



ORIGINAL RESEARCH

EFFICACY OF MULTIPARAMETRIC MRI TO INCREASE DETECTION OF CLINICALLY SIGNIFICANT PROSTATE CANCER IN COMPARISON WITH TRUS

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ABSTRACT

Background: Although prostate cancer is a very common cancer in men around the world, its cause is still not well known with multi-factor playing role, on the other hand, screening for the disease is still a matter of debate till now and the controversy about the current diagnostic methods which lead to overdiagnosis and overtreatment with the accompanying side effects and complications which could occur with the prostate biopsy and the treatment for the disease and minimal role of imaging in the diagnosis of prostate cancer encouraged the acceptance of multiparametric MRI (mpMRI) as the suitable tool to detect clinically significant prostate cancer.

Objectives: To evaluate the efficacy of multiparametric MRI for the detection of clinically significant prostate cancer compared to transrectal ultrasound.

Material and Methods: A cross-sectional comparative study, thirty-seven patients fulfilled our criteria with high PSA(4-15ng/ml), abnormal digital rectal examination, and no previous prostate biopsy or prostatic surgeries were included in our study at Azadi teaching hospital and Vajeen private hospital at Duhok city from March 2020 to December 2021, in which all patients underwent mpMRI and TRUS after taking informed consent from all patients

Results: The mean age of our patients was 66.35 ± 7.57 (54-81 years), and the mean PSA was 6.8470 ± 1.73278 (4-10 ng/ml). Our study revealed a significant correlation for both mpMRI and TRUS, with p-value (<0.001) and (0.003) for detection of prostate cancer and clinically significant prostate cancer respectively by TRUS, while the p-value was (0.003) and (<0.001) for the detection of prostate cancer and clinically significant prostate cancer respectively by mpMRI. mpMRI showed sensitivity (75%) and (92.3%) for prostate cancer in general and clinically significant prostate cancer respectively and the specificity for mpMRI was (76.5%) and (70.8%) for prostate cancer and clinically significant prostate cancer respectively, while TRUS showed low sensitivity (30%) and (38.5%) and low specificity (11.8%) and (33.3%) for prostate cancer in general and clinically significant prostate cancer respectively. mpMRI revealed negative predictive value (NPV) (72.2%) and (94.4%) and positive predictive value (PPV) (78.9%) and (63.2%) for prostate cancer in general and clinically significant prostate cancer respectively. While TRUS revealed negative predictive value (NPV) (12.5%) and (50%) and positive predictive value (PPV) (28.6%) and (23.8%) for prostate cancer in general and clinically significant prostate cancer respectively.

Conclusion: Multiparametric MRI showed high sensitivity, specificity, NPV, and PPV compared to transrectal ultrasound in detecting clinically significant prostate cancer. Therefore, it can be used to avoid unnecessary prostate biopsies in the future.

Keywords: mpMRI, TRUS, prostate cancer, prostate biopsy.

1 INTRODUCTION

Efficacy of multiparametric MRI to increase detection of clinically significant prostate cancer in comparison with TRUS

1.1. Prostate cancer

Prostate cancer is the top diagnosed

malignancy in men all over the world, with a lifetime incidence of 1 in 9 for developing the disease, also it's the second on the list for cancer-related death in men¹.

Since the enrollment of prostate specific antigen (PSA) for the diagnosis of prostate cancer in the early 1990s, the incidence of the disease and the number of

diagnosed cases show a dramatic increase, in which most of them are detected in their early stages ². Despite this increasing number of newly diagnosed prostate cancer cases, only 3-4% of them die from the disease itself. This means most of the diagnosed cases will not cause morbidity or mortality to the patient if not diagnosed or treated ³.

Prostate cancer has a very wide range of variations from indolent to highly aggressive diseases. According to the wide range of variations and progression of prostate cancer mentioned earlier the diagnosis and treatment of the disease are still a challenge ³.

Knowing the complications and side effects that can occur from the treatment of prostate cancer, it is very wise to determine the exact tumor stage and aggression for best clinical management selection and to avoid unnecessary treatment for clinically insignificant disease ³.

Most tumors of the prostate are adenocarcinomas (95%), and the other types like sarcoma, urothelial carcinoma, squamous cell carcinoma, and neuroendocrine tumors are rare (5%) ⁴.

1.2. Etiology

Although the cause of prostate cancer is still not known, there are several known risk factors. However, the mechanism leading to the development of prostate cancer is still unclear ^{5,6}.

Non-modifiable factors include (age, family history, ethnicity, and genetic factors), while modifiable factors include (smoking, obesity, sedentary lifestyle, and poor quality of diet) ^{5,6}.

The findings of recent studies highlight the importance of gene mutations in prostate cancer ⁷. Prostate cancer risk rises considerably with age when compared to other malignancies ⁸.

Prostate cancer is multifocal and genetically heterogeneous, with foci forming in different parts of the gland independently. The specific molecular pathways that cause prostate cancer are yet unknown. Changes in the expression of growth factors such as transforming growth factor (TGF), vascular endothelial growth factor (VEGF), or insulin-like growth factors (IGFs), particularly IGF-1, have been linked to the development of this disease ^{9,10}.

The prostate is a highly sensitive organ hormonally which stimulates its biological processes. Furthermore, the pathogenesis of prostate cancer is influenced by steroid hormones (androgens and estrogens) as well as IGFs. Male steroid hormones play a role in the early development of prostate cancer in roughly 70% of cases ¹¹⁻¹³.

1.3. Screening

Since its introduction three decades ago, the PSA test has transformed the face of prostate cancer, causing a huge increase in incidence and assisting in

shifting the stage of disease at the time of diagnosis to a far earlier and potentially curable stage ^{14,15}. However, testing for prostate cancer and early detection remains a matter of debate and skepticism. PSA screening was implemented based on fact that high PSA levels were linked to occult prostate cancer ¹⁶.

Although some have linked the decrease in mortality to screening, this is not the case. While the benefits of prostate cancer screening are uncertain, the costs of early detection and treatment of prostate cancer are well understood ¹⁶.

In the absence of screening, it is believed that between 23 percent and 42 percent of malignancies found on screens would never have been diagnosed ¹⁷, this level of possible overdiagnosis and overtreatment of the disease appears to be higher than any other cancer for which routine screening is now performed. Furthermore, the side effects of prostate cancer treatment are substantial and sometimes life-threatening.

Depending on the type of treatment chosen, there is a high possibility of sexual, urinary, and bowel-related complaints. As a result, the wealth of evidence now available on early diagnosis of prostate cancer supports neither a strong mandate to screen nor a prohibition against screening ¹⁶.

1.4. Clinically significant prostate cancer

There are many definitions for the clinically significant disease but the most accepted and validated one is the presence of Gleason score equal to or greater than 4+3 and positive biopsy core bigger than 0.5ml on histopathology or presence of extra prostatic extension ¹⁸.

The most common and the second most common histological pattern was used to determine Gleason score ¹⁸.

1.5. Diagnosis

The currently approved diagnostic pathway for the prostate cancer is transrectal ultrasound and biopsy (the gold standard) either transrectally or from the perineum in suspected cases of prostate cancer from abnormal PSA and /or digital rectal examination ¹⁸, by adopting this pathway without further imaging many biopsies are done which could be avoided and many significant cases will be missed while diagnosing many diseases at a stage that do not require treatment. Overall, this pathway led to overdiagnosis and overtreatment ¹⁸⁻²⁰.

1.5.1 Transrectal ultrasound

In the 1980s TRUS was established ²¹. Current transducers use 5–10 MHz frequencies for scanning. The prostate is labeled into separate anatomical zones by TRUS ^{22,23}. In contrast to the center zone (CZ) as well as the transition zone (TZ), which is poor in echogenicity, the peripheral zone (PZ) is echogenic ²³.

In a healthy adult, most of the prostate volume is the peripheral zone (75%), while (20%) is the central zone and the transition zone occupy only (5%) of the prostate,

the size of all zones is not constant and vary with age and with development of BPH. On longitudinal scans, the ejaculatory ducts can be seen as echogenic tramlines within the central gland²³.

The seminal vesicles connect in the ampulla of the vas, which can be followed backward (23).

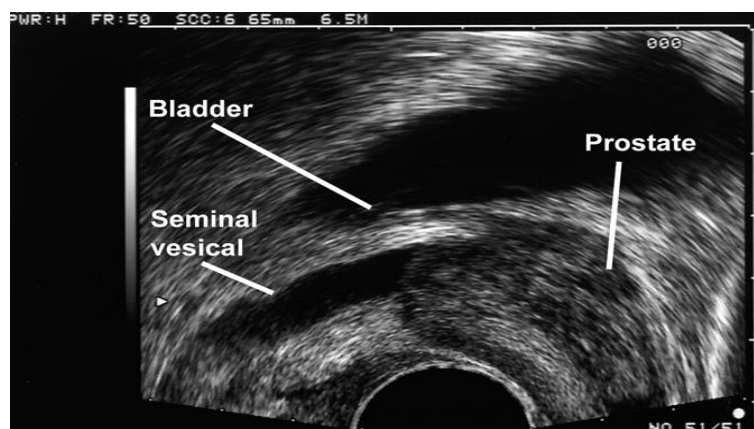


Figure 1. Transrectal ultrasound showing bladder, prostate, and seminal vesicles (24).

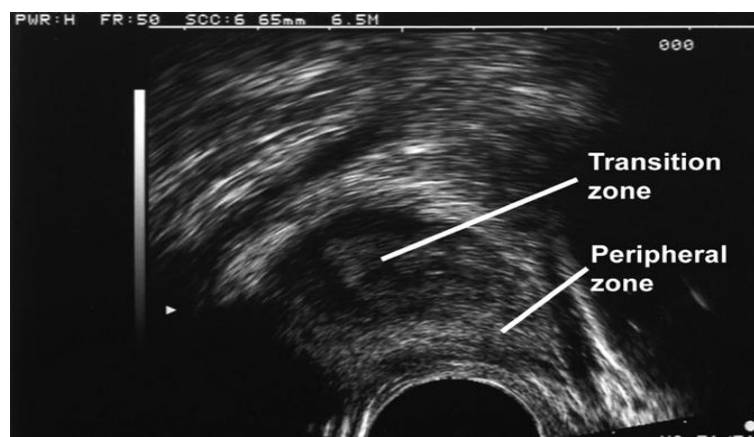


Figure 2. Transrectal ultrasound showing the transition and peripheral zone of the prostate (24).

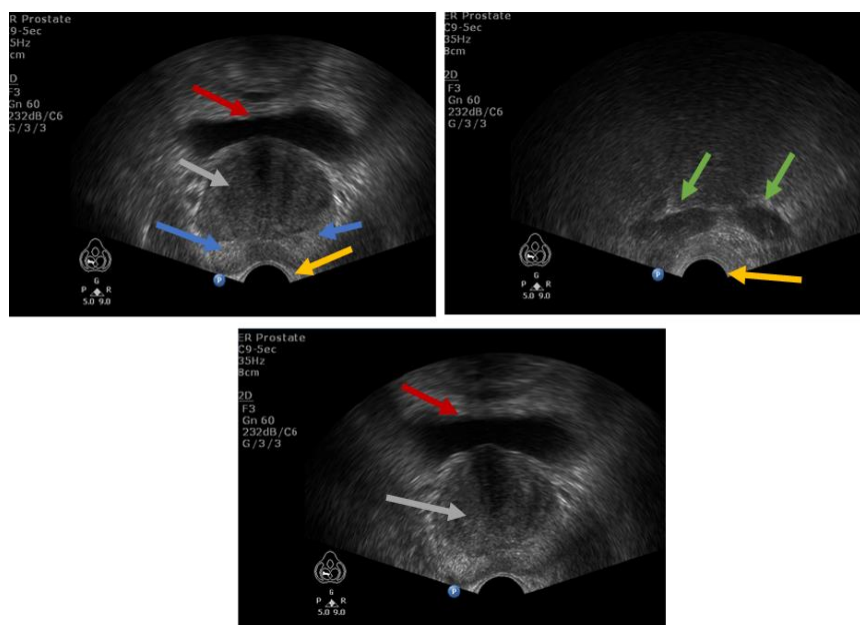


Figure 3. TRUS of prostate showing normal anatomy of the bladder (red arrows), transition zone (grey arrows), peripheral zone (blue arrows), seminal vesicles (green arrows), and rectum (yellow arrows)

1.5.2. Multiparametric MRI

Since the early 1980s, MRI was used for prostate imaging 25, but because of its poor-quality images and its inability to differentiate between the prostate and surrounding tissues, it was used for research only. Till the development of newer machines and improvements in the quality of imaging, it started to involve prostate imaging in clinical life ²⁶.

Multiparametric MRI Can be defined as images gained from T2-weighted (T2WI), dynamic contrast-enhanced (DCEI), and diffusion-weighted (DWI). To obtain a full and high-quality image from the prostate in many dimensions

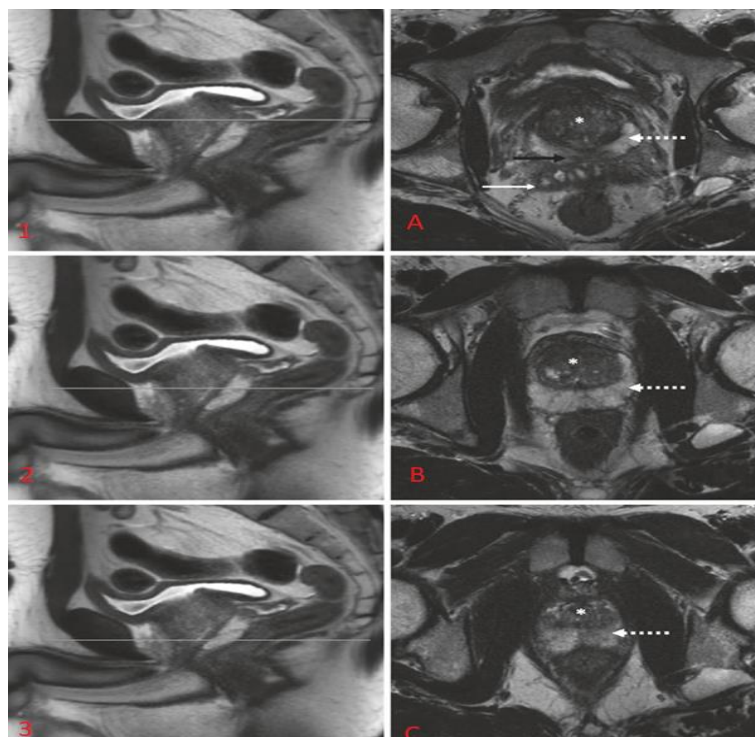


Figure 4. T2 weighted MRI at a different level of the prostate with sagittal sections (1,2,3) and axial sections (A, B, C) showing normal prostate anatomy, peripheral zone labeled by the white dotted arrow, and the transition zone labeled by (asterisk), while the (white arrow) shows seminal vesicles and the (black arrow) refer to the central zone (27).

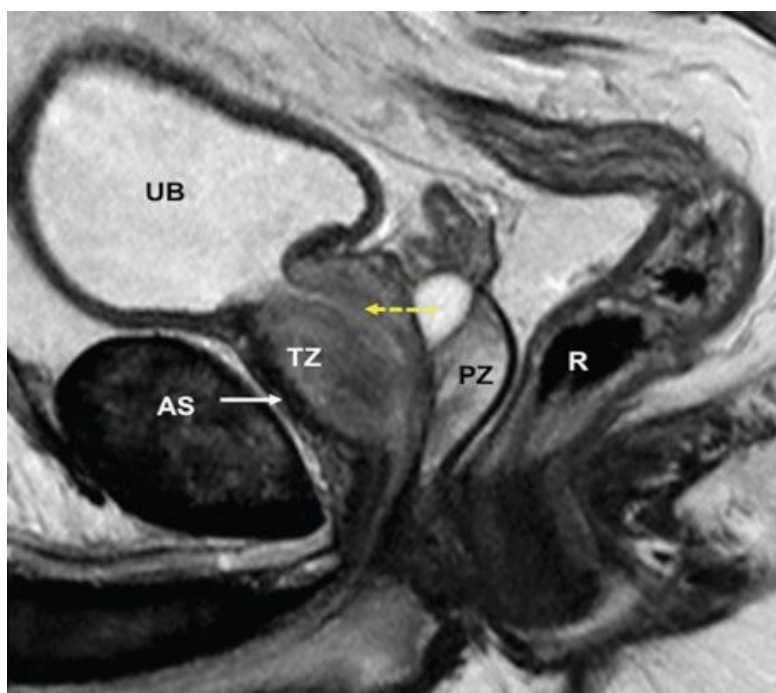


Figure 5. T2 weighted MRI film (sagittal section) showing the normal prostate anatomy and the surrounding structures, the (yellow dotted arrow) refers to the urethra, while (PZ) and (TZ) refer to the peripheral zone and transition zone respectively, (AS) is showing the anterior stroma while (R) and (UB) showing the rectum and urinary bladder respectively (27).

Prostate Imaging Reporting and Data System

High-resolution prostate imaging has been possible thanks to the introduction of mpMRI devices. However, there is no standard terminology for interpreting these data, which makes it difficult for clinicians to convert these non-standardized reports into therapeutic choices. The European Society of Uroradiology (ESUR) published the first version of PIRADS scoring at 2012, which aimed to provide a uniform system for interpreting MRI of prostate^{26,28}.

The images are taken in distinct sequences, the findings are obtained individually after first scoring, and the MRI score for the probable lesion is given a value of 1-5^{26,28}.

Table 1. Prostate Imaging Reporting and Data System assessment version 2

PIRADS	Meaning
1	Clinically significant cancer is highly unlikely to be present
2	Clinically significant cancer is unlikely to be present
3	The presence of clinically significant cancer is equivocal
4	Clinically significant cancer is likely to be present
5	Clinically significant cancer is highly likely to be present

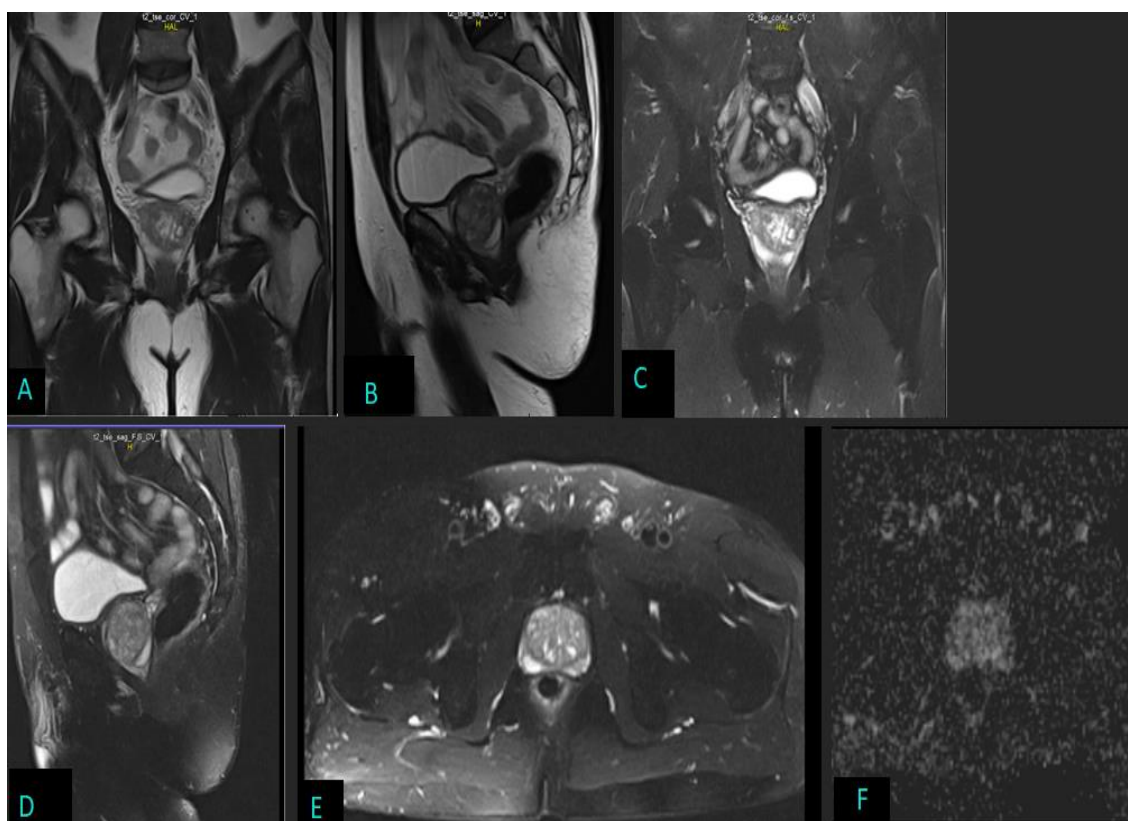


Figure 6. mpMRI showing coronal (a, c), axial (e,f) and sagittal (b,d) sections at prostate level with T2WI (A-D), DCEI (E), ADC map (F) showing BPH with PIRADS score 2 in 59 years old and a PSA of 5.39ng/ml

1.5.3. Prostate biopsy

The biopsy is still the gold standard for diagnosing prostate cancer. Abnormal digital rectal exam (DRE), elevated prostatic-specific antigen (PSA), and suspicion of prostate cancer clinically are the three common indications for biopsy²⁹.

Types of prostate biopsy

There are many types of prostate biopsy either the trans rectum or trans perineum either blind procedure or by imaging-guided biopsy. The transrectal ultrasound-guided prostate biopsy considered the procedure of choice with 12 core biopsies. But with the advancement of MRI and the availability of new ways to help in improving the accuracy of biopsy by the help of MRI many types of MRI-guided prostate biopsy have been developed for example (cognitive biopsy, Direct MRI-guided biopsy, and MRI–TRUS fusion biopsy)^{29,30}.

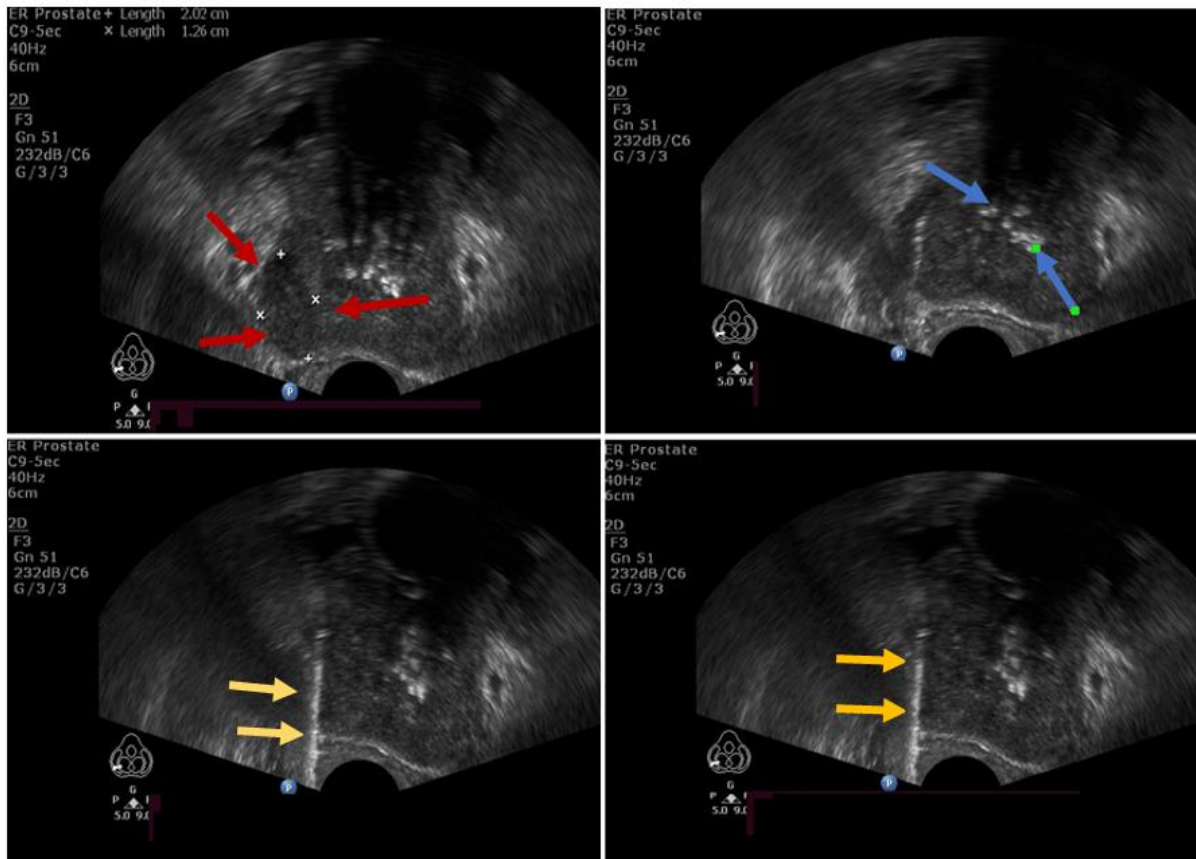


Figure 7. TRUS guided prostate biopsy to a suspected lesion (red arrows) on the right peripheral zone of the prostate showing the needle (yellow arrows) and the central zone calcification (blue arrows).

Complications of prostate biopsy

The biopsy is usually well-tolerated and has a low risk of major consequences. Minor complications such as discomfort and bleeding are common, and infectious complications have become more common over time. Bleeding, infection, discomfort, lower urinary tract symptoms (LUTS), urine retention, erectile dysfunction, and death are examples of biopsy complications³¹.

1.6. Aim of the study

In this study, we try to determine the ability of multiparametric MRI to detect clinically significant prostate cancer compared to TRUS.

Method and patients

2.1. Study design

A cross-sectional comparative study was done at Azadi teaching hospital and Vajeen private hospital at Duhok city from March 2020 till December 2021, with a total of 37 patients being studied for the detection of prostate cancer using mpMRI, TRUS, and prostatic biopsy.

2.1.1. Inclusion criteria:

- 1- Age > 18 years.
- 2- PSA 4-15 ng/ml.
- 3- Abnormal digital rectal examination (DRE).

2.1.2. Exclusion criteria:

- 1- Previous prostate biopsy.
- 2- Suspected advanced prostate cancer and /or metastasis.
- 3- Previous prostatic surgery.
- 4- Patients on finasteride.

2.2. Patients

All the patients who were suspected to have prostate cancer and included in the study underwent transrectal ultrasound (standard test), multiparametric MRI (index test), and prostate biopsy (reference test).

If there was suspicion of cancer on TRUS and mpMRI. After taking informed consent from all patients explaining the benefits, risks, and complications of each procedure done for them. Patients underwent TRUS by experienced radiologists, then they performed mpMRI which has been reviewed by experienced radiologists using PIRADS assessment version 2.

Prostate biopsies were done under local anesthesia with 12-core biopsies under TRUS-guided.

Results

3.1. Statistical analysis:

The descriptive purposes of the study were displayed in frequency and percentage for categorical and mean and standard deviation for continuous characteristics of the patients.

In this study, we calculate the specificity, sensitivity, negative predictive value (NPV), and positive predictive value (PPV) for both mpMRI and TRUS.

The P-value of less than 0.05 was regarded as significant, and SPSS 26 was used for statistical analysis.

3.2. Results

Thirty-seven patients fulfilled our criteria and were included in our study.

The mean age of our patients was 66.35 ± 7.57 (54-81), and the mean PSA was 6.8470 ± 1.73278 (4-10).

Table 2. comparison between age and PSA

Category	Mean	Standard deviation	Range
Age	66.35	7.573	54-81
PSA	6.8470	1.73278	4-10

Twenty-one patients (56.8%) were suspected to have prostate cancer on TRUS, while 16 patients had negative TRUS (43.2%).

Nineteen patients (51.4%) had suspected prostate cancer on MRI, and 18 patients (48.6%) had negative MRI.

Table 3. Frequency and percentage of Prostate cancer, TRUS, and MRI

Category	Subcategories	Frequency	Percentage
Prostate cancer	Positive	20	54.1
	Negative	17	45.9
TRUS	Suspected	21	56.8
	Negative	16	43.2
MRI	Suspected	19	51.4
	Negative	18	48.6

In contrast, 13 (35.14%) and 7 (18.92%) had clinically significant and nonsignificant prostate cancer respectively, on the other hand, 17 (45.95%) had no prostate cancer on biopsy.

Table 4. comparison of prostate cancer concerning frequency and percentage

Prostate cancer		
	Frequency	Percentage
No prostate cancer	17	45.9
Clinically significant prostate cancer	13	35.1
Clinically non-significant prostate cancer	7	18.9
Total	37	100

From 20 patients that proven to have prostate cancer 6 patients had suspected lesions on TRUS, while 14 of them had negative TRUS, in contrast, 15 had suspected lesions on mpMRI and 5 had negative mpMRI.

From 17 patients who had no prostate cancer 15 of them had suspected lesion on TRUS and 2 of them had negative TRUS, in contrast, 4 of them had suspected lesion on mpMRI and 13 had negative mpMRI.

The study showed significant relation for both mpMRI and TRUS for the detection of prostate cancer with a p-value of (<0.001) and (0.003) for detection of prostate cancer and clinically significant prostate cancer respectively by TRUS, while the p-value was (0.003) and (<0.001) for the detection of prostate cancer and clinically significant prostate cancer respectively by mpMRI.

Table 5. Comparison between MRI and TRUS according to Pearson Chi-square test concerning the presence of prostate cancer

Category	Sub categories	Prostate cancer	No prostate cancer	P value
MRI	Negative Suspected	5(25%) 15(75%)	13(76.5%) 4(23.5%)	0.003*
TRUS	Negative Suspected	14(70%) 6(30%)	2(11.8%) 15(88.2%)	0.000*
* Pearson Chi-square test.				

Table 6. Comparison between MRI and TRUS according to Pearson Chi-square test concerning clinically significant and non-significant prostate cancer

Category	Subcategories	Prostate cancer		P-value
		Clinically non-significant prostate cancer	Clinically significant prostate cancer	
MRI	Negative Suspected	17(70.8%) 7(29.2%)	1(7.7%) 12(92.3%)	0.000*
TRUS	Negative Suspected	8(33.3%) 16(66.7%)	8(61.5%) 5(38.5%)	0.003*
* Pearson Chi-square test.				

In our study, the sensitivity of MRI was 75% and 92.3% for prostate cancer in general and clinically significant prostate cancer respectively, while the sensitivity of TRUS was 30% and 38.5% for prostate cancer in general and for the clinically significant prostate cancer respectively.

The specificity of MRI was 76.5% and 70.8% for prostate cancer and for clinically significant prostate cancer respectively, in the meanwhile, the specificity of TRUS was 11.8% and 33.3% for prostate cancer and clinically significant prostate cancer respectively.

The negative predictive value (NPV) for MRI was 72.2% and 94.4% for prostate cancer in general and clinically significant prostate cancer respectively, in the meanwhile, the NPV for TRUS was 12.5% and 50% for prostate cancer and clinically significant prostate cancer respectively.

The positive predictive value (PPV) of MRI was 78.9% for prostate cancer and 63.2% for clinically significant prostate cancer, in the meanwhile, the PPV was low for the TRUS 28.6% and 23.8% for prostate cancer and clinically significant prostate cancer respectively.

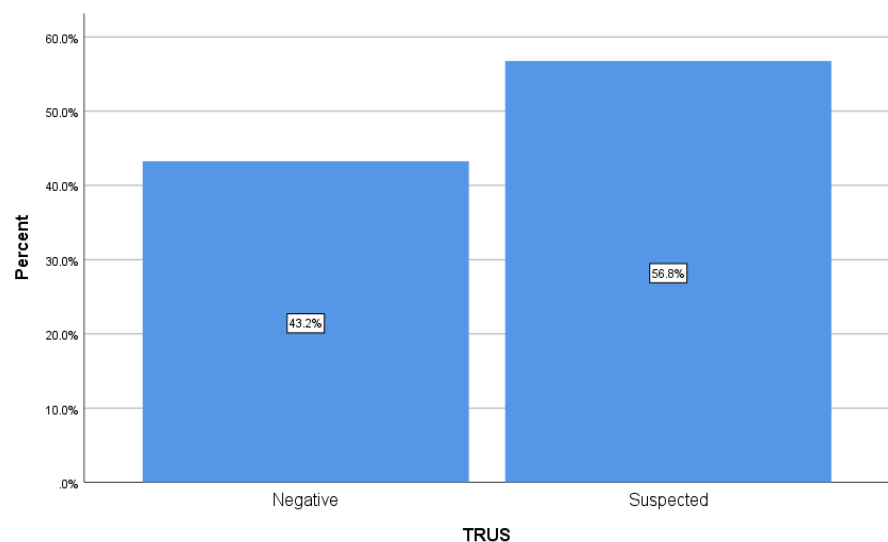


Figure 8. Bar chart of TRUS percentages

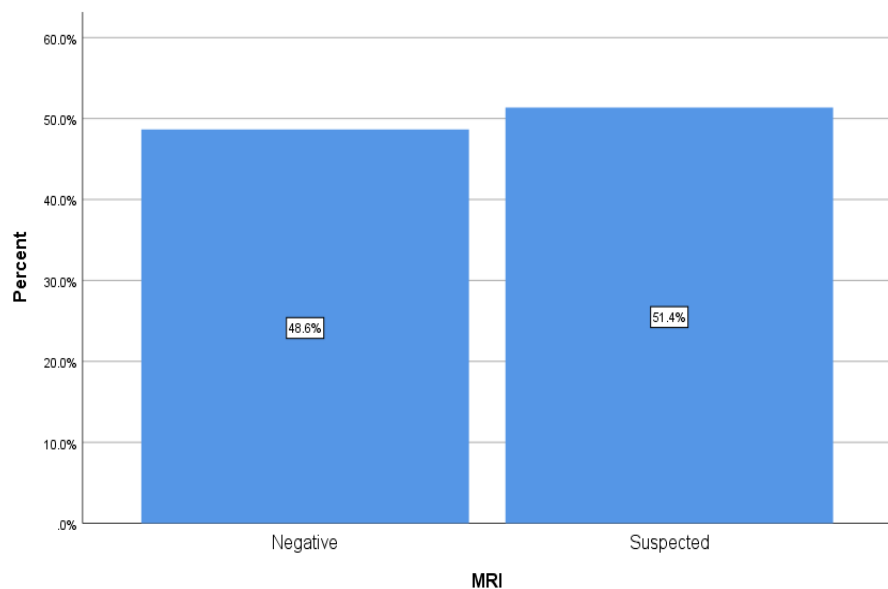


Figure 9. Bar chart of MRI percentages

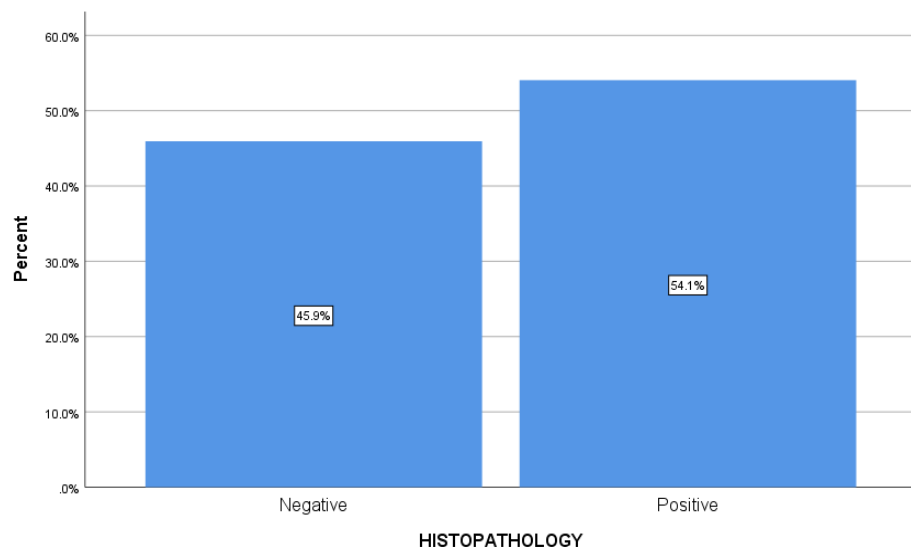


Figure 10. Bar chart of prostate cancer percentages

4.1 DISCUSSION

Prostate cancer is the most common cancer in men¹, its etiology is multifactorial and not clear^{5,6}, with the controversy whether to screen for the disease or not and the issues concerning the overdiagnosis and overtreatment(16). The treatment should be offered to those in danger of having an increased rate of morbidity and mortality with clinically significant prostate cancer³.

With the progression in the science development and MRI machines and the need for an imaging method to be able to detect prostate cancer and especially CS prostate cancer, this led to thinking about adding mpMRI in research studies to increase the detection of clinically significant prostate cancer²⁶.

The result of our study was relatively similar to (Ahmad *et al*,2017) regarding the sensitivity and negative predictive value of mpMRI for clinically significant cancer which shows 93% sensitivity and a negative predictive value of 89%. While our result showed higher specificity and negative predictive value, the specificity of mpMRI was 41% with a positive predictive value of 51% according to (Ahmad *et al*,2017)¹⁸.

(Pesapane *et al*,2021) reported 84% sensitivity and 76.5% specificity for mpMRI for any grade of prostate cancer, while considering high grade Prostate cancer only 83% sensitivity and 76% specificity was reported for mpMRI³².

Our study reported an overall sensitivity of 84.7% and specificity of 54.6% for the detection of all prostate cancer. Corresponding PPV and NPV were 82.3% and 58.8%, respectively. (Tsai *et al*,2020)³³.

Our results showed similar results to a study done by (Lopes *et al*, 2015) that reported low sensitivity (31%) to detect prostate cancer by TRUS, also reported low negative predictive value for TRUS³⁴.

CONCLUSION AND RECOMMENDATION

5.1. Conclusion

There is minimal role of imaging in prostate cancer diagnosis and there is well-known overdiagnosis and overtreatment in the diagnosis of prostate cancer, our study reveals that mpMRI has high sensitivity, specificity, NPV, and PPV especially for clinically significant prostate cancer, so mpMRI is a better tool for the detection of prostate cancer than TRUS and it can be used to avoid unnecessary biopsies.

5.2. Recommendation

We recommend adding MRI in the diagnosis of prostate cancer to overcome the issues of overdiagnosis and overtreatment.

5.3. Limitation of the study

Due to the limitation of the time, the size of the sample was small and based on a single center.

DECLARATIONS

Competing interest

The authors declare that there are no competing interest.

Funding

The work was not funded.

Ethical Approval

“Not applicable”

Consent for publication

“Not applicable” No funding was received from any financially supporting body

Competing interests

The authors declare no competing interests.

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