Single center results of magnetic resonance imaging ultrasound guided fusion prostate biopsy obtained patients

Manyetik rezonans görüntüleme-ultrason füzyon prostat biyopsisi tek merkez sonuçları

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Özet

Amaç: Çalışmamızda tek merkeze ait manyetik rezonans görüntüleme-ultrason füzyon prostat biyopsisi (MRI-US FPBx) sonuçlarını değerlendirmek ve güncel literatürle karşılaştırmak istedik.

Gereç ve Yöntemler: Ocak 2016 ile Temmuz 2019 arasında 358 erkeğin MRI-US FPBx sonuçları retrospektif olarak analiz edildi. PI-RADS skorları 222 (% 62), 107 (% 29.8) ve 29 (% 8.1) hastada sırasıyla 3, 4 ve 5 olarak tespit edildi. Toplam 454 lezyona MRI-US FPBx uygulandı. 303 (% 66,7) lezyon PI-RADS 3, 120 (% 26,4) lezyon PI-RADS 4 ve 31 (% 6,8) lezyon PI-RADS 5 olarak skorlandı. Lezyonların 315'i (% 69,3) periferik zonda, 26'sı (% 5,7) santral zonda, 111'i (% 24,4) geçiş zonu ve 2'si anterior fibromüsküler stromada idi.

Bulgular: Genel prostat kanseri (PCa) tespit oranı% 36.3 idi. Tek başına MRI-US FPBx ve tek başına transrektal ultrasonografi eşliğinde prostat biyopsisi (TRUS-Bx) kanser saptama oranları sırasıyla % 27.6 ve% 26.5 idi. PI-RADS-3 ve PI-RADS 4 & 5 için MRI-US FPBx'e özgü kanser tespit oranı sırasıyla % 6,9 ve% 20,6 idi. Klinik olarak önemli prostat kanseri (csPCa) oranları değerlendirildi ve TRUS-Bx, MRI-US FPBx ve kombine teknikler için csPCa ve PCa oranları sırasıyla % 16.8, % 35.4 ve % 39.2 idi. 11 hastanın biyopsi sonuçları benigndi.

Sonuç: MRI-US FPBx , prostat biyopsi prosedürünün başarı oranını önemli ölçüde artırır.

Abstract

Objective: We aimed to evaluate magnetic resonance imaging-ultrasound guided fusion prostate biopsy (MRI- US FPBx) results from a single center and to compare with current literature.

Material and Methods: Between January 2016 and July 2019, MRI-US FPBx pathological and imaging results of 358 men were retrospectively analyzed. PI-RADS scores were determined as 3, 4 and 5 in 222 (62%), 107 (29.8%) and 29 (8.1%) patients, respectively. Totally 454 lesions were underwent MRI-US FPBx. 303 (66.7%) lesions were scored as PI-RADS 3, 120 (26.4%) lesions were scored as PI-RADS 4 and 31 (6.8%) lesions were scored as PI-RADS 5. 315 (69.3%) of lesions were in peripheral zone, 26 (5.7%) were in central zone, 111 (24.4%) were in transitional zone and 2 of them were in anterior fibromuscular stroma.

Results: Overall prostate cancer detection rate was 36.3%. Concerning detection rates, MRI-US FPBx alone and transrectal ultrasonography guided prostate biopsy (TRUS-Bx) alone were 27.6% and 26.5%, respectively. Cancer detection rate only through MRI-US FPBx PIRADS-3 and PI-RADS 4&5 were 6.9% and 20.6%, respectively. Clinically significant prostate cancer (csPCa) rates were evaluated and csPCa to overall prostate cancer (PCa) rates for TRUS-Bx, MRI-US FPBx and combined techniques were 16.8%, 35.4% and 39.2%, respectively. Results of 11 patients were evaluated as benign.

The study was approved by the Ethics Committee of Gazi University (Approval number: 91610558-604.01.02) (Date: 2019.07.26). All research was performed in accordance with relevant guidelines/regulations, and informed consent was obtained from all participants.

Ancak mevcut MRI teknolojisine göre, MRI-US FPBx'i TRUS-Bx olmaksızın bağımsız bir biyopsi seçeneği olarak düşünmek uygun olmadığı görüşündeyiz.

Anahtar Kelimeler: prostat kanseri, biyopsi, MRI, füzyon

Conclusion: MRI-US FPBx significantly increases success rate of prostate biopsy procedure. Regarding current MRI technology, it is not appropriate to consider MRI-US FPBx as a stand-alone biopsy option without concomitant with TRUS-Bx.

Keywords: prostate cancer; biopsy; MRI; fusion

INTRODUCTION

Men with suspected clinical prostate cancer (PCa) based on abnormal digital rectal examination (DRE) or increased prostate specific antigen (PSA) level are conventionally recommended to undergo transrectal ultrasonography–guided biopsy of the prostate (TRUS-Bx) (1). However, TRUS-Bx has a false negative rate of 10-20% especially with lesions in transition zone, anterior and apex of the prostate (2). Moreover, final pathology upgrade rates after radical prostatectomy of patients obtained TRUS-Bx is 30-45% (3). Especially in the last decade, multiparametric magnetic resonance imaging (mpMRI), as an alternative diagnostic pathway on detection of PCa has become popular (4). PCa detection has become easier after the standardization of the mpMRI reporting system (5). With combination of 12-core cognitive biopsy and targeted biopsy increases PCa detection rate 10% more (6). In addition, targeted prostate biopsy provides significant lower upgrades in final pathology compared to standart biopsy and upgrading tumor laterality is also lower in patients performed magnetic resonance imaging-ultrasound guided fusion prostate biopsy (MRI-US FPBx) (7). Actually, MRI targeted biopsy increases the detection of clinically significant prostate cancer (csPCa) while decreases the detection of cancer that do not require treatment (8).

In this retrospective study, we aimed to present our MRI-US FPBx results from a single center and to evaluate benefits of the fusion biopsy.

MATERIAL AND METHODS

After institutional review board approval (ID: 2019-290), we retrospectively identified results of the patients obtained MRI-US FPBx between January 2016 and July 2019.

Patient Selection

Patients with suspected prostate cancer due to increased PSA value (threshold ≥4 ng/dL) or DRE findings or both were included the study. Biopsy naive patients and patients with prior negative biopsy were also included. The ethnicity of all patients was Turkish. The inclusion criteria was detection of at least one suspicious lesion of the prostate according to the Prostate Imaging Reporting and Data System version 2 (PI-RADS v.2) (9) classification in mpMRI determined as PI-RADS ≥3 (10). Patients who could not receive sedation anesthesia due to their comorbidities were excluded from the study. Age, PSA level, PSA density, prostate volume, DRE findings, zone of lesions, number of fusion biopsy cores taken and PI-RADS findings of the patients in mpMRI were recorded. Preprocedural urine culture was evaluated for all patients. In case of any growth detection in urine culture, required antibiotics was administrated to patients until urine culture became negative before the procedure. If any, anticoagulant or antiagregant were stopped and low molecular weight heparin (LMWH) was started 5 days before the procedure and restarted 3 days after the procedure unless postprocedural rectal or urethral bleeding occurred.

Magnetic Resonance Imaging

MpMRI was performed by 1.5 or 3.0 Tesla scanners with a pelvic phased - array coil. Dynamic contrast-enhanced (DCE), 2 - weighted, diffusion - weighted sequences were obtained according to minimum standards that have been set by consensus guidelines. All MRI images were evaluated by two uro-radiologists (AYO, MY) separately who have specialized and seven-year experience on prostate MRI and PI-RADS version 1&2 and did not have additional information

about patients' datas. All MRI images were reported according to PI-RADS v.2 scaling from 1 to 5. Regarding the patients with multiple lesions, in case of two equal PI-RADS score existence, the largest lesion was determined.

MRI-US FPBx Procedure

All procedures were performed under sedoanalgesia combined with local anesthesia and prophylactic antibiotics. Sedo-anesthesia combined with local anesthesia was applied to the patients during the procedure in order to minimize errors that may occur due to patients' movements. Propofol 4 mg/kg and 2% prilocaine hydrochloride (20 mg/ml) were administrated as sedoanalgesia and local anesthesia, respectively. LOGIQ E9© (General Electric, MA, USA) ultrasonography device with rigid fusion software was used during all procedures. Patients who have PI-RADS score of 3, 4 or 5 underwent MRI-US FPBx by a single uro-radiologist (HO) who has at least 25-years of experience on TRUS-Bx procedure. Before procedures, mpMRI images of the patients were obtained and uploaded to ultrasonography (US) software system and lesions were marked on T2-weighted axial images initially. The procedures were performed on left decubitus position. First, propofol was administrated through intravenous access and subsequently 1-2 minutes later sonographic examination of the prostate was performed. Any existence of suspicious lesions was evaluated. Before the software matching, periprostatic block was performed with 2% prilocaine hydrochloride into the neurovascular bundle on both sides of prostate using a 18-guage 20 cm Chiba© needle. Then, prostate boundaries were determined. MRI and US images of the prostate were matched using the software. Initially a total of 12-core cognitive TRUS-Bx was acquired from the peripheral zone and subsequently fusion biopsy was performed for each marked lesion. At least 3-core fusion biopsy was obtained from each lesion. In addition, according to radiologist's (HO) decision, number of fusion biopsy core was increased.

Pathologic Evaluation

A single pathologist who has more than 20 years of experience on uro-pathology has evaluated all pathologic samples according to 2014 International Society of Urological Pathology (ISUP) grading system (11). CsPCa was defined as ISUP ≥ 2 (Gleason score $\geq 3 + 4$) in the present cohort.

Statistical Analysis

Parametric and non-parametric data were presented as mean ± standard deviation or median (Interquartile Range (IQR)), respectively. Statistical analysis was done using Statistical Package for Social Sciences 23.0 Software (SPSS 23.0). Descriptive statistics of scale samples were expressed as median (IQR). Kolmogorov - Smirnov, Kurtosis, and Skewness Tests were used to assess the variables' normalization. The clinical characteristics of groups were compared with Mann Whitney U and Student t-tests for continuous variables and with Fisher Exact chi-square test for categorical variables. Probability of $p < 0.05$ was accepted as statistically significance.

RESULTS

The study included 358 patients.Median age was 60.5 (47-84) years, median PSA level was 8.04 (0.59-30.4) ng/dL, median PSA density was 0.11 (0.01-1.0) ng/dL/mL and median prostate volume was 60.6 (18-194) mL. DRE was detected as suspicious in 113 (31.6%) men while evaluated as normal in 245 (68.4%). PI-RADS scores were determined as 3, 4 and 5 in 222 (62%), 107 (29.8%) and 29 (8.1%) patients, respectively (Table 1). 21 patients had a history of TRUS-Bx and 5 patients had transurethral resection of the prostate (TUR-P)history.

Total of 454 lesions were evaluated through MRI-US FPBx. 303 (66.7%) lesions were scored as PI-RADS 3, 120 (26.4%) lesions were scored as PI-RADS 4 and 31 (6.8%) lesions were scored as PI-RADS 5. 315 (69.3%) of lesions were located at the peripheral zone, 26 (5.7%) were located at the central zone, 111 (24.4%) were located at the transitional zone and 2 were located at the anterior fibromuscular stroma (Table 2).

The overall PCa detection rate was 36.3%. Cancer detection rates of MRI-US FPBx alone and TRUS-Bx alone were 27.6% and 26.5% , respectively (Table 3).

The overall cancer detection rates of TRUS-Bx and MRI-US FPBx regarding PI-RADS 3, 4 and 5 lesions

were compared. The overall cancer detection rate of MRI-US FPBx was 27.6%, whereas 6.9% for PI-RADS 3 and 20.6% for PI-RADS 4&5 lesions (Table 4).

csPCa were evaluated and csPCa to overall PCa rates for TRUS-Bx, MRI-US FPBx and combined techniques were 16.8%, 35.4% and 39.2%, respectively (Table 5).

Table 1. Patient demographics and clinical characteristics

Median (IQR)	
Age (years)	60.5 (10)
PSA Level (ng/dL)	8.04 (4.44)
PSA Density (ng/dL/mL)	0.11 (0.09)
Prostate volume (mL)	60.6 (37)
DRE (n) %	
Normal	245 (68.4)
Suspicious	113 (31.6)
mpMRI PI-RADS scores (No.) %*	
PI-RADS 3	222 (62)
PI-RADS 4	107 (29.9)
PI-RADS 5	29 (8.1)
Median (IQR)	
Lesions per patient	2 (2)
TRUS-Bx per patient	12 (0)
MRI-US FPBx per lesion	4 (2)

**For patients with multiple lesions, the highest PI-RADS score is stated.*

***IQR:** Interquartile Range, **PSA:** Prostate Specific Antigen, **DRE:** Digital rectal examination, **mpMRI:** Multiparametric magnetic resonance imaging, **PI-RADS:** Prostate imaging reporting and data system*

Table 2. Zonal location of lesions according to the PI-RADS scores

	PI-RADS 3	***PI-RADS 4***	***PI-RADS 5***	***No.***
Peripheral Zone	*207*	*81*	*27*	315
Central Zone	*16*	*9*	*1*	26
Transitional Zone	*78*	*30*	*3*	111
Anterior Fybromuscular Stroma	*2*	-	-	2

***PI-RADS:** Prostate imaging reporting and data system*

Table 3: Pathology results of the patients

	No. (%)
Overall detected PCa	130 (36.3)
PCa patients detected by TRUS-Bx	95 (26.5)
PCa patients detected by MRI-US FPBx	99 (27.6)

***PCa:** Prostate cancer, **TRUS-Bx:** Transrectal ultrasonography–guided biopsy, **MRI-US FPBx:** Magnetic resonance imaging-ultrasound fusion prostate biopsy*

Table 4. The cancer detection rates of MRI-US FPBx and TRUS-Bx for specific PI-RADS groups

	TRUS-Bx	MRI-US FPBx	p value*
Overall Cancer Detection Rate (%)	95/358 (26.5)	99/358 (27.6)	0.001
PI-RADS 3 Cancer detection rate (%)	30/358 (8.3)	25/358 (6.9)	0.025
PI-RADS 4&5 Cancer detection rate (%)	65/358 (18.1)	74/358 (20.6)	0.001

PI-RADS: *Prostate imaging reporting and data system,* ***TRUS-Bx:*** *Transrectal ultrasonography–guided biopsy,*
MRI-US FPBx: *Magnetic resonance imaging-ultrasound fusion prostate biopsy *Statistical analyzed with Pearson Chi-Square test. Fisher's Exact test was used because two groups were not normally distributed. Although the ratios were close to each other, P value of 0.001 was considered normal.*

Table 5. Prostate cancer detection rates of transrectal biopsy, targeted fusion biopsy and combined of two techniques

	TRUS-Bx	MR-US FPBx	Combined Bx	p-value
Overall Prostate Cancer, No. (%)	95 (26.5)	99 (27.6)	130 (36.3)	0.099
Clinically significant PCa, No. (%)	16 (4.5)	35 (9.8)	51 (14.2)	0.003
csPCa/PCa, No. (%)	16/95 (16.8)	35/99 (35.4)	51/130 (39.2)	0.003
non-csPCa, No. (%)	79 (22)	64 (17.9)	89 (24.8)	0.003
Benign, No. (%)	16 (4.5)	7 (2)	11 (3.1)	0.099

PCa: *Prostate cancer,* ***csPCa:*** *Clinically significant PCa,* ***non-csPCa:*** *Non-clinically signficantPCa*

DISCUSSION

With advances in targeted biopsy technologies, MRI is increasingly playing a vital role in PCa diagnosis. Targeted biopsy detects more csPCa than systematic biopsy(12, 13). Recently, a systematic review showed that cancer detection rates using the traditional method ranges from 26.3% to 56.6% and this ranges from 33% to 79.5% with targeted biopsy(14). Ahmed et al. reported that mpMRI-targeted biopsy have greater sensitivity than TRUS - guided biopsy (87% vs 60%)(15). In addition, it is known that in case of targeted and systematic biopsies are combined, detection rates of PCa cases increase(12). Consistent with the literature, our study shows that the combination of MRI-US FPBx and TRUS-Bx provides the highest rate of overall PCa and csPCa detection.

European Association of Urology (EAU) guidelines strongly recommend the use of a combination of targeted and TRUS-guided biopsy in positive mpMRI cases(16). Fourcade et al. showed in a prospective study, targeted Bx combined with standard Bx, yielded a significantly higher PCa detection rate than systematic biopsy alone (45% vs. 33.5%, p = 0.02)(17). In a randomized controlled trial by Porpiglia et al. comparing the combination of TRUS-guided biopsy and mpMRI-targeted biopsy only through TRUS-guided biopsy in 212 biopsy-naive men, it was shown that the detection of PCa and csPCa was significantly higher in the combination group than the other group (50.5% vs. 29.5% ; 43.9% vs. 18.1%, respectively, p < 0.002)(18). Similarly, in our study, overall PCa and csPCa detection rates in combined group were higher than TRUS-Bx alone and MRI-US FBx alone (36.3% vs. 26.5% and 27.6% ; 14.2% vs. 4.5% and 9.8%; respectively).

MRI-US FPBx combines the real-time capabilities of TRUS with the superiority of mpMRI in lesion detection (19). Three approaches to perform MRI targeted biopsy are in use: visual registration (cognitive registration), software-assisted registration (fusion registration), and direct in - bore biopsy (13). Software - assistance enables shaping of the suspicious lesion and prostate gland in mpMRI. The purpose of software-assisted targeted biopsy is to overcome the limitations of the visually registrated strategy, to help operator easily identify the suspicious lesion detected in mpMRI on ultrasound images of the prostate and provide improved reproducibility (13). Software-assisted MRI-US FPBx has been shown to be superior to

standard TRUS-Bx and higher detection rates for csPCa (20). Pinto et al. reported that they were able to detect more PCa per core through software assisted MRI-US FPBx than standard biopsy (21% vs 12%) (21). In the study by Wysock et al., it was shown that software fusion biopsies detected more csPCa than cognitive fusion biopsies per-target (20.3% vs. 15.1%, P 5 .0523) (22). In another study, it was demonstrated that software-assisted targeted biopsy detected more csPCa than visually registrated-targeted biopsy (23). In our study, we performed software- assisted fusion biopsy, which is superior to other methods and the overall PCa rate detected by fusion biopsy was found to be significantly higher than detected by TRUS-Bx ($p < 0.001$).

PI-RADS score is the strongest predictor of csPCa detection and it is known that csPCa detection rate has a strong correlation with the PI-RADS score (24). In a prospective study by Murphy et al. involving biopsy-naïve 39 patients who underwent fusion biopsy, PI-RADS scores of detected lesions were found to be significantly higher than benign lesions (25). Sonmez et al. reported higher rates of PCa detection in patients with PI-RADS-4 or 5 lesions than those with PI-RADS-3 lesions (26). In our study, in accordance with the literature, it was observed that detected cancer rates in PIRADS-4 and 5 lesions were higher than PI-RADS-3 lesions. However, there was no significant difference between MRI-US FPBx and TRUS-Bx in terms of cancer detection rate in PI-RADS-3 lesions. This controversy may be the topic of another study.

Prior negative biopsy and ongoing PCa suspicion is still a challenging clinical situation for urology specialists. It is reported that cancer detection rates in patients with a prior negative biopsy can range 20–40% and is lower compared to biopsy-naive patients (27). Studies on this topic revealed that MRI-targeted biopsy is more successful in detection of cancer than systematic biopsy among men with prior negative biopsies (28). In the present study, there were patients with previous negative biopsy and biopsy-naive patients. We did not prefer to analysis datas of the two groups separately, since the number of patients with previous negative biopsy was lower.

One of the important topic concerning fusion biopsy is the ideal number of biopsy cores obtained. Kenigsberg et al. stated that although most of cancers detected through MRI-US FPBx were detected in the first 2 cores. They specified that there might also be a patient group that would benefit from more core sampling (29). Sonmez et al. reported that 2 or 3 cores could be efficient for PI-RADS 4 and 5 lesions, while at least 4 cores should be obtained from PI-RADS 3 lesions (30). In our study, the mean number of cores per lesion in MRI-US FPBx was 4 (3-5) and we believe that it is sufficient for the effectiveness of our biopsy results.

MRI-US FPBx can be performed under local anesthesia or under sedation anesthesia (7). In our center, we prefer sedo-anesthesia combined with local anesthesia application to the patients during biopsy in order to avoid errors that may rise due to patient movement.

Study Limitations

Our study has several limitations. First, our study has retrospective nature. Second, biopsy complications were not mentioned. Third, biopsy naive patients as well as patients who had previously undergone biopsy were included in our study.

CONCLUSION

According to our results, MRI-US FPBx significantly increases the success rate of both csPCa and overall PCa. However, MRI technology needs to be developed for better success rates. It would not be convenient to consider MRI-US FPBx as a stand-alone biopsy option without concomitant TRUS-Bx for now.

Acknowledgment

No acknowledgments to declare.

Conflict of Interest

All authors declared that there is no conflict of interest.

Financial Disclosure

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Ethical Approval

The study was approved by the Ethics Committee of Gazi University (Approval number: 91610558-604.01.02) (Date: 2019.07.26). The study protocol conformed to the ethical guidelines of the Helsinki Declaration.

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