ORIGINAL RESEARCH

Concordance of Multiparameteric MRI and MRI Ultrasound Fusion-guided Prostate Biopsy

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Multiparametric MRI (mpMRI) of the prostate is recently becoming more and more utilized in the detection of prostate cancer. Studies have shown that a higher PIRADS score correlated to a higher chance of obtaining a clinically significant prostate cancer but few studies have correlated PIRADS score to a specific Gleason score.

Objective: This study aimed to determine the concordance of PIRADS score to the Gleason score result of MRI ultrasound fusion-guided prostate biopsy.

Methods: All patients who had at least a PIRADS 2 lesion on mpMRI and underwent MRI ultrasound fusion-guided biopsy of the prostate from August 2018 up to November 2019 at St. Luke's Medical Center, Global City were included in the study. An ambispective collection of data was done until the ideal sample size of greater than 100 positive lesions was obtained, in order to derive concordance rate.

Results: One hundred and sixty-two patients were included in the study with a total of 212 lesions analyzed. Forty three percent were benign while 57% were found to be malignant. PIRADS 2 lesions had zero high grade cancers, and the percentage steadily increased with 37.8% of PIRADS lesions considered high grade. Concordance was computed to be 0.38 showing a fair, direct concordance between PIRADS and Gleason score with significant result ($p<0.05$).

Conclusion: A result of PIRADS 4 or 5 lesion on mpMRI will have a higher urgency of doing a prostate biopsy and subsequent management to prevent unfavorable outcomes as opposed to PIRADS 3 lesions.

Key words: Multiparametric MRI, fusion biopsy, prostate biopsy

Introduction

Prostate cancer is the second most common cancer in males worldwide.[1] In patients with elevated PSA or a rectal examination suspicious for malignancy, a biopsy of the prostate is recommended. In recent years, this practice has been influenced by the emergence of multiparametric magnetic resonance imaging (mpMRI) of the prostate. This technique is being used to improve cancer detection rates as suspected lesions can be better identified and localized.[2] Several studies have already shown that mpMRI is a reliable method for detecting clinically significant prostate cancer.[3-5]

One of the first reports of detecting prostate cancer using MRI was in 1983 as reported by Hricak, et al. The authors described the prostate cancer lesion to have a higher intensity signal than the surrounding gland. Radiologists have developed the Prostate Imaging-Reporting and Data System (PIRADS) score

as a reporting scheme for the evaluation of suspected prostate cancer.[3] Lesions on prostate mpMRI were scored from PIRADS 1-5 followed by focused lesion biopsy. The results showed that a higher score on mpMRI corresponded with a higher chance of obtaining a positive prostate cancer result. In addition to this, higher PIRADS score was associated with a greater likelihood of obtaining a Gleason 7 or greater result.[6] Cash, et al. conducted a similar study which correlated the PIRADS score with MRI ultrasound fusion biopsy result.[7] Their results were consistent with other reports where PIRADS 2 had the lowest cancer detection rate and PIRADS 5 had the highest cancer detection rate. PIRADS 2 and 3 lesions were more commonly biopsied with a Gleason 6 prostate cancer whereas PIRADS 5 lesions appeared to be more commonly biopsied as Gleason 8 and above. A review of literature by Futterer, et al. concluded that mpMRI can detect clinically significant prostate cancer with rates ranging from 44% to 87% and a high negative predictive value which may eliminate the role of biopsy in patients with negative MRI results.[5] In the PROMIS trial, they concluded that up to 27% of men may avoid prostate biopsy and 5% fewer clinically insignificant cancers are detected.[8]

The PIRADS score has been used to detect prostate cancer but only a few studies have correlated PIRADS score to a specific Gleason score. This study focuses on the PIRADS score on mpMRI and its concordance with the MRI ultrasound fusion biopsy Gleason score.

Methods

This study includes all patients who underwent MRI ultrasound fusion biopsy of the prostate from August 2018 up to November 2019 at St. Luke's Medical Center, Global City. All patients had at least a PIRADS 2 lesion detected on mpMRI analyzed by a single MRI consultant reader. An ambispective collection of data was done until the ideal sample size of greater than 100 positive lesions was obtained, in order to derive concordance rate.

MRI/ Ultrasound Fusion Guided Prostate Biopsy

All mpMRI results were contoured by a single radiologist. MRI ultrasound fusion guided biopsy was facilitated using the Koelis Trinity Prostate Biopsy System. Targeted biopsy of the suspected lesions was done as well as random sampling on the rest of the prostate gland. Each lesion was labeled properly and sent for histopathology, and analyzed by a single pathologist. Once the pathology report came out, each lesion was paired with its respective reading. Non-prostate adenocarcinoma lesions were excluded from this study. When the target sample size had been reached, concordance between the PIRADS score and Gleason score was then calculated.

Results

A total of 162 patients were included in the study with a mean age of 66.8 years (SD 8.73). Average PSA was 14.1ng/dL (SD 22.81) while mean prostate size was 53.8grams (SD 29.79). Two hundred and twelve (212) lesions were included and analyzed accordingly (Table 1).

Out of the 212 lesions sampled, 43% were classified as benign prostatic tissues. Fifty seven percent or 120 lesions were positive for prostate adenocarcinoma (Table 2).

The 120 positive lesions were then correlated to their respective histopathology results and tabulated below. None of the lesions biopsied showed a Gleason 10 histopathology (Table 3).

Statistical analysis was done using Kendall tau due to the data being ordinal and not normally distributed. Kendall's tau-b was computed to be 0.38 showing a fair, direct concordance between PIRADS and Gleason score with significant result ($p<0.05$). Generally, concordance values can be separated into ranges of 0.8 – 1, 0.6 – 0.8, 0.4 – 0.6, 0.2 – 0.4 and 0 – 0.2 which mean a strong, good, moderate, fair and insignificant relationship, respectively.

Of the 162 patients that were biopsied, random sampling of the rest of the prostate was done which showed 30 patients (18.5%) had an incidental finding of prostate adenocarcinoma, apart from the lesions identified on mpMRI. Breakdown per Gleason score is shown in Table 4.

Two patients had a benign targeted biopsy but had prostate cancer Gleason 6 on random sampling. Six had a higher Gleason score on random sampling compared to the lesion directed biopsy. Of these, three had a Gleason grade 2 levels higher than the

Table 1. Patient demographics

Patient Demographics	Mean	Range	Standard Deviation
Age	66.8	44-95	8.73
PSA	14.1	0.37-186.82	22.81
Prostate size	53.8	15-166	28.79
Lesions per prostate	1.31	1-3	0.53

Table 2. Stratification of PIRADS lesions with biopsy outcomes

PIRADS	Benign	Malignant	Total
2	8 (72.7%)	3 (27.3%)	11
3	53 (57.6%)	39 (42.4%)	92
4	25 (34.7%)	47 (65.3%)	72
5	6 (16.2%)	31 (83.8%)	37

Table 3. PIRADS lesion with corresponding Gleason score result

PIRADS * Histopath Cross-tabulation									
	Histopath								
	Benign	Gleason 6 (3+3)	Gleason 7 (3+4)	Gleason 7 (4+3)	Gleason 8	Gleason 9	Gleason 10	Total	Average Gleason score per PIRADS
PIRADS SCORE	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
2	8 (72.7)	3 (27.3)	0	0	0	0	0	11 (100)	6.00
3	53 (57.6)	26 (28.3)	8 (8.7)	2 (2.2)	1 (1.1)	2 (2.2)	0	92 (100)	6.46
4	25 (34.7)	14 (19.4)	13 (18.1)	7 (9.7)	10 (13.9)	3 (4.2)	0	72 (100)	7.04
5	6 (16.2)	8 (21.6)	6 (16.2)	3 (8.1)	9 (24.3)	5 (13.5)	0	37 (100)	7.35
Total	92 (43.4)	51 (24.1)	27 (12.7)	12 (5.7)	20 (9.4)	10 (4.7)	0	212 (100)	

Table 4. Gleason score of incidental findings on random biopsy samples

	n	%
Gleason 6	18	11.1
Gleason 7 (3+4)	4	2.4
Gleason 7 (4+3)	2	1.2
Gleason 8	3	1.9
Gleason 9	3	1.9
Gleason 10	0	0
Total	30	18.5

identified lesion while the rest had a 1 level higher Gleason score.

Discussion

Prostate biopsy is the gold standard in diagnosing prostate cancer.[9] Before prostate biopsy is done, evaluation of the risk of the patient for prostate cancer is done through history, physical exam and PSA determination. In recent years, multiparametric

MRI has been used as an adjunct in determining whether a prostate biopsy is indicated. It has been postulated that a higher PIRADS score on mpMRI corresponds to a higher chance of prostate cancer.[6,7] Similar results were obtained in the present study where PIRADS 2 lesion resulted in a 27.3% cancer detection rate and this percentage steadily increased up to 83.8% for PIRADS 5 lesions (Table 2). These percentages have also been computed to be the positive predictive value per PIRADS score. Comparing these results to other studies, the overall cancer detection rate of the PIRADS 2, 3, 4 and 5 lesions were 0-22%, 10-33%, 30-77% and 78-95% respectively.[7,10-12] Cancer detection rate was better in PIRADS 2 and 3 lesions in this study, while PIRADS 4 and 5 lesions were comparable to other studies.

As for the relationship of PIRADS score to Gleason score, it was determined that with a higher PIRADS score, the Gleason score also tended to be higher (Table 3).

There were zero high grade cancers (Gleason 8 and 9) on PIRADS 2 lesions while 37.8% of PIRADS 5 lesions were considered high grade. On statistical analysis, this was found to have a fair concordance (0.38) with statistically significant result ($p<0.05$). This is consistent with a positive correlation between the two categories.

Other studies had similar results with PIRADS 1-2 lesions having 0-6% clinically significant prostate adenocarcinoma (Gleason 7 and above); PIRADS 3 lesions 11.5 to 42% (0.7-14% high grade), PIRADS 4 lesions 48.2-56% (10.8-17% high grade) and PIRADS 5 lesions 72.2-86% (23-49% high grade).[7,13] Another study determined the concordance between PIRADS and Gleason score and was determined to be 0.33.[12]

Van den Bergh, et al. [2013] reviewed several studies on the timing of treatment for localized prostate cancer.[14] It concluded that men with low-risk prostate cancer may have a treatment delay of several months to years with no compromise in the long-term oncological effects. This explains the option of active surveillance where very low and low risk patients can be monitored until there is evidence of disease progression. For patients with intermediate to high-risk disease, mixed results were obtained but a delay of 2.5 to 9 months may lead to unfavorable outcomes. Berg, et al. had a similar conclusion with intermediate risk cancers having adverse pathological outcomes with a delay more than 60 days and high-risk cancers delayed more than 30 days.[15] Low risk cancers on the other hand also resulted in a worse pathological outcome at 150 days delay of treatment with radical prostatectomy. Abern, et al. noted that low-risk men who underwent radical prostatectomy did not significantly affect their outcome.[16] For intermediate risk men with treatment delayed more than 9 months had greater biochemical recurrence and positive surgical margins. The latest EAU guidelines on Covid 19 have also recommended to start treatment on intermediate to high-risk patients no later than 3 months from diagnosis.[17]

The clinical significance of the result of this study will be on the urgency of performing the biopsy and subsequent management if the result will indeed be positive for malignancy. PIRADS 3 and higher lesions should still be biopsied according to the recommendations for Prostate Cancer Diagnosis and Management in the European Association of Urology 2020 guidelines. These lesions have a greater than 42% risk of being malignant. Having a patient with mpMRI result of PIRADS 4 or 5 will have a higher urgency as opposed to a patient with PIRADS 3 lesion. Biopsy and definitive management for localized disease may prevent unfavorable outcomes if done within 3 months, preferably within 1-2 months.[15] PIRADS 3 lesions may need to be biopsied within 6 months as most of the lesions are benign or low risk, but there is still a 14.2% chance of obtaining a clinically significant prostate cancer result. This information may be useful in clinical decision making as to whether or not one should proceed with urgent biopsy especially in the light of the COVID-19 pandemic.

The result also supports the use of mpMRI in active surveillance. A repeat mpMRI with PIRADS 3 or lower with relatively stable PSA suggests that the patient is not progressing and may decrease the need for repeat prostate biopsies. This is opposed to mpMRI results of PIRADS 4 or 5 which may need to be re-biopsied so that treatment may be delivered in a timely manner.

An incidental finding of 18.5% prostate adenocarcinoma was detected on random sampling of the prostate. As seen in other studies, targeted biopsy of the lesion together with systematic random biopsy is recommended.[18,19] A random sampling of the rest of the prostate is still needed as there may be significant cancer lesions that are not detected on

mpMRI. The significance of these tumors missed on mpMRI are not yet characterized and future studies may need to be done to properly identify these lesions.[20] These may be especially important for lesions that are at least 2 grades higher the identified primary lesion.

Conclusion

A fair concordance between PIRADS score and Gleason score means that mpMRI may be used as a tool to predict the aggressiveness of prostate adenocarcinoma. A PIRADS score of 4 or 5 would necessitate doing biopsy and subsequent management promptly to avoid unfavorable outcomes. PIRADS 3 lesions would still need to be biopsied although not as urgent as the higher PIRADS scores.

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