e-ISSN: 2791-8815

Original Article

Evaluating Seminal Vesicle Invasion with Multiparametric Magnetic Resonance Imaging in Patients Diagnosed with Prostate Cancer: Is Radiologist Experience Effective?

Prostat Kanseri Tanılı Hastalarda Multiparametrik Manyetik Rezonans Görüntüleme ile Seminal Vezikül İnvazyonunu

Değerlendirme: Radyolog Deneyimi Etkili Mi?

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Abstract

Bacground: Predicting seminal vesicle invasion (SVI) in patients diagnosed with prostate cancer with multiparametric magnetic (mp) resonance imaging (MRI) provides more accurate local staging and thus more appropriate treatment management. Because mpMRI has a steep learning curve, radiologist experience is crucial. Our study aimed to show the difference that the experience of the uroradiologist would create in the detection rate of mpMRI and SVI by comparing it with radical prostatectomy tissue histopathology.

Materials and Methods: Patients with positive SVI in radical prostatectomy specimen were included in the study. The group of radiologists less experienced in genitourinary radiology was defined as Observer I, and experienced uroradiologists as Observer II (5 years and more than 2000 MR experience) and Observer III (4 years and more than 1000 MR experience). The groups were compared in terms of accurately predicting SVI positivity.

Results: Ninety (11.22%) patients were included in the study. All patients were positive for SVI, 80 patients (88.9%) had extraprostatic spread, 21 (23.3%) patients had lymph node (LN) invasion, and 20 (22.2%) patients did not undergo LN dissection. The rates of correctly predicting SVI positivity were 25.9%, 73.8%, 81% for Observer I, II, and III, respectively. The accuracy rate of Observer II and Observer III was significantly (p<0.05) higher than the Observer I group. The accuracy rate did not differ significantly (p>0.05) between Observer II and III groups.

Conclusion: The ability of mpMRI to detect local factors such as SVI is enhanced by the radiologist's experience, which has the potential to create significant differences in proper staging and treatment plans.

Keywords: Seminal vesicles, multiparametric magnetic resonance imaging, prostate neoplasms

Öz

Amaç:Prostat kanseri tanılı hastalarda multiparametrik (mp) manyetik rezonans görüntüleme (MRI)'yle seminal vezikül invazyonunu (SVI) öngörme, daha doğru lokal evrelemeyi, böylece daha uygun tedavi yönetimini belirlemeyi sağlamaktadır. mpMRI belirgin bir öğrenme eğrisi gösterdiğinden, radyolog deneyimi önem arz etmektedir. Çalışmamızda, üroradyoloğun deneyiminin mpMRI ile SVI saptama oranında yaratacağı farkı, radikal prostatektomi doku histopatolojisi ile karşılaştırarak göstermeyi hedefledik.

Gereç ve Yöntemler: Radikal prostatektomi spesmeninde SVI pozitifliği saptanan hastalar çalışmaya dahil edildi. Genitoüriner radyolojide daha deneyimsiz radyologlardan oluşan grup Gözlemci I olarak, deneyimli üroradyologlar ise Gözlemci II (5 yıl ve 2000'in üzerinde MR deneyimi) ve Gözlemci III (4 yıl ve 1000'in üzerinde MRI deneyimi) olarak tanımlandı. Gruplar, SVI pozitifliğini doğru tahmin etme açısından karşılaştırıldı.

Bulgular:Doksan (11,22%) hasta çalışmaya dahil edildi. Tüm hastalar SVI pozitif olup, 80 hasta (88,9%) ekstraprostatik yayılım, 21 (23.3%) hastada lenf nodu (LN) invazyonu mevcut olup, 20 (22.2%) hastaya LN diseksiyonu yapılmamıştır. SVI pozitifliğini doğru tahmin etme oranları sırasıyla Gözlemci I, II ve III için, 25.9%, 73.8%, 81%'dir. Gözlemci II ve Gözlemci III'ün doğruluk oranı Gözlemci I grubundan anlamlı (p < 0.05) olarak daha yüksektir. Gözlemci II ve Gözlemci III grupları arasında doğruluk oranı anlamlı (p > 0.05) farklılık göstermemiştir.

Sonuç: Radyoloğun deneyimi, mpMRI'ın SVI gibi lokal faktörleri tespit etme gücünü arttırmakta, bu durum doğru evreleme ve tedavi planında önemli farklar yaratma potansiyeli taşımaktadır.

Anahtar Kelimeler: Seminal veziküller, multiparametrik manyetik rezonsans görüntüleme, prostat neoplazileri

Introduction

The fundamental goal of prognosis and therapeutic management in prostate cancer (PCa) is to distinguish the localized disease from locally advanced disease. The extraprostatic extension (EPE) and seminal vesicle invasion (SVI) have a worse prognosis due to a higher risk of post-surgical biochemical recurrence (BCR), increased risk of lymph node metastases, and positive surgical margins (1). SVI is directly associated with local recurrence and distant metastasis (2). In these patients, 5-year BCR development rates range from 8% to 68%, with the effect of factors such as Gleason grade, Prostate-specific antigen (PSA) and positive surgical margin (3,4).

Predictive models such as the Kattan nomogram (5) and the Partin tables (6) are used to assess the pre-treatment risk of SVI. Moreover, patients are divided into risk groups based on Gleason grade, clinical T stage and PSA values. In addition to all of these, the widespread use of multiparametric (mp) Magnetic Resonance Imaging (MRI) and the advancement of its techniques have accelerated the process by providing advantages in the diagnostic evaluation of local staging of PCa (7).

When MRI was first employed in prostate cancer in the 1980s, it was limited to T1 and T2-weighted scans, with the primary goal of gaining insight into local staging in patients diagnosed with PCa via biopsy. However, with mpMRI technology, this measurement combined with diffusion-weighted imaging (DWI), diffusion coefficient (ADC) and dynamic contrast-enhanced imaging (DCI) sequences created the possibility of functional and physiological evaluation of the prostate. With the publication of Prostate Imaging and Reporting and Data System (PIRADS) Version 2 in 2014, the evaluation of prostate cancer with MRI has been standardized (8). The precision of MRI in detecting parameters such as SVI and EPE reflects its power in local staging.

The disadvantage of MRI regarding its consistency is due to the interobserver agreement. This problem may be due to the difference in experience among radiologists, as mpMRI shows a marked learning curve (9). Our study aimed to show the difference that the experience of the uroradiologist will create in the detection rate of mpMRI and SVI by comparing it with radical prostatectomy tissue histopathology.

Materials and Methods

Following the ethics committee approval (2020/234), the data of 806 patients who underwent radical prostatectomy for prostate cancer in Bakırköy Dr. Sadi Konuk Training and Research Hospital, Department of Urology, of from January 2017, when the routine use of mpMRI started in our centre, to December 2020, were retrospectively analyzed. The study was carried out in compliance with the Helsinki Declaration. Patients with unilateral or bilateral SVI in the postoperative pathology specimen (n=99, [12,34%]) were included in the study. Patients with a diagnosis of prostate cancer who received chemotherapy, radiotherapy or hormonal therapy before surgery, patients who did not have preoperative mpMRI and whose mpMRI was found in an external centre, patients who had visual deterioration and artefacts in their mpMRI due to lack of cooperation were excluded. Age, body mass index (BMI), PSA levels and prostate volumes (PV) measured by MRI were recorded. The reference standard for SVI was taken as the histopathological evaluation after radical prostatectomy. Histopathological examination was performed by two experienced uropathologists unaware with mpMRI interpretations. All specimens were graded according to the International Society of Urological Pathology (ISUP) grade system, and SVI was defined as cancer invasion into the extraprostatic portion of the seminal vesicles (10). Moreover, the presence of EPE, lymph node (LN) invasion, and surgical margin positivity were recorded. Prostate cancer staging was performed according to the 2017 TNM classification with MRI, ISUP grade, and PSA level (11). Patients were classified as low, intermediate, and high risk according to the European Association of Urology (EAU) 2021 Guideline (11). In the interpretation of the patients' MRIs, the observer assignments were random and no special settings were made according to the risk group. Radical prostatectomy procedures were performed using open retropubic, open perineal, laparoscopic, perineoscopic, robot-assisted transperitoneal laparoscopic radical prostatectomy (RARP) or robot-assisted perineal radical prostatectomy (r-PRP) methods. Surgical techniques have been previously mentioned in the literature (12).

MRI technique

The presence of claustrophobia, a pacemaker, or an estimated GFR of ≤ 30 mL/min/1.73 m2 were considered as contraindications for MRI. All mpMRI imaging was performed with a 3 Tesla MRI device (Magnetom Verio; Siemens,

Erlanger, Germany) with 16 channel phased array coils. T2 weighted turbo spin echo (TSE) sequence (Slice thickness, 3.5 mm with no intersection gap; TR, 5800 ms; TE, 100 ms; number of signals acquired, 2; resolution, 0.8 mm \times 0.8 mm) in 3 planes (axial/ sagittal/ coronal) were obtained. Diffusion-weighted images were acquired as spin echo planar images (Slice thickness, 3.5 mm with no intersection gap; TR 3900/TE 75 ms; number of signals acquired, 1; resolution, 1.4 mm \times 1.4 mm; b - factor, 50/ 500 /1000/ 1500 s/mm2). Apparent Diffusion Coefficient (ADC) mapping was performed from the b50, b500, b1000 and b1500 diffusion images using SyngoVia workstation software. T1-weighted high-resolution, fat saturated, isotropic volume imaging was used for dynamic perfusion imaging (Slice thickness, 3 mm; no intersection gap; TR, 5.08/TE 1.77 ms; number of signals acquired, 1; resolution, 1.4 mm \times 1.4 mm; contrast injection. The sequence started 24 seconds after initial acquisition; temporal resolution, 8 seconds; number of dynamic time points, 25; total DCE time, 200 seconds). DCE imaging was performed after intravenous injection of 0.1 mmol/kg gadoterate meglumine (Dotarem, Guerbet, Villepinte, France), followed by a 10-ml saline flush, at an injection rate of 3 ml/sec. Endorectal coil (ERC) was not used. SVI was reported as low signal intensity in the seminal vesicles on T2-weighted sequences or a prominent mass on diffusion-weighted and contrast-enhanced sequences confirming findings on T2, as described in PIRADS v2 (8).



Figure 1. Example of a true positive SVI MRI finding. 68-year-old man with high PSA level (14.8 ng/ml): on mp-MRI which is performed 2 months after positive prostate biopsy (Gleason score was 3+3 on three cores and 3+4 on one core). Axial T2WI (**Fig. 1a**) showing a homogeneous, hypointense mass in bilateral seminal vesicles. Axial DWI (**Fig. 1b**), ADC map (**Fig. 1c**) showing hyperintense signal on high b-value (b 1500) and markedly hypointense mass on ADC map. Sagittal T2WI (**Fig. 1d**) and coronal T2WI (**Fig. 1e**) MRI showing bulging of prostatic capsule, which is a sign of extraprostatic extension, and invasion to bilateral seminal vesicles. Histopathological analysis after radical prostatectomy confirmed bilateral seminal vesicle invasion and extraprostatic extension with Gleason score 4+4.

Both MRI acquisitions made before or after prostate biopsy were considered eligible for inclusion, as in both scenarios, staging information is provided. In patients who had previously undergone transrectal ultrasound-guided biopsy, hyperintense signal on pre-contrast T1-weighted sequences and hypointense areas on T2-weighted sequences were associated with bleeding in the seminal vesicles or prostate (Figure 1). Patients' PSA levels, clinical data, and, if a biopsy was performed before imaging, the histopathological data were all provided to the uroradiologists who conducted the evaluation. The uroradiologists were divided into groups based on their experience. The group of radiologists less experienced in genitourinary radiology was classified as Observer I. The radiologists in this group were those who worked in the field of general radiology and were not dedicated to uroradiology, had no experience with transrectal ultrasound and prostate biopsy, and had less than 500 prostate mpMRI

experience in total. Whereas experienced uroradiologists were defined as Observer II (5 years and more than 2000 MRI experience) and Observer III (4 years and over 1000 MRI experience). The groups were compared in terms of accurately predicting SVI positivity.

Categorical data were given as numbers and percentages. Means and standard deviations were calculated for continuous variables. The frequency of categorical variables was compared using Pearson chi-square, ANOVA and Post-hoc test. The p values of less than 0,05 were regarded as statistically significant. Statistical analysis was performed using Statistical Package of Social Sciences version 21 (IBM SPSS Statistics; IBM Corp., Armonk, NY).

Results

After applying the exclusion criteria, 90 (11.22%) patients with SVI positivity in radical prostatectomy pathology were included in the study. The mean age of the patients was 61.2 ± 6.7 (range: 49-75) years and the mean BMI as 26 ± 2.6 kg/m² (range: 20,5–31,9). Preoperative mean PSA level was 21.7 ± 24.2 ng/dl (range: 4,1-280). In the preoperative evaluation of the whole patient group, 9 (10%) patients are in the low-risk group, 48 (53.3%) patients are in the medium-risk group and 33 (36.7%) patients are in the high-risk group. In postoperative pathology, all patients were positive for SVI, 80 patients (88.9%) had EPE and 45 (50%) had positive surgical margins. There were 21 (23.3%) patients with LN invasion and 20 (22.2%) patients who did not undergo LN dissection. Preoperative demographic data, biopsy, and radical prostatectomy pathologies of the patients are presented in Table 1. The preoperative MRI findings are shown in Table 2. The prostate volume measured by MRI is 35.8 ± 16.8 cc (range: 17-140). In the entire group, 55 (61.1%) patients had a suspicion of SVI by MRI, compared to 41 (45.6%) for suspected EPE and 14 (15,6%) for LN metastasis. The number of patients reported for MRI by Observer I was 27 (30%), the number of Observer II was 42 (46.7%), and Observer III was 21 (23.3%).

The numbers and rates of radiologists reporting the presence of SVI in the MRI report are given in Table 3 and Figure 2. Observer I reported positive SVI in seven patients with a 25.9% accuracy rate, compared to 73.8% for Observer II and 81% for Observer III. The accuracy rate of Observer II and Observer III was significantly (p<0.0001) higher than the Observer I group. The accuracy rate did not differ significantly (p>0.05) between Observer II and III groups.

Table 1: Demographic data of patients	, preoperative and	l postoperative	pathology data
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Parameters		Mean ± SD (n; %)
Age		61.2 ± 6.7
BMI		26 ± 2.6
PSA		21.7 ± 24.2
	Low-risk	9 (10)
Preoperative Risk	Intermediate-risk	48 (53.3)
	High-risk	33 (36.7)
PSM	(-)	45 (50)
	(+)	45 (50)
EPE	(-)	10 (11.1)
	(+)	80 (89.9)
SVI	(-)	0 (0)
	(+)	90 (100)
T stage	3b	65 (72.2)
	4	25 (27.8)
	(-)	49 (54.5)
LNI	(+)	21 (23.3)
	Not dissected	20 (22.2)

BMI: Body mass index, *PSA*: Prostate-spesific antigen, *PSM*: Positive surgical margin, *EPE*: extraprostatic extension, *SVI*: seminal vesicle invasion, *LNI*:

Lymph node invasion

Table 2. MRI data and staging findings

Parameters		Mean ± SD (n; %)		
Prostate volume measured on MRI		35.8 ± 16.8		
SVI on MRI	(-)	35 (38.9)		
	(+)	55 (61.1)		
EPE on MRI	(-)	49 (54.4)		
	(+)	41 (45.6)		
LNI on MRI	(-)	76 (84.4)		
	(+)	14 (15.6)		
Observer I		27 (30)		
Observer II		42 (46.7)		
Observer III		21 (23.3)		

MRI: Magnetic resonance imaging, SVI: seminal vesicle invasion, EPE: extraprostatic extension, LNI: Lymph node invasion

Table 3. Rates of observers accurately predicting SVI with MRI	Table 3. R	ates of obso	ervers accura	ately predict	ting SVI with	n MRI
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		Observer I n(%)	Observer II n(%)	ObserverIII n(%)	Р
SVI on MRI	(-)	20 (74.1)	11(26.2)	4(19)	< 0.0001x2
					ObserverI<
					Observer2=
					Observer 3
	(+)	7(25.9)	31(73.8)	17(81)	

MRI: Magnetic resonance imaging, SVI: seminal vesicle invasion x2Chi-square test



Figure 2. Accuracy rates in predicting SVI on MRI among Observers

Discussion

In the case of PCa, staging is crucial in determining treatment options and minimizing risks such as under- or over-treatment. In the classical management of PCa, the decision is made by a combination of parameters such as the histological grade of the tumour obtained by biopsy, PSA level, and rectal examination. However, when using these methods to determine tumour aggressiveness, the risk of under-staging is common, and locally progressed disease can be undetected (13). Suspicion of EPE or SVI in terms of local staging also directly affects the definitive treatment decision, as it brings risks such as insufficient resection in radical prostatectomy and low dosage to seminal vesicles in brachytherapy (7). It will also determine the surgical technique or the dose, template, and adjuvant treatment decisions in radiotherapy, such as defining locally advanced disease, performing extended lymph node dissection, avoiding nerve-sparing surgery to avoid surgical margin positivity (9).

Current patterns in staging PCa are shifting as MRI becomes more widely used in clinical staging. The use of MRI guides definitive treatment and improves surgical, oncological, and functional management (14). In the literature, the sensitivity of

mpMRI in PCa ranges from 53% to 89%, and the specificity ranges from 71% to 90.3% (15,16). When it comes to detecting SVI, sensitivity ranging between 34.9-100% and specificity ranging from 86.1% to 99% have been reported (13, 17-21). A recent meta-analysis showed that even at low sensitivity rates (58%), MRI can detect SVI with high specificity (96%) (13). One factor contributing to the accuracy rates may be the high field strength acquisition of MRI using the 3T system. Ruprecht et al. reported 78% sensitivity and 92.8% specificity in their study using a 1.5 T MRI device (20). However, in the study of Sahin et al., SVI was detected with 85% sensitivity and 96% specificity. The authors attributed this difference to the use of the 3T device and the experience of the uroradiologist (21). In our study, due to its higher magnetic strength, we used a 3T MRI device in all patients, and we aimed to create a more homogeneous patient group by excluding all patients who used ERC.

Gupta et al., in their study comparing mpMRI with the Partin nomogram in organ confined PCa, found the area under the curve (AUC) values to be 0.82 and 0.62, respectively. However, predictive values for SVI were not specifically examined in this study (22). Morlocca et al., in their study in which they compared clinical prediction models such as Partin and CAPRA with mpMRI, discovered that while AUC values were 0.75 and 0.82 in the Partin and Partin + MRI models, respectively, these values were 0.75 and 0.83 in the CAPRA and CAPRA + MRI models (23).

According to guidelines jointly revised by EAU, The European Society for Radiotherapy and Oncology (ESTRO), and The International Society of Geriatric Oncology (SIOG), mpMRI can influence treatment decision by detecting SVI and be used in high-risk or locally advanced PCa (24). Furthermore, MRI also provides excellent soft-tissue separation and is the best approach for preoperative local T staging, according to EAU recommendations (11).

There are also studies stating that mpMRI is still doubtful in making the treatment decision and does not show significant superiority over the clinical parameters used in the Partin tables (9,13,25). More than half of the patients (55%) in Jansen et al.'s study could not be diagnosed with preoperative mpMRI despite being locally advanced (T3-4). Nearly half of these patients did not undergo lymph node dissection and the nerve-sparing surgery approach was chosen. This indicates the potential for undertreatment of false radiological evaluation (9). In our study, although there was locally advanced disease, the rate of patients who did not undergo lymph node dissection was found to be 22.2%. Of course, this low rate cannot be attributed to understaging alone because surgical variables and the operator's perioperative decision will also be influential in the lymph node dissection. However, more accurate preoperative staging offers the potential to prevent undertreatment by providing a more effective treatment plan. Again, in the study of Jansen et al., 24% of patients with organ confined PCa gave false positivity in MRI in local further evaluation. The authors concluded that using mpMRI in patients at increased risk of locally advanced disease did not result in a significant improvement in diagnostic accuracy (9).

A strong relationship between SVI and other preoperative clinical characteristics such as EPE has been demonstrated previously. Both conditions can be explained by similar pathological mechanisms that push the tumour to grow invasively (26). The mpMRI has been shown to have good diagnostic accuracy in EPE. Tay et al. showed that radiologists experienced in uroradiology were more likely to predict EPE with mpMRI than inexperienced radiologists, and they found the AUC value as 0.91 and 0.72, respectively (27).

In the study of Popita et al., the interobserver agreement in terms of SVI was examined, and a higher agreement was obtained among the radiologists in the evaluations where mpMRI was taken before the biopsy or without the use of ERC. The authors reported that changes such as post-biopsy haemorrhage may be the cause of this. The accuracy of SVI detection differed according to the use of ERC during mpMRI. While sensitivity and negative predictive value were higher in the group with ERC, higher accuracy rates were achieved with high specificity and positive predictive value in the group without ERC (18). According to a meta-analysis of 75 studies including 9,796 patients, 18 of which were prospective, the use of ERC provided no additional benefit for EPE detection, but slightly improved the sensitivity of SVI detection (13). These examples demonstrate the necessity of MRI technology as well as the radiologist's experience.

There are limited studies in the literature about the learning curve of mpMRI in local staging. A meta-analysis showed that the multiplicity of procedures included had no effect on diagnostic accuracy (13). In another recent study, it is reported that the sensitivity for the locally advanced disease does not improve over the years, despite increasing experience with mpMRI and the increasing number of procedures performed (9). The authors thought that the reason why the accuracy rate did not increase

at the same rate as expected as the number of procedures increased may be the decrease in the time spent by radiologists for evaluation. Given the marked increase in the number of scans, the time available per scan could have been built to possibly offset a potential learning effect. In the patient series of Grivas et al, 72% of the mpMRIs taken were interpreted by radiologists experienced in uroradiology, and higher sensitivity and specificity rates were obtained in the detection of SVI in this group (84.4%, 95.6%, respectively) (7). Ruprecht et al., in their study comparing a uroradiologist with 15 years of experience and an inexperienced radiologist in genitourinary radiology, found a significant difference in local staging efficiency with MRI in favour of an experienced radiologist (86.96% vs. 56.52%). As a result, the interobserver agreement detected a rather weak agreement (20). We also found in our study that the experience of the uroradiologist significantly increased the rate of accurate estimation of SVI with mpMRI. In our patient group with SVI histopathologically verified, the rate of true positive for experienced uroradiologists (Observer II and III) is almost three times higher than those without experience in genitourinary radiology (Observer I) (73.8%, 81% vs. 25.9%, respectively). Although Observer II is more experienced than Observer III, true positive rate was detected with lower accuracy. This may be because the Observer II's MRI reports are older, and the PIRADS scoring system has evolved and become more standardized since then. Of course, this situation can be considered as a limitation of the study. Another reason may be that the distribution of patients according to risk groups is random and not homogeneous. But it should also be noted that the difference between observer II and III is not statistically significant.

The most important limitation of our study is that since the patient group was only SVI positive patients, there was no control group and data such as sensitivity, specificity, false positive, true negative and predictive values could not be given. This situation prevented us from making sensitive and specificity comparisons with the literature. In addition, the radiologists' knowledge of patients' clinical data such as PSA and biopsy is another factor that may affect the results of the study. The fact that the patient distribution was made randomly to the radiologists and the available data were used retrospectively can be presented as another limitation. In addition, mpMRI technology still has limitations. SVI can also occur only microscopically, and low-volume invasion cannot be detected on MRI (7).

Conclusion

The diagnostic accuracy of mpMRI will increase as imaging technology, the PIRADS scoring system, and the experience of radiologists improve. The ability of mpMRI to detect local factors such as SVI is enhanced by the radiologist's experience, which has the potential to create significant differences in proper staging and treatment plans.

Acknowledgments: None

Ethical Approval: Bakırköy Dr. Sadi Konuk Training and Research Hospital 2020/234 Author Contributions: Concept: İE, DNÖ, RT Literature Review: ME,AH,YÇ Design : İE, ÖY, RT Data acquisition: DNÖ, SK, TK Analysis and interpretation: TK,HP,RT Writing manuscript: İE, DNÖ, ME, ÖY Critical revision of manuscript: ME, AH, SK, TK, HP Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: Authors declared no financial support

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