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ORIGINAL ARTICLE

The role of the digital rectal examination as diagnostic test for prostate cancer detection in obese patients

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Summary

Purpose: *Digital rectal examination (DRE) is a routine part of prostate cancer (PCa) screening and provides important prognostic information. The purpose of this study was to analyse the potential association between obese patients and DRE findings for PCa detection.*

Methods: *We retrospectively reviewed the medical records of patients who underwent an initial prostate needle biopsy for abnormal DRE, high prostate specific antigen (PSA) levels (≥4 ng/mL), or both at the Department of Urology. Patients with a history of biopsy, surgical treatment of prostatic disease, or incomplete clinical data were excluded from this study. A total of 1113 patients were included in the analysis. Before the biopsy procedure body mass index (BMI) was calculated. Age, PSA, BMI, DRE findings, prostate volume and Gleason score were analysed to assess the potential association between obesity and PCa detection.*

Results: *The mean ± SD BMI was 28.3 ± 4.1 kg/m^2. A total of 373 (33.5%) patients were classified as obese (BMI ≥30 kg/m^2). No significant difference was noted in the number of biopsy cores between obese and non obese patients. The obese men were older, had a lower PSA concentration, a large prostate volume, and were less likely to have abnormal DRE findings. Patients with high grade prostate cancer (HGPCa) had higher BMI. Age, PSA and prostate volume were not significantly associated with a higher risk of cancer at biopsy.*

Conclusions: *Our data demonstrated that obese patients have lower PSA levels, larger prostates and abundant perirectal fat. Lower PSA serum levels and large prostate size associated with high BMI, indicated a potential risk for delayed diagnosis and poor pathological outcomes.*

Key words: *body mass index, digital rectal examination, obesity, prostate biopsy, prostate cancer, prostate volume*

Introduction

DRE is a routine part of PCa screening [1]. Many authors have shown that DRE is still important in diagnosing clinically important PCa and continues to provide important prognostic information [2,3]. The positive predictive value of DRE ranges from 4 to 11% in men with PSA levels of 0 to 2.9 ng/mL and from 33 to 83% in men with PSA levels greater than 3.0 to 9.9 ng/mL [4,5]. However, many studies have demonstrated that obese patients have lower PSA levels and large prostate size [6,7]. Therefore, patients with high BMI who underwent prostate biopsy based on standard schemes are less likely to detect a PCa [6,8]. In addition, obese patients may have a diagnostic delay in the routine screening visit because it is more difficult to observe abnormal DRE findings due to the presence of perirectal fat.

The purpose of this study was to assess and analyse the potential association between obese patients and DRE findings for PCa detection.

Methods

Clinical and pathological studies

We retrospectively reviewed the medical records

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of patients who underwent an initial prostate needle biopsy for abnormal DRE, high PSA levels (≥ 4 ng/mL), or both at the Department of Urology between May 2011 and October 2014. DREs were performed by four experienced urologists for all patients. Patients with a history of biopsy, surgical treatment of prostatic disease, or incomplete clinical data were excluded from study. A total of 1113 patients were included in the analysis. Before the biopsy procedure, patients underwent a physical examination, including height and weight measurements. BMI was calculated as weight in kilograms divided by height in meters square (kg/m^2). Obesity was defined as BMI ≥30 kg/m^2. Transrectal ultrasound (TRUS)-guided prostate biopsy (TPB) was performed with the patient in left lateral decubitus position using a General Electric Logiq 7 machine equipped with a 5-9MHz multi-frequency convex probe "end-fire". Each TRUS performed included an assessment of the prostatic diameter, the volume of the whole prostate, the transition zone, capsular and seminal vesicle characteristics, as well as morphological description of potential pathological features.

After prostate imaging, sampling was carried out with a 18-Gauge Tru-Cut needle powered by an automatic spring-loaded biopsy disposable gun.

Two experienced urologists performed a 14-core biopsy, as first intention, including 2 lateral peripheral (1 basal and 1 apical), 3 conventional parasagittal, and 2 midline peripheral samples (1 basal and 1 apical) on each side. Each patient was treated under local anesthesia with lidocaine spray (10g/100ml), applied 2 min before the procedure [9]. Age, PSA, BMI, DRE findings, prostate volume estimated by TRUS, and Gleason score were analysed to assess the potential association between obesity and PCa detection.

The primary goal of our study was to validate the correlation between obesity and risk of PCa in a biopsied population. Subsequently, we have considered the relationship between BMI and DRE findings as a possible cause of diagnostic delay for PCa in obese patients.

Statistics

We categorized BMI (kg/m^2) as < 25 for normal weight, 25-30 for overweight, and ≥ 30 for obese patients. We also examined BMI as a continuous variable and performed tests for associations between BMI and clinical variables using the rank sum test for continuous variables and chi square test for categorical variables. We used logistic and linear regression analysis to verify the association between DRE findings and PCa in obese patients. All statistical analyses were conducted on Microsoft Excel 2010 platform. A p value <0.05 was considered to indicate statistical significance.

Results

A total of 1113 patients underwent 12.1±2.6 TBPs in the study period. The mean ± SD and median age was 64.4±6.3 and 63.2 years, respectively. Median total PSA was 4.9 ng/mL (range 2.2–20), median prostate volume was 43.7 (range 17-145) and 383 (34.5%) patients presented had positive DRE. The mean ± SD and median BMI was 28.3 ± 4.1 kg/m^2 and 27.6 kg/m^2, respectively. A total of 373 (33.5%) patients were classified as obese (BMI ≥30 kg/m^2). No significant difference was noted in relation to the number of biopsy cores between obese and non obese patients. The obese men were older, had a lower PSA concentration, a large prostate volume, and were less likely to have abnormal DRE findings (Table 1). Histological evaluation of biopsy cores showed PCa in 513 (46.1%) patients and a diagnosis of benign prostatic hyperplasia/chronic prostatitis in 437 patients (39.2%) or high-grade prostatic intraepithelial neoplasia (HGPIN)/atypical small acinar proliferation (ASAP) in 163 patients (14.7%). In univariate analysis, BMI ≥30 kg/m^2 was signifi-

Table 1. Clinicopathologic features of 1113 patients undergoing prostate biopsy

Features	*Normal weight (<25 kg/m^2) (N: 348)*	*Overweight (25-30 kg/m^2) (N: 392)*	*Obese (≥30 kg/m^2) (N: 373)*	*p value*
Age (years), mean±SD	63.2±7.1	64.4±6.3	65.2±7.6	NS
Positive family history, N(%)	77 (22.1)	81 (20.6)	93 (24.9)	NS
Mean prostate volume, cm^3 (range)	30.2 (17-42)	59.3 (32-98)	72.5 (60-145)	<0.001
Mean PSA level, ng/mL (range)	6.7 (2.5-17)	6.3 (2.2-20)	5.2 (3.2-19)	<0.003
Mean free-to-total PSA,% (range)	15.8 (7-21)	15.4 (8-33)	16.3 (9-28)	NS
Abnormal DRE, N(%)	102 (29.3)	111 (28.3)	67 (17.9)	<0.001
N° biopsy cores, mean±SD	12.7±2.9	11.9±2.5	12.2±2.7	NS
Gleason score, N(%)				
≤6	76 (21.9)	87 (22.2)	101 (27.1)	<0.002
7	67 (19.3)	74 (18.9)	72 (19.3)	NS
≥8	9 (2.6)	11 (2.8)	16 (4.3)	<0.001

SD : standard deviation, PSA : prostate-specific antigen, DRE: digital rectal examination, PCa : prostate cancer, NS: not significant

Table 2. Patient characteristics according to prostate biopsy diagnosis

Characteristics	*No cancer (N:600)*	*Cancer (N:513)*	*p value*
Age (years), mean ± SD	64.7±7.2	63.9±6.5	NS
PSA (ng/mL), mean ± SD	7.1±4.3	8.6±5.4	NS
PV (cm^3), mean ± SD	56.8±23.8	57.5±24.2	NS
Abnormal DRE, N(%)	56 (9.3)	224 (46.7)	<0.001
BMI (kg/m^2), mean ± SD	25.6±3.5	29.6±3.8	<0.002

SD: standard deviation, PSA: prostate-specific antigen, DRE: digital rectal examination, PV: prostate volume, NS: not significant

cantly associated with detection of PCa through TBP (p<0.002). Patients with high-grade PCa (HG-PCa) had higher BMI, compared to patients with normal weight. Sixteen patients with Gleason score ≥8 were obese compared with 9 non obese patients (p<0.001). Multivariate analysis showed that age, PSA and prostate volume were not significantly associated with a higher risk of cancer at biopsy (Table 2).

Discussion

Obesity is a major public health problem and it is associated with several chronic medical conditions such as hypertension, heart disease, and diabetes [10]. Obesity has also been associated to several cancers (e.g. breast [11], colon [11]), and an increased risk of PCa in large prospective cohort studies [12,13]. However, the relationship between obese patients and PCa development is less clear. Masuda et al. [14] analysed 3966 Japanese patients and showed a significant positive association between BMI and PCa risk at biopsy, with a higher risk observed in patients whose BMI was ≥27 kg/m^2 compared with the control group. In contrast, Lee et al. [15] reported that obesity (≥25 kg/m^2) was significantly associated with lower odds of PCa detection through biopsy in 3113 South Korean men. Also, obesity was significantly associated with a lower rate of high grade (Gleason score > 7) biopsy-detected disease.

There have been some studies that investigated the effects of BMI on PSA level and prostate cancer detection [8,16], but few studies have evaluated DRE accuracy for PCa detection according to BMI [7,17]. Freedland et al. [8] examined the association between BMI and PSA levels among patients who underwent radical prostatectomy for PCa. They found no relationship between BMI and PSA. However, Benez et al. [18] suggested that the PSA level was underestimated in obese men and that lower PSA levels were largely due to hemodilution by the large plasma volume in men with BMI ≥30 kg/m^2. In addition, obesity was associated with lower serum testosterone concentrations. Given that PSA production is under androgenic control, this consideration suggests that obesity may be associated with decreased PSA level concentrations [19].

In our study, patients with a higher BMI were older, had a lower PSA concentration, a larger prostate volume, and were less likely to have abnormal DRE findings (p<0.001). We found that patients with higher BMI were statistically significantly more likely to have PCa on standard biopsy scheme (14 cores). Moreover, among patients diagnosed with PCa, men with a higher BMI were more likely to have HGPCa.

Early PCa detection depends on prostate biopsy, which is implied by elevated PSA levels (≥4 ng/mL) or abnormal DRE findings. However, many studies have proved that obese men have lower PSA levels and large prostate size; additionally, it is more difficult to have abnormal DRE findings in obese patients due to the presence of perirectal fat [5]. Our data are in line with prior studies [20,21], and showed that obese patients had larger prostate size and ample perirectal fat. The clinical implication is that at the time of DRE and prostate biopsy it is more difficult to find the cancer, assuming a cancer exists. Remzi et al. [22] reported that prostate volume was the greatest contributor to missing cancers in obese patients. Moreover, the reduced detectability of PCa among obese men is only relevant for asymptomatic clinically localized disease.

Several limitations need to be acknowledged. A first limitation of our study concerns the race: the majority of the participants were white and Italians, therefore the present results might not be generalizable to other races. Second, this is a single center study with a limited number of patients and small number of obese subjects. Our results apply to our study cohort only (men undergoing prostate biopsy) and cannot be extended to all men at risk for PCa. No follow-up results were

available in our patients. Therefore, it is possible that some patients with a negative biopsy actually harbored PCa.

Obesity is a frequent condition in Italian population. We believe that evaluation of the BMI should be part of the standard physical examination of patients in the urological outpatient clinic. Numerous factors contribute toward the difficulty of detecting PCa in obese men. First, obese men have lower PSA values, resulting in reduction of PSA-driven biopsy rates. Hypothetically, this is due to increased blood volume in obese individuals, leading to PSA hemodilution. Second, obesity may make it more challenging to perform a thorough DRE, leading to more missed cancers. Lastly, obese men have larger prostates, reducing the likelihood of finding cancer at biopsy. Lower PSA values combined with difficulties in performing a through DRE can lead to lower biopsy rates among obese men; larger prostates can result in more missed cancer cases that collectively lead to reduced detection of early stage cancers. In the literature the relationship between obesity and HGPCa is conflicting and hence detection bias does not fully explain the link between obesity and aggressive PCa [23,24]. Therefore, our data suggest that high BMI may be biologically associated with an increased risk of PCa development, but it is also associated with a reduction of detection rate during DRE at the time of the urologic examination. Our results demonstrated that obese patients have lower PSA levels, larger prostates and abundant perirectal fat. For these reasons, this study suggests a positive correlation between BMI and PCa detection, particularly HGPCa detection, at biopsy. Lower PSA serum levels and large prostate size associated with high BMI indicated a potential risk for delayed diagnosis and poor pathological outcomes in obese men.

We believe that larger studies with a longer follow-up are needed to determine the effectiveness of the proposed diagnostic strategy in obese men for PCa detection.

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