate cancer diagnosis. This confirms results from earlier studies showing inverse associations between BMI and serum PSA [13, 14, 12, 5–8]. Obesity plays a key role in developing abnormalities in sex hormone metabolism and insulin levels, as the excess accumulation of adipose tissue or body fat. It can lead to benign prostatic enlargement by raising estrogen and estradiol levels, while lowering testosterone and serum globulin binding protein levels [15]. The elevated estrogen/testosterone ratio associated with obesity might increase the stromal/epithelial cell ratio in benign prostatic hyperplasia nodules [16].

Previous studies presented that higher BMI might have larger BV [8, 12], which could bias real PSA serum concentrations, and this findings were confirmed in present study. The theory behind the hypothesis is that the same total amount of PSA released from cells in the prostate should be diluted into lower concentrations in men with larger as opposed to smaller BV. Moreover, we found that the BMI was positively correlated with PV and the PV was positively correlated with the level of PSA. However, the BMI

was negatively correlated with PSA level. One explanation is following: on the one hand, higher BMI might cause larger PV, and then increase PSA levels. On the other hand, higher BMI could cause hemodilution because the BV has increased, and the hemodilution effect of blood volume on PSA was greater than the increasing effect of PV on PSA [8, 17]. Our results also supported the hypothesis.

Based on the impact of BV and PV on PSA levels, it is necessary to make a comprehensive judgment by combining BV and PV. Some new PSA parameters had been proposed to eliminate the effects of these factors on PSA and improve the sensitivity and specificity of prostate cancer screening. We separately estimated PSA density and PSA mass as PSA concentration divided by PV and PSA concentration times BV, showed that PSA density concentration showed an inverse correlation with BMI, but PSA mass showed no significant correlation to BMI. Our analysis results indicated that using PSA mass to assess PSA concentration will not be affected by obesity in Chinese general men.

There were some limitations in our study, such as being a cross section study. Second, because the study participants were Chinese, the data may not necessarily represent populations outside China. Moreover, our study did not do other analysis of other obesity indices apart from BMI. In addition, we did not investigate the socioeconomic factors and other potential confounders which might influence the BMI and PSA levels. However, our findings are consistent with those of numerous studies conducted in other regions.

Conclusion

The results of this large-sample, hospital-based study in China indicated that PV was positively associated with PSA concentration, but BMI and BV were inversely correlated to PSA concentration. Otherwise, PSA mass might be the best parameters to estimate the PSA concentration without the effect of obesity in Chinese general men.

Declarations

Acknowledgements

Not applicable.

Authors' Contributions

Zongtao Chen: Project development; Luling Chen: Manuscript editing; Dandan Lin and Ting Liu: Data Collection, Data analysis and Manuscript writing

Funding

This study was not supported by any funding.

Availability of data and materials

The data of the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no conflict of interest.

Consent for publication

Not applicable

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study protocol was approved by the Ethics Committee of the first Affiliated Hospital of Army Medical University.

References

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F (2015) Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *International journal of cancer* 136 (5):E359-386. doi:10.1002/ijc.29210
2. All Cancers Estimated Incidence, Mortality and Prevalence of All Cancers (excluding non-melanoma skin cancer) in 2012 (2017). *Journal of the National Cancer Institute* 109 (9). doi:10.1093/jnci/djx205
3. Dunn MW (2017) Prostate Cancer Screening. *Seminars in oncology nursing* 33 (2):156-164. doi:10.1016/j.soncn.2017.02.003
4. Catalona WJ, Smith DS, Ratliff TL, Dodds KM, Coplen DE, Yuan JJ, Petros JA, Andriole GL (1991) Measurement of prostate-specific antigen in serum as a screening test for prostate cancer. *The New England journal of medicine* 324 (17):1156-1161. doi:10.1056/NEJM199104253241702

5. Fowke JH, Matthews CE (2010) PSA and body composition by dual X-ray absorptiometry (DXA) in NHANES. *The Prostate* 70 (2):120-125. doi:10.1002/pros.21039
6. Loeb S, Carter HB, Schaeffer EM, Ferrucci L, Kettermann A, Metter EJ (2009) Should prostate specific antigen be adjusted for body mass index? Data from the Baltimore Longitudinal Study of Aging. *The Journal of urology* 182 (6):2646-2651. doi:10.1016/j.juro.2009.08.041
7. Price MM, Hamilton RJ, Robertson CN, Butts MC, Freedland SJ (2008) Body mass index, prostate-specific antigen, and digital rectal examination findings among participants in a prostate cancer screening clinic. *Urology* 71 (5):787-791. doi:10.1016/j.urology.2007.11.036
8. Banez LL, Hamilton RJ, Partin AW, Vollmer RT, Sun L, Rodriguez C, Wang Y, Terris MK, Aronson WJ, Presti JC, Jr., Kane CJ, Amling CL, Moul JW, Freedland SJ (2007) Obesity-related plasma hemodilution and PSA concentration among men with prostate cancer. *Jama* 298 (19):2275-2280. doi:10.1001/jama.298.19.2275
9. Martinez-Pineiro L, Garcia Mediero JM, Gonzalez Gancedo P, Taberner A, Lozano D, Lopez-Tello JJ, Alonso-Dorrego JM, Nunez C, Picazo ML, Madero R, De La Pena JJ (2004) Probability of prostate cancer as a function of the percentage of free prostate-specific antigen in patients with a non-suspicious rectal examination and total prostate-specific antigen of 4-10 ng/ml. *World journal of urology* 22 (2):124-131. doi:10.1007/s00345-003-0393-5
10. Yang HJ, Doo SW, Yang WJ, Song YS (2012) Which obesity index best correlates with prostate volume, prostate-specific antigen, and lower urinary tract symptoms? *Urology* 80 (1):187-190. doi:10.1016/j.urology.2012.04.003
11. Yessel K, Alma E, Eken A, Gulum M, Ercil H, Ayyildiz A (2015) Effect of obesity on International Prostate Symptom Score and prostate volume. *Urology annals* 7 (3):371-374. doi:10.4103/0974-7796.152056
12. Grubb RL, 3rd, Black A, Izmirlian G, Hickey TP, Pinsky PF, Mabie JE, Riley TL, Ragard LR, Prorok PC, Berg CD, Crawford ED, Church TR, Andriole GL, Jr., Team PP (2009) Serum prostate-specific antigen hemodilution among obese men undergoing screening in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology* 18 (3):748-751. doi:10.1158/1055-9965.EPI-08-0938
13. Bonn SE, Sjolander A, Tillander A, Wiklund F, Gronberg H, Balter K (2016) Body mass index in relation to serum prostate-specific antigen levels and prostate cancer risk. *International journal of cancer* 139 (1):50-57. doi:10.1002/ijc.30052
14. Sarma AV, Jaffe CA, Schottenfeld D, Dunn R, Montie JE, Cooney KA, Wei JT (2002) Insulin-like growth factor-1, insulin-like growth factor binding protein-3, and body mass index: clinical correlates of prostate volume among Black men. *Urology* 59 (3):362-367. doi:10.1016/s0090-4295(01)01546-1
15. Pasquali R, Casimirri F, Cantobelli S, Melchionda N, Morselli Labate AM, Fabbri R, Capelli M, Bortoluzzi L (1991) Effect of obesity and body fat distribution on sex hormones and insulin in men. *Metabolism* 40 (1):101-104. doi:10.1016/0026-0495(91)90199-7

16. Giovannucci E, Rimm EB, Chute CG, Kawachi I, Colditz GA, Stampfer MJ, Willett WC (1994) Obesity and benign prostatic hyperplasia. *Am J Epidemiol* 140 (11):989-1002.
doi:10.1093/oxfordjournals.aje.a117206
17. Walsh PC (2005) The association of body mass index and prostate-specific antigen in a population-based study. *The Journal of urology* 174 (5):1825