Efficacy of Pelvic Diffusion Weighted MRI Prior to Prostate Biopsy in Patients with tPSA Level of 2,5-20 ng/ml for Determination of Malign Lesions

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Citation

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Abstract

OBJECTIVES: The aim of this study is to increase the diagnosis rate of prostate cancer by using transrectal ultrasonography (TRUS) guided biopsy samples from pre-determined lesions in diffusion-weighted magnetic resonance imaging (MRI).

METHODS: 100 patients with serum total prostate-specific antigen (tPSA) levels of 2.5 to 20 ng/ml and without any prior biopsy were randomly assigned into two groups.
1.group; 50 patients have undergone to 10 quadrant needle TRUS guided prostate biopsy.
2.group; 50 patients have undergone to diffuse weighted MRI before TRUS guided prostate. Along with 10 quadrant biopsy, additional tissue samples were collected in suspicious lesions detected with MRI. Pathology results were compared with diffuse MRI results in order to determine the sensitivity and specificity of MRI in diagnosis of prostate cancer.

RESULTS: 8 (16%) out of 50 patients in group 1 were diagnosed with prostate cancer after histopathologic examination of TRUS guided biopsy samples. 13 out of 50 patients in group 2 were diagnosed with prostate cancer after histopathologic examination of TRUS guided biopsy samples. Cancer cells were detected in 10 out of these 13 patients (76.9%) at lesions that were determined with diffuse weighted MRI. There was no suspected area in MRI examination of the remaining 3 patients. Only one of 37 patients, who were not diagnosed with cancer, had suspected lesions in MRI examinations, however biopsy results were negative only for this particular patient.

Results of TRUS guided prostate biopsy and diffusion weighted MRI were statistically compatible (p=0.0001). Sensitivity and specificity of diffuse weighted MRI prior to TRUS guided prostate biopsy were found as 77% and 97%, respectively. The possibility of positive TRUS guide biopsy result in a patient with positive MRI examination finding was found 28.46 times higher compare to a negative MRI examination finding.

CONCLUSION: In brief, we strongly recommend taking extra samples from the suspicious lesions detected by diffusion MRI in prostate biopsy, however multicentric studies in wider populations are needed in order to advise this technique.

INTRODUCTION

Prostate cancer is most common type of solid cancer in European male population besides the second common reason of cancer related death after lung cancer.

In a study, conducted in US it was demonstrated that the risk of having prostate cancer during lifetime period for a male was 16% while disease related mortality was 3% (1).

As a result of negative biopsy results in patients with normal PSA levels and abnormal rectal examination findings revealed in prostate cancer screening programs, clinicians faced with diagnostic challenges (2).

Similar patient PSA levels in both BPH and prostate cancer as well as insufficient specificity and sensitivity of PSA level in determination of prostate cancer lead to the development of PSA based differentiation for investigators in order to be used early diagnosis, stating and follow up of prostate cancer. Parameters, developed for increasing the

efficacy of PSA levels in clinical practice can be summarized as; PSA density (PSAD), PSA velocity-PSAV, age related PSA reference values and ratio of free PSA to total PSA (s/tPSA) (3, 4, 5, 6). However, it should be bear in mind that the risk of undiagnosed cancer with increasing PSA specificity and number of redundant biopsies with increasing sensitivity can be high.

Rate of cancer diagnosis in TRUS guided biopsies is incremental; 22%, 25% and 50% in tPSA threshold values of 2,6 to 4 ng/ml, 4 to 20 ng/ml and >20 ng/ml, respectively (7).

Magnetic Resonance Imaging (MRI) has the highest soft tissue resolution out of available imaging techniques. Using MRI in prostate cancer is efficient for staging of disease, determination of local dissemination and lymph node metastasis. Recent studies revealed that diffusion-weighted MRI is superior to dynamic contras enhanced MRI in diagnosis of prostate cancer (8).

The aim of this study is to increase the rate in diagnosis of prostate cancer by using TRUS guided biopsy samples from pre-determined lesions in diffusion-weighted MRI.

MATERIALS AND METHODS

100 patients with serum tPSA levels of 2.5 to 20 ng/ml and without any prior biopsy were included in the study prospectively from outpatients of Bagcilar Training and Research Hospital, Urology Clinic between July 2012 and December 2012. Age, tPSA levels and Prostate volumes were shown in table 1.

Table 1

Age, tPSA and PV variables of all patients

	N	Minimum	Maximum	Mean	Sd.
Age (year)	100	46	80	62.10	7.58
tPSA (ng/ml)	100	2.7	19	5.88	3.19
PV (cm³)	100	10	107	50.65	22.81

Sd: Standard Deviation

Patients were randomly assigned to;

1.group; 50 patients have undergone to 10 quadrant needle TRUS guided prostate biopsy.

2.group; 50 patients have undergone to diffuse weighted MRI before TRUS guided prostate. Along with 10 quadrant biopsy, additional tissue samples were collected in suspicious lesions detected with MRI.

Patients with prior history of open prostatectomy or TUR-P operation and who already have been followed with diagnosis of prostate cancer were excluded from the study.

The difference between two groups in terms of average age (p:0,325), tPSA (p:0,539) and prostate volumes (p:0,654) was not statistically significant (Table 2).

Table 2

Comparison of two groups in terms of age, tPSA and PV

	Group 1	Group 2	p
Age (year)	62,82±7,25	61,38±7,32	0,325
PSA (ng/ml)	6,07±3,79	5,68±2,48	0,539
PV (cm³)	49,61±24,71	51,69±20,95	0,654

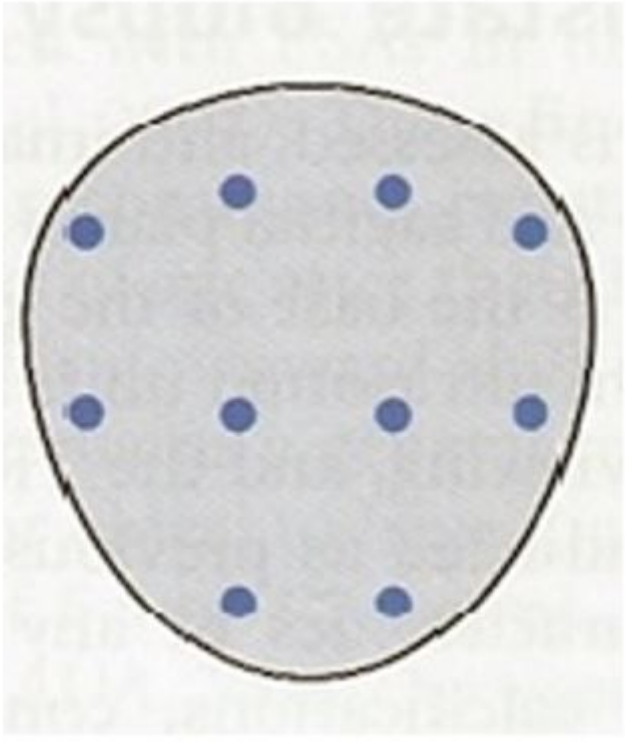
p<0.05 significant

Diffusion enhanced MRI (Philips Intera 1.5T MRI device, Best, Holland) were evaluated by same radiologist (M.O.).

In all patients, 10 quadrant prostate biopsies were performed by using the technique, represented by Presti et all (image 1) (9).

Figure 1

10 quadrant prostate biopsy schema of Presti et. all.

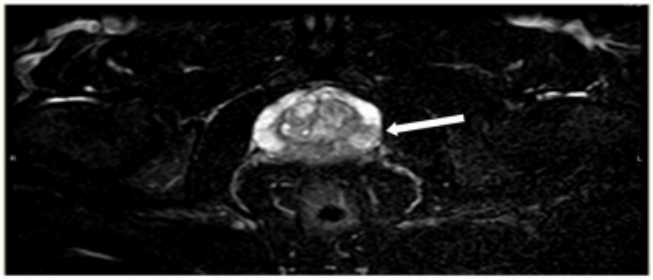


Suspected lesions in MRI findings were defined as prostate

basis, media and apex and were also separated to central and peripheral topographical areas. Hypodense areas in T2A images were detected. . TRUS biopsy (BK pro-focus 2202 color, Herlev, Denmark) was made by using 12 MHz wavelength transrectal probe. All TRUS guided prostate biopsies were performed by same urologist (S.Y.)

Figure 2

Hypodense lesion in T2A images of prostate located in right peripheral zone (ok). (PSA:6,27 ng/ml, age:59, result of TRUS guided biopsy: Gleason 3+4 Prostat Adenoca)



All patients started treatment with a quinolone group antibiotic-ofloxacine at a dose of 400 mg/day in once daily regimen for 3 days prior to biopsy and they continued the treatment 2 more days after the procedure. Libalax gr enema was administrated to all patients 2 hours prior to the procedure and anticoagulant medication was terminated 1 week prior to the procedure the for patients taking anticoagulation treatment. Patients were undergone to bilateral peripheral nerve blockage TRUS biopsy in left decubitis position after anesthesia (20%) administration consisting of 20 mg 2 ml lidocaine, diluted with 8 ml serum physiologic. Tissue samples were obtained with automatic biopsy gun (MegaCore, Pekin, China) and 18G biopsy needle (Gallini Mirandol, Italy) following this procedure. Each was delivered to pathology department separately in one eppendorph containing 10% formaldehyde.

Prostate volumes in TRUS were calculated by using ellipsoid formula (anterior-posterior diameter X transverse diameter X longitudinal diameter x 0,523).

Pathology results were compared with diffuse MRI results in order to determine the sensitivity and specificity of MRI in diagnosis of prostate cancer.

Statistical Analysis:

SPSS (Version 22.0, SPSS Inc., Chicago, IL, USA) was used all statistical analysis. Descriptive statistics were presented as mean ± standard deviation when data were normally distributed; otherwise, were presented as median, minimum–maximum (min–max). Nominal variables were presented as number of cases and percentage. The data obtained were analysed for normal distribution using the Shapiro Wilks normality test. The significances of the difference between the two groups were evaluated with Independent t-test for means and Mann Whitney U test for medians. The McNemar test was used to test for significance differences between paired results of TRUS guided prostate biopsy and diffusion weighted MRI and to evaluate the levels of agreement was calculated by the Kappa Coefficient (K). Sensitivity, Specificity, Positive predictive value (PPV), Negative predictive value (PPV), Accuracy and Positive Likelihood Ratio (LR+) were calculated for each test using the numbers of patients with true positive (TP), true negative (TN), false positive (FP) and false negative (FN) results. P value <0.05 was considered statistically significant.

RESULTS

8 (16%) out of 50 patients in group 1 were diagnosed with prostate cancer after histopathologic examination of TRUS guided biopsy samples.

13 out of 50 patients in group 2 were diagnosed with prostate cancer after histopathologic examination of TRUS guided biopsy samples. Cancer cells were detected in 10 out of these 13 patients (76.9%) at lesions that were determined with diffuse weighted MRI. There was no suspected area in MRI examination of the remaining 3 patients.

Only one of the 37 patients, who were not diagnosed with cancer, had suspected lesions in MRI examinations, however biopsy results were negative only for this particular patient.

Results of TRUS guided prostate biopsy and diffusion weighted MRI were statistically compatible (kappa correlation coefficient 0.781 p=0.0001)

Table 3

Results of both groups

1.Group	TRUS-BX Positive		TRUS-BX Negative		
	8	(16%)	42	(84%)	
2.Group					
MR Positive	10	(76.90%)	1	(2.70%)	**p*=0.625**
MR Negative	3	(23.10%)	36	(97.30%)	**κ_w:0.781, p**<0.001**

*McNemar p value ** Kappa p value, **κ**: Kappa value, Strength of agreement according to the value of **κ** (0.00 < **κ** < 0.20: poor; 0.21 < **κ** < 0.40: fair; 0.41 < **κ** < 0.60: moderate; 0.61 < **κ** < 0.80: good; 0.81 < **κ** < 1.00: very good).

Sensitivity and specificity of diffuse weighted MRI prior to TRUS guided prostate biopsy were found as 77% and 97%, respectively (table 4).

Table 4

Sensitivity and specificity results of diffuse weighted MRI prior to TRUS guided biopsy (TRUS-BX) in 2. Group. (PPV: positive predictive value, NPV: negative predictive value)

	Sensitivity	Specificity	PPV	NPV	Accuracy	LR(+)
TRUS-BX / MR	0.77	0.97	0.91	0.92	0.92	28.46

PPV: positive predictive value, **NPV**: negative predictive value, **LR(+)**: Positive Likelihood Ratio

The possibility of positive TRUS guide biopsy result in a patient with positive MRI examination finding was found 28.46 times higher comparing with a negative MRI examination finding.

DISCUSSION

Over last two decades, widespread screening of serum PSA levels lead not only the increase of cancer detection rate but also the increase in treatment success due to early diagnosis (10). On the other hand, the number of redundant biopsies also increased. Moreover, the specificity of TRUS guided biopsy samples is restrictive in terms of representing the whole tissue. Today, investigations are ongoing for finding different diagnostic methods and modifications in current techniques, in order to eliminate the disadvantages and increasing the efficacy of PSA screening for detection of prostate cancer. Despite having the maximum positive predictive value for prostate cancer, PSA screening also has some deficiencies in diagnosis. In resent studies conducted in parallel to those findings, it was also aimed to find out new diagnostic techniques for prostate cancer. The value of MRI in diagnosis, staging and follow up of prostate cancer is still remaining to be controversial (8).

Because only a very tiny part of the tissue can be sampled with TRUS guided biopsy technique, it is reported that the specificity of the process in detecting cancer is decreasing with the increasing prostate volume (11, 12). In the studies conducted in respect to this information, it was advised to increase the number of samples in higher prostate volumes (13,14,15). However, the increase in the number of sampling is correlated with the increasing morbidity, which led the investigators to seek new techniques that capable of higher cancer detection rate with a less sampling number. Determination of suspected lesions with diffuse weighted MRI has become a pioneer in this quest. MRI also reveals the invasion of seminal vesicle and adjacent tissue as well as presence of pelvic lymph nodes and bone metastasis in patients who will be undergone to surgery. For this purpose, contrast enhanced MRI, endo-coil MRI and diffuse weighted MRI are being used. While using contrast enhanced MRI, caution should be exercised in terms of contrast material related hypersensitivity reactions and renal failure. Furthermore, currently published studies suggested that diffuse weighted MRI is superior to contrast enhanced pelvic MRI in diagnosis of prostate cancer. Endo-coil MRI has some disadvantages in terms of difficult and time-consuming process and patient miscooperation. This is why recent studies are focused on diffuse weighted MRI (8). Kozlowski et. all. compared diffuse weighted MRI and dynamic contrast enhanced MRI by using 1.5T MRI device in 14 patients with a suspicion of cancer before performing biopsy. The sensitivity of diffuse weighted MRI and contrast enhanced MRI was found as 54% and 59% while their specificity was found as 100% and 74%, respectively (16). In a smilar study, conducted by Iwaza et. all. in 178 patients the sensitivity of diffuse weighted MRI and contrast enhanced MRI was found as 74.8% and 52.8% while their specificity was found as 79.8% and 83%, respectively. When diffuse weighted MRI is used together with dynamic contrast enhanced MRI sensitivity was 72.9% and specificity was 80.1%.

Investigators proved that diffuse weighted MRI is more efficient in determining prostate cancer (8).

In our study, 6 patients in group 2 were diagnosed with prostate cancer from samples taken with 10-core biopsy in suspected lesions which were determined in both diffuse weighted MRI and TRUS. In those patients, diagnosis was not affected by MRI examination as 10-core biopsy sampling was including the lesions in MRI findings. Distinguishingly, the other 4 patients were diagnosed with extra samples taken from outer range of 10-core biopsy diagram. It is obvious that combination use of diffuse weighted MRI and TRUS guided biopsy is increasing the cancer detection rate in patients with high tPSA level. As a result, sampling from suspected lesions in MRI examination, in addition to standard sampling schemes decreases the possibility of undiagnosed cases.

In our study, we found the sensitivity and specificity of diffuse weighted MRI prior to TRUS guided biopsy as 77% and 97%, respectively.

CONCLUSION

In brief, we strongly recommend taking extra samples in biopsy, however multicentric studies in wider population are needed in order to advise biopsy sampling from solely the

lesions detected with MRI examination.

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