ORIGINAL RESEARCH

Prevalence of Prostate Cancer Following an Initial Negative MRI-Fusion Biopsy of the Prostate from 2018-2022: A Single-Center Retrospective Descriptive Cohort

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Objectives: To determine the incidence of prostate cancer on follow up after an initial negative MRI-fusion biopsy of the prostate, and to determine the change in PSA and MRI results on follow-up.
Methods: MRI-fusion prostate biopsy registry from 2018 to 2022 was obtained then histopathology, MRI results, and PSA results were obtained. Repeat PSA and MRI results at extracted at <1 year, 1-2 years, 2-3 years, and >3 years. PSA mean, range, and change were then determined. MRI results were extracted to determine progression, regression, or persistence.
Results: A total of 670 prostate biopsies were done in the study period, of which 70 were included. PSA on biopsy 9.93 (3.35 – 55.0) with corresponding PIRADS lesions 3, 4, and 5 (n=55, n=19, and n=6). No patient was subsequently diagnosed with prostate cancer on follow-up. PSA mean 7.03, 6.44, 5.27, and 6.07 at <1year, 1-2years, 2-3years, and >3years interval from biopsy. Repeat prostate MRI showed persistence in 1 and regression in 6 patients.
Conclusion: After a negative MRI-fusion biopsy of the prostate no patient developed prostate cancer with a general decrease in trend in PSA and MRI on follow-up. These patients may have longer interval follow-up periods given the clinical scenario but would be best to test this method in prospective trials first.

Key words: negative prostate biopsy, multiparametric prostate imaging, prostate cancer

Introduction

Prostate cancer screening involves a shared decision making guided by clinical factors such as PSA levels, digital rectal examination (DRE), and personal risk of prostate cancer with definitive diagnosis deferred until with histopathologic confirmation. These clinical factors, when combined, increase the possibility of advanced prostate cancer.[1] However, the standard random biopsy is prone to sampling error and has a high false negative result.[2,3,4,5] To address this issue, adjuncts like MRI of the prostate have been developed.

Multiparametric MRI (mpMRI) of the prostate is an imaging tool used to detect clinically significant prostate cancer (csPCa). The interpretation of the mpMRI follows the Prostate Imaging Reporting and Data System (PI-RADS Version 2.1).[6] Results stratify the likelihood of detecting csPCa into categories PIRADS 1-5 with an increasing positive predictive value on results with higher PIRADS categories.[2-5] MRI of the prostate has a pooled sensitivity of 0.91 and a pooled specificity of 0.37 for detecting csPCa.[1]

Clinically significant prostate cancer refers to a prostate cancer that poses risk of morbidity

and mortality to patients compared to those that do not.[1] This distinction was made to avoid overtreatment to patients with prostate cancer as the treatment itself may expose additional risks.[1]

MRI-Fusion biopsy is an outpatient procedure done under local or general anesthesia. MRI images are pre-loaded into the in-house KOELIS Trinity® MRI/US Prostate Biopsy System. A transrectal ultrasound is positioned to capture real-time ultrasound images and then contoured with the pre-loaded MRI images to indicate the area of concern (PIRADS lesion). Biopsy samples are then acquired using a Max Core TM Disposable Core Biopsy Instrument (G18 x 25 cm) from the targeted lesion followed by systematic sampling. Final histopathology determines the subsequent management of patients with prostate cancer, however, there are no established guidelines on patients with negative results.

Multiple heterogenous studies were previously done to follow-up patients with initial negative biopsy results but with high suspicion of prostate cancer. A large prospective trial by Pepe, et al looked at 256 cases of patients with a PIRADS 3 or 4 with an initial negative biopsy and then were subjected to a repeat biopsy. The overall cancer detection rate was 14% with a csPCa detection rate of 10.1%.[7] Another large trial by Barletta, et al looked at 308 patients with PIRADS score of 3 or more and negative biopsy results for cancer. Patients were monitored with PSA and MRI, and 118 men underwent subsequent biopsy revealed a csPCa incidence of 4.9%.[8] Other smaller trials reported a wide range of overall cancer detection rate, from 7.5-87.5% and a csPCa detection rate ranging from 0-48%. These findings were summarized in a recent mini-systematic review by Grivas, et al which recommended that all initial biopsy-negatives with MRI results of PIRADS 3 or higher should be re-read for confirmation since there are concerns whether prostate cancers are missed on initial biopsies. For patients with persistent concerns, clinical follow-up with PSA, repeat MRI, and possible biopsy is advised.[9]

As of this writing, there is no local report on the follow-up and monitoring of these patients.

This study aimed to determine the incidence of overall prostate cancer and csPCa on follow up after an initial negative result on MRI-fusion biopsy.

Methods

The records from the Stone and Prostate Center for all MRI-fusion prostate biopsies conducted between 2018 to 2022 were retrieved including their follow-up data from the hospital and outpatient clinic archives following the IERB ethical clearance. Inclusion criteria comprised patients who underwent MRI-fusion biopsy of the prostate, were negative for cancer on histopathology, and had mpMRI results of PIRADS 3-5. Exclusion criteria were as follows: Incomplete data on repeat PSA or MRI within 1 year, 2-3 years, or >3 years post-biopsy. The computed sample size was 247, based on the overall incidence of csPCa of 35% with a confidence interval of 90%. Follow-up data on PSA, MRI and histopathology were tabulated. Changes in PSA and MRI findings were compared to baseline at <1 year, 1-2 years, 2-3 years, and >3 years intervals.

Results

After reviewing the records of 670 prostate biopsies performed between 2018 to 2022, six hundred eighteen (618) biopsies were done via MRI Fusion guidance. After applying the inclusion and exclusion criteria, a total of 70 cases were included as shown in Figure 1. Baseline characteristics are listed in Table 1. Mean PSA, prostate size, and PSAD were 9.93 ng/dL, 622.95 mL and 0.2, respectively. Out of the 70 patients included in the study, none was diagnosed with prostate cancer on follow-up.

Repeat PSA measurements on follow-up, were requested from 53 patients within the first year after the biopsy with a mean PSA of 7.03 ng/dL and a mean PSAD of 0.13. At 1-2 years, 36 patients had a mean PSA of 6.44 ng/dL and a mean PSAD of 0.13. At 2-3 years, 25 patients had a mean PSA of 5.27 ng/dL and mean PSAD of 0.10. In 14 patients followed for more than 3 years, the mean PSA was 6.07 ng/dL and the mean PSAD was 0.10.

Repeat MRI was done 7 times in 5 patients. Change in prostate size ranged from -4 ml to +36mL. PIRADS lesion remained stable in 1 patient and downgraded in 6. Among patients with an initial PIRADS lesion of 3, there were 2 with lesions downgraded to PIRADS 2, one showed no PIRADS, and another one remained stable at 3. On

2 patients with an initial PIRADS 4 lesion, one was downgraded to PIRADS 2 and another one showed no PIRADS. No patient with an initial PIRADS 5 lesion had a repeat MRI.

Discussion

The advent of multiparametric MRI (mpMRI) has improved the detection of clinically significant

Table 1 – Descriptive characteristics of patient cohort at initial MRI-Fusion prostate biopsy.

Baseline Characteristics		
65.08 (50 – 83)		
9.93 (3.35 – 55.0)		
0.2 (0.04 - 1.76)		
62.95 (30 -129)		
PIRADS 3 n = 55 (68.8%)	*PIRADS 4* n = 19 (24.8%)	*PIRADS 5* n = 6 (7.5%)

Table 2. Mean and range of PSA, PSAD and change in PSA at select time intervals.

		PSA	PSAD	Change in PSA
<1 year	n = 53	7.03 (1.47 – 42)	0.13 (0.03 – 0.84)	-2.31 (-52.44 – 33.71)
1-2 years	n = 36	6.44 (1.42 – 17.7)	0.13 (0.03 – 0.43)	-1.90 (-53.39 – 12.8)
2-3 years	n = 25	5.27 (1.48 – 11.2)	0.10 (0.03 – 0.29)	-2.21 (-8.92 – 4.63)
>3 years	n = 14	6.07 (0.08 – 14.94)	0.10 (0.002 – 0.3)	-2.54 (-19.28 – 2.32)

Table 3 – Repeat multiparametric MRI with prostate size and PIRADS at different time intervals.

Repeat Multiparametric MRI of the Prostate		
	Prostate Size (previous)	PIRADS (previous)
<1 year	64 (71)	3 (3)
	77 (77)	2 (4)
1-2 years	46 (50)	2 (3)
	86 (77)	3 (4)
	53 (39)	2 (3)
2-3	74 (77)	No PIRADS (4)
>3 years	131 (95)	No PIRADS (3)

prostate cancer (csPCa). However, there is a subset of patients negative for cancer on subsequent prostate biopsies even with the sensitivity and specificity of prostate mpMRI for prostate cancer at 0.91 and 0.37, respectively.[1] There is currently no high-quality data on the optimal timing and protocol for following up these patients with PIRADS 3 or higher lesions on mpMRI and without cancer on biopsies. The decision to repeat the MRI or biopsy is left to the discretion of the physician.

In a study by Barletta, et al, 308 patients were followed-up after negative biopsies.[8] The overall incidence of csPCa was 4% within 24 months. Additionally, 66% of patients showed downgraded PIRADS Score on repeat MRI and with 56% of those results read as negative. Among patients with persistent positive MRI findings, 35% had csPCa compared to 3% in those with negative MRI findings. The study showed that a small number of patients may miss the diagnosis of cancer on initial biopsies and repeat MRI on follow-ups help determine the need to do repeat biopsies.

St. Luke's Medical Center is one of the first institutions in the country to utilize MRI-fusion biopsies of the prostate for early cancer detection with the longest follow-up available locally. Among patients of the current study who initially had a positive MRI and subsequent negative biopsy, none was diagnosed with prostate cancer on follow-up. The PSA and PSAD decreased from the initial compared to subsequent determinations up to 3 years post-biopsy. Among the few patients that underwent repeat MRI of the prostate, 86% showed a downgraded PIRADS score with 33% of which had no PIRADS lesion, compared to 66% and 56%, respectively in the study by Barletta, et al[8]. Current data support the current standard of detection of csPCa and patients with negative-biopsies can be followed-up with PSA and MRI. The limitation of this study is the sample size, broad follow up time intervals, and number of repeat MRI done. Nonetheless, this is the first locally available dataset in this population. The authors recommend future prospective studies and randomized studies with regular PSA monitoring and prostate MRI to guide follow-up of these patients.

Conclusion

The data indicate that no patient with a PIRADS 3 or higher lesion with a negative biopsy developed suspicion of prostate cancer on follow-up. PSA decreased slightly but remained relatively stable and imaging studies further supported this trend. For this subset of patients, it may be safe to extend follow-up intervals based on the clinical scenarios but would need additional data and prospective studies to confirm these findings.

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