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Original Article

Body mass index, prostate volume and health condition are associated with the risk of prostate cancer detectionin a biopsy population

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Abstract: Purpose: Ultrasound-guided biopsy is the standard method for diagnosing prostate cancer. However, according to the literature, the positive predictive value of prostate biopsy is very low when PSA < 30 ng/mL. We assessed the association of prostate cancer detection rates with age, prostate volume, and health condition in a referral-based biopsy population when PSA < 30 ng/mL. Materials and methods: We retrospectively reviewed the records of 546 men who underwent prostate biopsy at Shanghai Tenth People's Hospital with a total PSA of 4 to 30 ng/mL. The age, body mass index, biopsy results, and health condition including diabetes mellitus, hypertension, and other chronic diseases were collected. Cancer detection rates with respect to age, body mass index, and health condition were analyzed. Results: A total of 546 patients were included in the analysis. The mean age was 71.1 years, and the median PSA level was 14.7 ng/mL. Prostate cancer was detected from the biopsy in 198 patients (36.26%). A higher prostate cancer detection rate was found in obese patients than in normal patients (81% vs 16.7%). No significant difference was found for age and the odds of being diagnosed with prostate cancer (P = 0.211). However, patients with prostate volume < 50 cc had a higher prostate cancer detection rate than patients with prostate volume > 50 cc (49.1% vs. 13.3%). Our data also indicated that DM and hypertension are risk factors for the development of prostate cancer. Logistic analysis showed that prostate nodules, BMI, PSA, and prostate volume were the significant predictors of a positive biopsy. Conclusion: BMI, prostate volume, DM, and hypertension were associated with an increased prostate cancer detection rate. However, age did not affect the rate of prostate cancer biopsy detection.

Keywords: Prostate cancer, biopsy, BMI, DM, hypertension

Introduction

Ultrasound-guided biopsy is the standard method for diagnosing prostate cancer (PCa) in patients with increased total prostate specific antigen (PSA) or abnormal digital rectal examination (DRE). However, according to literature, the positive predictive value of prostate biopsy is very low when PSA < 30 ng/ml [1, 2]. In addition, biopsy is an invasive examination, causing a series of complications such as infection, pain, bleeding, and urinary symptoms following the examination [3]. For these reasons, many patients are reluctant to undergo prostate biopsy.

At present, some factors influencing the risk of prostate cancer detection have been investigated including body mass index (BMI) [4, 5], diabetes mellitus (DM) [6], and hypertension [7]. However, the results of these studies over the past decade were highly inconsistent. In the study of Presti et al. [4], they found that normal BMI correlates with a higher cancer detection rate and larger cancers in men undergoing prostate biopsy. Moreover, higher BMI was associated with lower risk of detection of prostate cancer, including high-grade cancer, independent of patient age, PSA, DRE finding, and prostate volume [5]. However, a recent study demonstrated that among men without a known family history of prostate cancer, increased BMI was not associated with a higher risk of prostate cancer, but was significantly associated with a higher risk of high-grade prostate cancer; while among men with a known family history of prostate cancer, the

Table 1. Patients characteristics

Parameter	Value	Biopsy detection rate	Range
No. patient	546	36.30%	
Mean Age	71		33-95
Mean PSA (ng/mL, range)	14.7	36.30%	1.51-30
No. abnormal DRE finding	66	45.50%	12.09%
Mean prostate volume (mL, range)	49		17-185
No. DM (%)	78	65.40%	14.29%
No. Hypertension (%)	105	57.10%	19.23%
No. Other diseases (%)	130	56.90%	23.81%
No. overall Pca (%)	198		36.26%
GS 6	68		12.45%
GS 7	99		18.13%
GS 8	18		3.30%
GS 9	13		2.38%

risks of prostate cancer and high-grade prostate cancer increased rapidly as body mass index increased. For DM, Park [6] reported that poor glycemic control of DM was associated with a higher risk of prostate cancer detection in the biopsy population. In contrast, another study showed that obese patients, in combination with DM, were more likely to present with more aggressive prostate cancer [8]. Yilmaz et al. [9] reported that there is a significant relationship between high-grade prostate cancer and decreasing prostate volume. However, the relationship between prostate cancer detection and BMI, age, prostate volume, DM, and hypertension remains unclear.

In this study, the association of BMI, DM, prostate volume, and age with the risk of prostate cancer detection in a biopsy population when PSA < 30 ng/mL was investigated.

Materials and methods

We retrospectively reviewed the medical records of patients who underwent prostate biopsy in Shanghai Tenth People's Hospital between January 2009 and October 2014 after institutional review board approval. Inclusion criteria of medical records were a serum PSA level 4 to 30 ng/ml, and patients who underwent prostate biopsy. We excluded medical records of patients with a history of surgical treatment for prostatic disease, and incomplete clinical data. A total of 546 men who underwent prostate biopsy at Shanghai Tenth People's Hospital with a total PSA of 4 to 30 ng/ml were selected. Clinical information was abstracted from the patient records, including patient age, height, weight, DRE findings, PSA, DM or not, hypertension or not, and prostate volume estimated by transrectal ultrasonography. Pathologic information included the presence or absence of cancer and the Gleason sum. The BMI was calculated as the weight in kilograms divided by the height in meters squared.

Statistical analysis

According to Asian BMI recommendations [10], we defined normal weight as a BMI < 23 kg/m^2, overweight was defined as a BMI = 23-25 kg/m^2, and obesity was defined as a BMI > 25 kg/m^2. We used Pearson's Chi-square test to test BMI category, age, PSA level, DM, hypertension, and prostate volume between other clinical variables. Pearson's Chi-square test, Fisher's exact test, and a linear regression model were used to describe the relationships between the variables. Logistic analysis was performed, treating BMI as a continuous variable, to study the interrelationships between BMI, age, prostate volume, DM, hypertension, and PSA for predicting a positive biopsy. Statistical significance was considered as $P \leq 0.05$. All statistical analyses were performed using SPSS 20 software (IBM SPSS-Chicago).

Results

A total of 546 patients were included in the analysis. The mean age was 71.1 years, and the median PSA level was 14.7 ng/ml. There were 78 men (14.29%) with a history of DM, and 105 men (19.23%) with a history of hypertension. Prostate cancer was detected from the biopsy in 198 men (36.26%). The detailed information of the patients is presented in **Table 1**.

BMI and prostate cancer detection rate

A statistically significant trend was found for BMI and the odds of being diagnosed with prostate cancer (P = 0.000). Our data showed that statistically significant differences were found in the prostate cancer detection rate between obese patients and normal patients regardless of age, PSA level, DM, hypertension, and pros-

Table 2. BMI and detection rate

	Normal	Overweight	Obese	*p* Value (chi-square test)		
				All	Normal vs Overweight	Normal vs Obese
All pts	27/162 (16.7)	60/247 (24.3)	111/137 (81)	0.000	0.083	0.000
Age						
< 60	2/20 (10.0)	7/33 (21.2)	11/16 (68.8)	0.000	0.456	0.000
60-70	11/58 (19.0)	17/74 (23.0)	39/49 (79.6)	0.000	0.67	0.000
> 70	14/84 (16.7)	36/140 (25.7)	61/72 (84.7)	0.000	0.137	0.000
PSA (ng/mL)						
0-10 ng/mL	9/95 (9.5)	18/115 (15.7)	24/32 (75)	0.000	0.217	0.000
10-20 ng/mL	9/48 (18.8)	13/76 (17.1)	30/48 (62.5)	0.000	0.814	0.000
20-30 ng/mL	9/19 (47.4)	29/56 (51.8)	57/57 (100)	0.000	0.795	0.000
DM						
Yes	9/14 (64.3)	12/34 (35.3)	30/30 (100)	0.001	0.109	0.002
No	18/148 (12.2)	48/213 (22.5)	81/107 (75.7)	0.000	0.013	0.000
Hypertension						
Yes	14/32 (43.8)	18/41 (43.9)	28/32 (87.5)	0.000	1.000	0.000
No	13/130 (10)	42/206 (20.4)	83/105 (79.0)	0.000	0.015	0.000
Prostate vol (cc)						
< 50 cc	18/100 (18)	56/143 (39.2)	98/107 (91.6)	0.000	0.000	0.000
≥ 50 cc	9/62 (14.5)	4/104 (3.8)	13/30 (43.3)	0.009	0.018	0.004

Table 3. Age and detection rate

	< 60	60-70	> 70	*p* Value (chi-square test)		
				All	< 60 vs 60-70	< 60 vs > 70
All pts	20/69 (29)	67/181 (37)	111/296 (37.5)	0.402	0.298	0.211
BMI						
Normal	2/20 (10)	11/59 (19)	14/84 (16.7)	0.650	0.496	0.731
Overweight	7/33 (21.2)	17/64 (23)	36/140 (25.7)	0.821	1.000	0.661
Obese	11/16 (68.8)	39/49 (79.6)	61/72 (84.7)	0.321	0.495	0.157
PSA (ng/mL)						
0-10 ng/mL	5/33 (15.2)	19/80 (23.8)	27/129 (20.9)	0.594	0.449	0.625
10-20 ng/mL	8/22 (36.4)	17/59 (28.8)	27/91 (29.7)	0.794	0.592	0.610
20-30 ng/mL	7/14 (50)	31/44 (73.8)	57/76 (75)	0.152	0.113	0.104
DM						
Yes	4/5 (80)	19/29 (65.5)	28/44 (63.6)	0.767	1.000	0.646
No	16/64 (25)	48/152 (31.6)	83/252 (32.9)	0.472	0.415	0.291
Hypertension						
Yes	7/12 (58.3)	22/40 (55)	31/53 (58.5)	0.941	1.000	1.000
No	13/57 (22.8)	45/141 (31.9)	80/243 (32.9)	0.327	0.23	0.154
Prostate vol (cc)						
< 50 cc	17/46 (37)	67/116 (52.6)	94/188 (50)	0.188	0.083	0.138
≥ 50 cc	3/23 (13)	6/65 (9.2)	17/108 (15.7)	0.473	0.692	1.000

tate volume. However, there was no statistical significance in the prostate cancer detection rate between overweight patients and normal patients (**Table 2**).

Table 4. PSA and detection rate

	0-10 ng/mL	10-20 ng/mL	20-30 ng/mL	p Value (chi-square test)		
				All	0-10 vs 10-20 ng/mL	0-10 vs 20-30 ng/mL
All pts	51/242 (21.1)	52/172 (30.2)	95/132 (72)	0.000	0.038	0.000
Age						
< 60	5/33 (15.2)	8/22 (36.4)	7/14 (50)	0.036	0.106	0.025
60-70	19/80 (23.8)	17/59 (28.8)	31/42 (73.8)	0.000	0.559	0.000
> 70	27/129 (20.9)	27/91 (29.7)	57/76 (75)	0.000	0.154	0.000
BMI						
Normal	9/95 (9.5)	9/48 (18.8)	9/19 (47.4)	0.000	0.180	0.000
Overweight	18/115 (15.7)	13/76 (17.1)	29/56 (51.8)	0.000	0.842	0.000
Obese	24/32 (75)	30/48 (62.5)	57/57 (100)	0.000	0.331	0.000
DM						
Yes	4/18 (22.2)	13/26 (50)	34/0 (100)	0.000	0.114	0.000
No	47/224 (21)	39/146 (26.7)	61/98 (62.2)	0.000	0.210	0.000
Hypertension						
Yes	4/22 (18.2)	28/51 (54.9)	28/32 (87.5)	0.000	0.005	0.000
No	47/220 (21.4)	24/121 (19.8)	67/100 (67)	0.000	0.782	0.000
Prostate vol (cc)						
< 50 cc	51/171 (29.8)	43/92 (46.7)	78/87 (89.7)	0.000	0.007	0.000
≥ 50 cc	0/71 (0)	9/80 (11.2)	17/45 (37.8)	0.000	0.003	0.000

Age, PSA, and prostate cancer detection rate

Our data showed that there was no significant relationship between age and prostate cancer detection rate (**Table 3**). When we divided patients by BMI, PSA, DM, hypertension, and prostate volume, no statistically significant trend was found in these groups (**Table 3**). However, a statistically significant difference was found between PSA and the odds of being diagnosed with prostate cancer (**Table 4**). Interestingly, when we divided patients by BMI, DM, and hypertension, there was no significant difference between the 0-10 ng/ml and 10-20 ng/mL groups, but a statistically significant trend was found between the 0-10 ng/mL and the 20-30 ng/mL groups.

DM, hypertension, and prostate cancer detection rate

Between the groups of men with DM and without DM, the prostate cancer detection rate (P = 0.000), PSA (P = 0.003), BMI (0.002), and mean prostate volume (P = 0.028) showed significant differences. Between men in the groups with hypertension and without hypertension, the prostate cancer detection rate (P = 0.001), mean PSA (0.015), and BMI (P = 0.004) had significant differences. Our data also showed that in both the DM and hypertension groups, the prostate cancer detection rate (71%) was significantly higher than in the only DM (65.4%) or only hypertension (57.1%) groups (**Table 5**).

Prostate volume and prostate cancer detection rate

When we took the prostate volume as a variable to analyze the prostate cancer detection rate, we found a significant difference between prostate volume ≥ 50 cc and prostate volume < 50 cc. The positive rate of prostate biopsy in the ≥ 50 cc prostate volume group was 13.3%, while the positive rate of prostate biopsy in prostate volume < 50 cc was 49.1% (P = 0.001).

Certain variables influence prostate cancer detection rate

We performed logistic analysis to evaluate the variables that may influence the prostate cancer detection rate. When the entire population was considered, multivariate analysis demonstrated that prostate nodules, BMI, PSA, and prostate volume were the significant predictors of a positive biopsy (**Table 6**).

Table 5. Patient characteristics and biopsy outcomes according to DM and Hypertension

Variables	DM-	DM+	*P* Value	Hypertension-	Hypertension+	*P* Value	DM+ Hypertension
No. Patient biopsy outcomes	147/468 (31.4)	51/78 (65.4)	0.000	138/441 (31.3)	65/105 (57.1)	0.001	22/31 (71)
Mean Age	70.98	72	0.369	71.17	70.92	0.804	69.39
Mean PSA	13.99	18.97	0.003	14.13	17.11	0.015	19.8
Mean prostate volume	50	43	0.028	49	48	0.755	43
BMI	23.9	24.8	0.002	23.9	24.7	0.004	23.7

Table 6. Patient characteristics and biopsy outcomes according to DM and Hypertension

Variables	DM-	DM+	*P* Value	Hypertension-	Hypertension+	*P* Value	DM+ Hypertension
No. Patient biopsy outcomes	147/468 (31.4)	51/78 (65.4)	0.000	138/441 (31.3)	65/105 (57.1)	0.001	22/31 (71)
Mean Age	70.98	72	0.369	71.17	70.92	0.804	69.39
Mean PSA	13.99	18.97	0.003	14.13	17.11	0.015	19.8
Mean prostate volume	50	43	0.028	49	48	0.755	43
BMI	23.9	24.8	0.002	23.9	24.7	0.004	23.7

Discussion

The relationship between prostate cancer and obesity has produced conflicting patterns of results and remains a topic of debate [11-13]. Some studies indicate that obesity is associated with an increased risk of high-grade disease and a reduced risk of low-grade disease [14]. However, one Netherlands cohort study showed that the incidence of prostate cancer increased with increasing BMI [15]. Some Chinese studies also reported that increased BMI correlates with a higher cancer detection rate in the Chinese population. In our study, we found that BMI was significantly associated with an increased prostate cancer detection rate. Several hypotheses can be suggested to explain the association between obesity and prostate cancer. Data from the literature indicate that obesity could be associated with biological modifications of adipokine levels related to a more aggressive PCa phenotype [8]. The important influencing factor is that adipose tissues release reduced anti-inflammatory adipokines and increased inflammatory adipokines, causing a chronic inflammatory state and increased cancer progression [16]. Possible reasons for the differing results in different studies are that the obese Chinese population may experience different biological changes than other populations, and that different studies had varying inclusion criteria.

At present, the widely accepted concept is that older patients have a higher median PSA. Recently, Sarıkaya S [17] reported that cancer was diagnosed in 7.5% of patients under the age of 50, 14.4% of patients between the age of 50 and 60, and 27% of patients over the age of 70 when PSA values ranged between 4 and 10 ng/dL. In the study of Murray et al. [18], they reported that men over 70 years had a higher median PSA and a higher frequency of cancer detected when PSA values ranged between 4 and 10 ng/dL. In contrast, when we compared prostate cancer biopsy rate in patients with PSA between 4 and 30 ng/dL, no relationship was found between age and prostate cancer detection. The possible reason is that PSA levels will rise with increasing age. When we selected patients PSA < 30 ng/mL, elderly man with prostate cancer may have been excluded.

Additionally, our data showed that when prostate volume was more than 50 cc, the prostate cancer detection rate decreased from 49.1% to 13.3%. This indicated that prostate volume was an important factor that effected a positive detection rate. Other studies [19, 20] have also indicated that prostate volume is an important marker in prostate biopsy.

Furthermore, we found that DM and hypertension also can affect the prostate cancer detection rate. Francesco [8] reported that DM was associated with high-grade prostate cancer only in obese subjects. They found DM possibly conferring no risk in non-obese men, but increased risk in obese men. In our study, we also found that patients with DM have a higher

BMI than without DM. These findings have been reported similarly by other recent studies [21, 22]. Whether DM or anti-diabetic agents are associated with prostate cancer is still unclear. In the study of Margel [23], the data indicated that there was no association between metformin use and the risk of prostate cancer, regardless of cancer grade. However, Franciosi et al. [24] reported that metformin might be associated with a significant reduction in the risk of cancer and cancer-related mortality. The reason causing these observed disparities may be associated with the combined effect of obesity and DM on PCa aggressiveness [8]. Several hypotheses can be suggested to explain the influence of DM on prostate cancer. One is that DM has a strong association with insulin resistance; hyperinsulinemia can increase the bioavailability of IGF-1 (insulin-like growth factor-1), steroid and peptide hormones, and inflammatory markers [8]. These can affect the immune system, which plays an important role in prostate cancer physiology and pathology [25]. The other hypothesis is that chronic inflammation and oxidative stress associated with DM may also contribute to PCa development and progression [26]. In the study of Ohwaki [27], they found uncontrolled hypertension was independent risk factors for biochemical recurrence after prostatectomy while control of hypertension could be an important treatment strategy for preventing biochemical recurrence. Whether hypertension is associated with prostate cancer detection rate was answered in the study of Takeshita et al [28]. They found that risk of prostate cancer in rats with high blood pressure was significantly higher than that in rats without hypertension. Although the anti-hypertensive effects of prazosin were rather weak, there appeared to be some reduction in the incidence of adenocarcinomas. However, Fitzpatrick et al. [29] reported that an inverse association was found between the risk of incident prostate cancer and use of any antihypertensive medication. At present, the relationship between hypertension and prostate cancer development are still conflicting. The positive relationship were reported in a population-based cohort study in Norway [7] and a case-control study in the United States [30]. Data from cohort studies in Sweden [31] and the United States demonstrated no obvious connection between hypertension and prostate cancer [32]. However, in our study, we found a relationship between positive rate of prostate biopsy and hypertension. Logistic analysis showed that prostate nodules, BMI, PSA and prostate volume were the significant predictors of a positive biopsy. These results indicate that positive rate of prostate biopsy prostate is very complicated and need further study to avoid unnecessary prostate biopsy.

In conclusion, we found that BMI, prostate volume, DM and hypertension are associated with increased risk of prostate cancer detection rate, but age has not effect on the rate of prostate cancer biopsy detection. Logistic analysis shows that prostate nodules, BMI, PSA and prostate volume are significant predictors of a positive biopsy.

Disclosure of conflict of interest

None.

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