Evaluation of the Role of Digital Rectal Examination and Transrectal Ultrasonography in Diagnosis of Prostate Cancer in Turkish Men

Türk Erkeklerinde Prostat Kanseri Tanisinda Transrektal Ultrasonografi ve Rektal Muayenenin Rolunun Değerlendirilmesi

Prostat Kanseri / Prostate Carcinoma

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Özet

Amaç: Farklı prostat patolojilerinde prostat spesifik antijen(PSA), Parmakla rektal muayene(PRM) ve Transrektal ultrasonografi(TRUS) bulguları arasındaki ilişkinin araştırılması. Gereç ve Yöntem: Ağustos 2008-Ocak 2009 tarihleri arasında polikliniğimize prostatizm yakınmasıyla başvuran ve PSA 4ng/ml üzerinde olan 229 hastadan 12 kadran biyopsi alındı. Histopatolojik değerlendirmede; 91 hastada benign prostat hiperplazi (BPH), 60 hastada BPH ile birlikte kronik prostatit, 63 hastada prostat kanseri (PCa) saptandı. PSA değeri 4-9.9ng/ml (grup1) ile 9.9ng/ml üzerinde olan gruplarda (grup2), PRM ve TRUS bulguları yönünden BPH, PCa ve kronik prostatit patolojik tanısı alanlar arasındaki ilişki değerlendirildi. Bulgular: Grup1'de PRM'de sertlik saptanması patolojik tanılar yönünden farklılık göstermediği halde grup2'de sertlik, diğer patolojik tanılara kıyasla PCa lehine daha yüksek oranda bulunmuştur. PRM'de nodül varlığında(PRM:1), PSA <10 ng/ml olan 3 hastanın ikisine BPH tanısı birine ise PCa tanısı konduğu halde, PSA>9.9 ng/ml olan 3 hastanın hepsine de PCa tanısı konmuştur. Grup1 için TRUS bulgusu (+) yada (-) olması ile patoloji sonuçları arasında istatistiksel olarak anlamlı ilişki saptanmadığı halde (p>0,05), grup2 için TRUS bulgusu ile patoloji sonuçları arasında istatistiksel anlamlı bir ilişki (p<0,001) tespit edilmiştir. Sonuç: PCa, tanısında PRM ve TRUS'nin değeri tartışılmaz olmasına rağmen tanıdaki etkinlikleri PSA değerine bağımlı bulunmuştur.

Anahtar Kelimeler

Adenokarsinom; Adenomatöz Hiperplazi; Prostat Spesifik Antijen; Transrektal Ultrasonografi

Abstract

Aim: Investigation of the relationship between Prostate Specific Antigen (PSA) and digital rectal examination(DRE) and transrectal ultrasonography(TRUS) findings in different prostate pathologies. Material and Method: 12-quadrant prostatic biopsy was performed for 229 patients who were admitted to our outpatient clinic between August 2008-January 2009, with lower urinary tract symptoms (LUTS) and PSA levels over 4 ng/ml. Histopathological evaluation were as benign adenomatous hyperplasia (BPH) in 91, BPH with chronic prostatitis in 60 and adenocarcinoma in 63 patients. PSA levels between 4.0 and 9.9 ng/ml and PSA level higher than10 ng/ml were determinated as Group1 and Group 2. The relationship between pathologic diagnosis and DRE /TRUS findings were evaluated. Results: While the determination of toughness in DRE didn't show any difference in terms of pathological diagnosis in group-1, the rate of toughness in group-2 was higher in favor of PCa. In 3 patients, there was nodule in DRE and PSA was below 10ng/ml, 2 of them were diagnosed as BPH and the other one was diagnosed as PCa. PSA was above 9.9ng/ml in other 3 patients and all of them were diagnosed as PCa. While there was no statistically significant relationship between pathologic results and positive or negative TRUS findings in group-1, group-2 had statistically significant relationship. Discussion: TRUS and DRE are more valuable tests for PCa diagnosis but these tests effectiveness is related to PSA.

Keywords

Adenocarcinoma; Adenomatous Hyperplasia; Prostate Specific Antigen; Transrectal Ultrasonography

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Introduction

After the introduction of prostate-specific antigen (PSA) measurement in the late 1980s, increased screening for prostate cancer began and resulted in changes that include an increase in prostate cancer incidence and in the number of prostate biopsies performed [1-3]. Regarding the indications for prostate biopsies, it has been shown that abnormal clinical findings (abnormal DRE) have markedly decreased and biochemical findings (elevated PSA) have increased over the last 20 years [4]. Although the true sensitivity of transrectal biopsy is not known, further testing is required after combined PSA and DRE which is typically followed by transrectal ultrasonography with transrectal biopsy. The combined use of PSA, DRE, and ultrasound-guided biopsy may result in earlier detection; however, randomized trials have not shown that it reduces morbidity or disease specific mortality. On the other hand, infection (20%), bleeding (20%), and hospitalization (1%) which are the complications of biopsy may occur [5]. The aim of this study is to evaluate the value of DRE and TRUS in the diagnosis of prostate cancer in patients who have a TRUS biopsy and PSA > 4ng/ml using the literature.

Material and Method

214 patients; aged between 48-80 years and with mean age of 63,99±7,12 years, mean total-PSA of 15,82±22ng/ml, mean free-PSA of 2,36±3,30ng/ml, free/total PSA ratio of 16,04±7,33 %, mean prostatic volume of 55,63±2,10 ml were performed 12-quadrant prostatic biopsy because of high PSA levels between August-2008 and January-2009. Serum samples were stored at -20 ºC and were tested for fPSA within 4 days. Free PSA was estimated by sandwich ELISA technique using high affinity Biotin-Streptavidin system, with analytical sensitivity of 0.05ng/mL Histopathological evaluation were as adenomatous hyperplasia (BPH) in 91, BPH with chronic prostatitis in 60 and adenocarcinoma in 63 patients. DRE and TRUS were performed to all 214 patients. DRE findings were classified as 0: benign, 1: palpable nodule, 2: endurated, 3: endurated+fixed. TRUS findings were classified as 0:absence of nodule, 1:presence of nodule (hypo or hyper-echogenic). PSA levels between 4.0 and 9.9 ng/ml and PSA level higher than 10.0 ng/ml were determinated as group-1 and group-2, respectively. The relationship between pathologic diagnosis (BPH, PCa and chronic prostatites) and DRE /TRUS findings were evaluated. T-test and chi-square test were used for the comparison of independent groups. P values <0.05 were considered as statistically significant. Data were analysed by using the Statistical Packages for the Social Sciences 11.5 for Windows (SPSS-11.5).

Results

While the determination of toughness in DRE didn't show any difference in terms of pathological diagnosis in group-1, the rate of toughness in group-2 was higher in favor of PCa. In 3 patients, there was nodule in DRE (DRE:1) and PSA was below 10ng/ml, 2 of them were diagnosed as BPH and the other one was diagnosed as PCa. PSA was above 9.9ng/ml in other 3 patients and all of them were diagnosed as PCa [Table 1]. In other words, DRE findings has provided less positive foresight for cancer diagnosis in 4.0-9.9 ng/ml group than in ≥10.0 ng/ml group. On the other hand, distribution of DRE findings was not homogenous between the histopathological groups. This is a clinical pre-study about digital rectal examination (DRE) and TRUSG findings of the patients with PSA levels over 4.0 ng/ ml and clinical follow-up of all patients still continued.

In our study, TRUSG findings have provided more positive foresight for cancer diagnosis in PSA 10.0 ng/ml group. In patients with presence of pathological nodule/s in TRUSG, PCa was determined in 34% of PSA 4.0-9.9 ng/ml group, while in 69.7% of ≥10.0 ng/ml group. The positiveness of TRUS findings (TRUS:1) was 18% in group-1 and 38% in group-2. Similarly, in one third of the patients who were diagnosed as PCa within group-1, TRUS findings were positive and in group-2, TRUS findings were positive in 2/3 patients who were diagnosed as PCa [Table 2]. In PSA 4,0-9,9ng/ml group, histopathological reports of the patients with no nodules in TRUSG were as BPH, PCa and chronic prostatitis in 56%, 16% and 26% of the patients, respectively. Also in the same group, histopathological reports were as BPH, PCa and chronic prostatitis in 59%, 17% and 23% of the patients with normal DRE respectively. When nodule was present in TRUSG in this group, BPH, PCa and chronic prostatitis were detected in 52%, 34% and 13% of the patients, respectively. The rates of BPH, PCa and chronic prostatitis in patients who had palpable prostate nwith PSA range between 4-9.9ng/ml were 36.8%, 36.8% and 26.3%, respectively. However, in PSA≥ 10.0 ng/ml group, histopathological diagnoses of the patients with no nodules in TRUSG were as BPH, PCa and chronic prostatitis in 30%, 27% and 41% of the patients, respectively. Also in the same group, histopathological reports were as BPH, PCa and chronic prostatitis in 35%, 18% and 45% of the patients with normal DRE, respectively. When nodule was present in TRUSG in this group, BPH, PCa and chronic prostatitis were detected in 9%, 69% and 21% of the patients, respectively The rates of BPH, PCa and chronic prostatitis in patients who had palpable prostate nodule with PSA range over 10ng/ml were 8%, 68% and 24%, respectively. Diagnostic values of DRE and TRUSG increase in patient with PSA ≥ 10.0 ng/ml. However, our study is a pre-study and the distribution of DRE findings is not homogenous. Data of our study in the future will be helpful in the evaluation of DRE and TRUSG findings of two different PSA groups [Table 1,2].

However, TRUSG was more effective in cancer diagnosis with presence of nodule while DRE was more effective with presence of n=2 findings, especially in PSA 10 ng/ml group. Also in patients with absence of TRUSG findings, detection rate of chronic prostatitis was high in PSA≥10ng/ml group (41.3%). Detection rate of chronic prostatitis in patients with no pathological findings on examination was 45,3% in PSA≥10ng/ml group. While there was no statistically significant relationship (p>0,05) between pathologic results and positive or negative TRUS findings in group-1, group-2 had statistically significant relationship (p<0,001) [Table 1,2].

Table 1. Histopathological results of the patients in PSA groups of 4,0-9,9 ng/ml and ≥10,0 ng/ml, according to DRE findings

	DRE	BPH	PCa	Ch.Prostatitis
Group-1	0 n= 104	61 %59,4	18 %17,0	25 %23,6
PSA 4,0-9,9 ng/ml n=127	1 n= 3	2 %66,7	1 %33,3	–
	2 n= 20	7 %36,8	7 %36,8	6 %26,3
	3 n= 0	–	–	–
Group-2	0 n= 52	19 %35,8	10 %18,9	23 %45,3
PSA ≥10,0 ng/ml n=87	1 n= 3	–	3	–
	2 n= 25	2 %8	17 %68	6 %24
	3 n= 7	–	7	–

Table 2. Histopathological results of the patients in PSA groups of 4,0-9,9 ng/ml and ≥10,0 ng/ml, according to TRUSG findings

	TRUSG	BPH	PCa	Ch. Prostatitis	P Value
Group-1 PSA 4,0-9,9 ng/ml n=127	0 n=104	59 (% 56,6)	18 (%16,9)	27 (%26,5)	p > 0.05
	1 n=23	12 (%52,1)	8 (%34,8)	3 (%13,1)	
Group-2 PSA ≥10,0 ng/ml n=87	0 n=54	17 (%30,9)	14 (%27,8)	23 (%41,3)	p < 0.001
	1 n=33	3 (%9,1)	23 (%69,7)	7 (%21,2)	

Discussion

The diagnosis of early prostate cancer comprises of a PSA assay, a DRE and TRUS-guided biopsy of the prostate. PSA remains the most important tool for investigating and manging patients with suspected and confirmed carcinoma of the the prostate. The DRE is considered to be mandatory in the dşagnosis of and staging of prostate cancer but studies investigating the accuracy of a DRE for these purposes have yielded conflicting reports [6] . DRE is the primary method of examination of the prostate. This technique allows the examiner to appreciate the gland's morphology, including any irregular, nodular, or indurated areas , that may be suspicious for malignancy [7]. Palpation of the prostate by DRE was the traditional manner by which a diagnosis of prostate cancer was suspected. Up to 50% of palpable masses were attributable to prostate cancer in historical series [8,9]. Digital rectal examination by itself is a poor method for diagnosing this malignancy [10]; however, it is still important in diagnosis as 25% of tumors are detected in men with normal PSA levels [11]. However, on the other hand, diagnosis of prostate cancer with biopsies of isolated PSA elevation and normal DRE range between 30% and 40% [4]. Unfortunately, when a prostate cancer is diagnosed based on a palpable tumor, the risk of the patient already harboring metastatic or locally advanced malignancy is considerable [12-14]. However, some curable cancers may be missed if prostate cancer is detected only by PSA without DRE [15].

In most of the cases the histological diagnosis of prostate cancer is made by prostate needle biopsy. Thus, in patients who have abnormalities found on digital rectal examination (DRE), or serum prostate-specific antigen (PSA) elevations, suspicious of prostate cancer is most often raised. Routine measurement of PSA is valuable as it increases the detection of prostate cancer over that of DRE, improves the predictive value of the DRE for cancer, and increases the detection of prostate cancers that are organ confined yet significant in terms of size and grade. The single test with the highest positive predictive value for prostate cancer is PSA [16]. Studies on the accuracy of DRE have resulted in contradictory reports . Prostate cancer detection rates are reportedly 49-60% in patients with an abnormal DRE and an elevated PSA level of 4>ng/ml. The present study shows that the positive predictive value of a DRE for prostate cancer is only 47% in patients with a PSA level of 2.5-10 ng/ml. Previous investigators reported higher cancer detection rates , as >20 % of patients in those studies had PSA levels of >10 ng/ml. In the present study there was a poor cancer detection rate in patients with an abnormal DRE despite the DRE being carried out by either of two experienced urologists [6]. In our study, prostate cancer was detected in 17% of the patients with normal DRE and in 36.8% of the patients with palpated nodule. Also in PSA 4-9.9ng/ml and in PSA ≥10 ng/ml group, cancer detection rates were 18.9% and 69%, respectively.

The present study also showed a very poor agreement between the DRE and pathological staging in those patients who chose to have a radical prostatectomy. Almost 40% of the patients who were considered to have a normal prostate on DRE were pathologically staged as T2 in 24 and T3 in seven. Thus the DRE was not only poor in detecting prostate cancer but also in predicting pathological staging [6]. In a study with 601 men undergoing RRP, only 52% of the 565 men with cT2 disease had organ-confined tumors whereas 19% of 36 men with cT3 disease had organ-confined lesions [12]. There are reports of cure by RRP for cT3 disease however, if there is a bulky extraprostatic tumor, the outcome is generally poor with the high associated risk of metastatic disease [17,18].

In a study, the patients had a history and physical examination done except digital rectal examination (DRE), which was carried out after blood for PSA had been drawn. All suspicious lesions at DRE underwent a biopsy and confirmed the disease at a high pick up rate [9].On the other hand, because of the significant risk of prostate cancer, prostate biopsy is recommended for all men who have DRE abnormalities, regardless of the PSA level, since there is still a chance, however small of prostate cancer even when PSA level is less than 4 ng/ml [3]. It is of paramount important to note here that till now clinical presentation and abnormal DRE remains the main way of diagnosis of prostate cancer in most of the hospitals in those countries. However, that DRE misses from 23% to 45% of the cancers that are subsequently found with prostatic biopsies done for serum PSA elevation or transrectal ultrasound abnormalities [19,20]. In 1987, the first literature appeared describing the us eof TRUS with transrectal biopsy. Since then, as ultrasound technology has become more refined, this technique has been described as a superior method of performing a core biopsy of the prostate [7] .Presently, the incidence of an abnormal TRUS, suggestive of a positive biopsy, is not so frequent, and findings may vary from 49 to 95% according to the authors . In fact, while the overall positive biopsy rate is 50%, it increased to 69% in cases of TRUS-suspected lesions. In cases of normal ultrasound patients of the prostatic fossa, only 20% of patients had a positive biopsy, while 62% of those with suspected lesions had proven local recurrences. In fact, while the overall positive biopsy rate is 50%, it increased to 69% in cases of TRUS-suspected lesions. Retrospective a study showed that TRUS was more sensitive than DRE (75% vs 50%) and, conversely, DRE proved more discriminating than TRUS (85% vs. 64%) [21]. On the other hand, In our study, prostate cancer was detected in 34% of the patients with positive TRUSG findings in PSA 4-9.9 ng/ml group and in 69.7% in PSA≥10 ng/ml group. But, in patients with palpated nodule on DRE, cancer detection rates were 36.8% and 68% in PSA 4.0-9.9 ng/ml and PSA ≥10 ng/ml groups, respectively. Many studies demonstrate that the higher the serum PSA level, the higher the positive biopsy rate. the PSA levels of patients with a positive biopsy were significantly higher than the PSA levels of those with a negative biopsy [21].Only 60% of the cancers detectable by PSA are organ-confined at radical prostatectomy. When DRE is added to PSA, only 60% of the newly diagnosed tumors are clinically localized [22-25]. However, TRUS is essential in ensuring accurate sampling of the gland and can be helpful in tailoring the number of cores and their distribution based on the size of the gland and patient risk stratification. Although the ideal number of cores is not clear. TRUS is an in-

tegral facet of prostate biopsy and will continue to contribute to our understanding of the optimum regimen fort he diagnosis of prostate cancer. With more patients presenting earlier for biopsy as a result of PSA screening, together with potentially earlier diagnosis resulting from increased gland sampling, prostate cancer may be diagnosed at an earlier and more treatable point in the disease process [7].

As a conclusion, there is however a need to establish the true prevalence of prostate cancer in our country by a well planned randomized study using PSA, DRE and TRUS. Although PSA levels, DRE, TRUS have no distinct superiority to each other when evaluated alone, it will provide more benefit when used together.

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