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Implementation of multiparametric magnetic resonance imaging technology for evaluation of patients with suspicion for prostate cancer in the clinical practice setting

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Objectives

To investigate the impact of implementing magnetic resonance imaging (MRI) and ultrasonography fusion technology on biopsy and prostate cancer (PCa) detection rates in men presenting with clinical suspicion for PCa in the clinical practice setting.

Patients and Methods

We performed a review of 1 808 consecutive men referred for elevated prostate-specific antigen (PSA) level between 2011 and 2014. The study population was divided into two groups based on whether MRI was used as a risk stratification tool. Univariable and multivariable analyses of biopsy rates and overall and clinically significant PCa detection rates between groups were performed.

Results

The MRI and PSA-only groups consisted of 1 020 and 788 patients, respectively. A total of 465 patients (45.6%) in the MRI group and 442 (56.1%) in the PSA-only group underwent biopsy, corresponding to an 18.7% decrease in the proportion of patients receiving biopsy in the MRI group ($P < 0.001$). Overall PCa (56.8% vs 40.7%; $P < 0.001$) and clinically significant PCa detection (47.3% vs 31.0%; $P < 0.001$) was significantly higher in the MRI vs the PSA-only group. In logistic regression analyses, the odds of overall PCa detection (odds ratio [OR] 1.74, 95% confidence interval [CI] 1.29–2.35; $P < 0.001$) and clinically significant PCa detection (OR 2.04, 95% CI 1.48–2.80; $P < 0.001$) were higher in the MRI than in the PSA-only group after adjusting for clinically relevant PCa variables.

Conclusion

Among men presenting with clinical suspicion for PCa, addition of MRI increases detection of clinically significant cancers while reducing prostate biopsy rates when implemented in a clinical practice setting.

Keywords

magnetic resonance imaging, prostate cancer, biopsy

Introduction

Multiparametric MRI (mpMRI) has emerged as a promising tool in the detection of clinically significant prostate cancer (PCa) [1–3]. Limitations associated with the recognition of low-grade, low-volume pathology can be considered a strength, as this allows the selection of patients with high-risk disease features, for which mpMRI exhibits remarkable specificity [2,4]. In view of current criticisms by the US Preventative Services Task Force (USPSTF) that PSA screening invites unnecessary intervention and treatment, the use of mpMRI as an adjunct to PSA creates an opportunity to consider prostate biopsy primarily for those patients with highest suspicion for clinically significant disease [5,6].

Although level 1 evidence supports the ability of mpMRI to detect higher-risk disease preferentially in patients with elevated PSA levels, results from existing trials are generated

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in highly idealized settings where comparison with cohorts evaluated by PSA alone involves the universal biopsy of all study patients for the purposes of sensitivity and specificity analyses [1,6]. In this respect, our understanding of the advantages of MRI to help guide biopsy decision in men with elevated PSA remains theoretical as, to date, no large-scale study has evaluated its performance when integrated into a true clinical practice setting, where decisions for biopsy are not necessarily driven by defined protocols, but are often based on personalized patient assessments.

In the present study, we investigated how the implementation of mpMRI and MRI/ultrasonography fusion-guided technology in two large academic and community urology practices in the USA influenced patterns of prostate biopsy and cancer detection in a large cohort of men who presented with elevated PSA level. With the USPSTF guidelines highlighting the inherent weaknesses of PSA-based screening, we contend that use of mpMRI to triage patients with elevated PSA would address these legitimate concerns in true clinical practice by decreasing biopsy rates, minimizing risks inherent in indiscriminate systematic prostate sampling, and enabling the preferential detection of clinically significant PCa when compared with men in whom biopsy decisions are guided by conventional clinical metrics centred around PSA assessment [5,7].

Methods

After obtaining institutional review board approval, data were retrospectively collected from patients (aged ≥18 years) referred for elevated PSA level between June 2011 and November 2014 to two large independent academic community practices in New York City and Long Island, NY, USA (the Smith Institute for Urology and Integrated Medical Professionals). The study population was divided into MRI and PSA-only groups based on whether patients underwent mpMRI of the prostate at any point during the specified accrual period. All patients were counselled on the use of mpMRI as a secondary test in the evaluation of elevated PSA level. Reasons for MRI not being performed included lack of patient desire, medical contraindication to MRI, physician decision to defer imaging, or inability to obtain insurance approval for the MRI study (Table S1). Both cohorts were followed longitudinally until October 2016. Patients with a history of PCa, history of prostate MRI prior to initial visit during the enrolment period, or <1-year follow-up were excluded. Patients in the PSA-only group who had a negative biopsy during the accrual period and underwent subsequent mpMRI during follow-up comprised a distinct cohort and were not included in the primary analysis; this was carried out to enable a more representative description of biopsy practice and cancer detection in a population evaluated purely based on conventional clinical metrics without MRI imaging.

Variables evaluated included age, race, family history of PCa, prior negative prostate biopsy, DRE, baseline PSA level, and prostate volume. Patients undergoing MRI were stratified into two groups (positive or negative) based on the presence of suspicious lesions. Suspicious findings were defined, based on a five-point Likert scale, as any lesions on MRI, categorized using the Simplified Qualitative System (SQS) score ranging between 1 and 5, with an SQS score of ≤2 corresponding to a negative MRI and an SQS score between 3 and 5 corresponding to a positive MRI and prompting fusion biopsy [8]. The SQS has been previously described and was used because implementation of our institutional MRI programme predated publication of the Prostate Imaging Reporting and Data System (PI-RADS) classification. Nevertheless, we have demonstrated similar overall risk stratification of MRI lesions based on SQS and PI-RADS V2 scoring systems [8].

Patients were evaluated for use of post-MRI or post-PSA prostate biopsy in the MRI and PSA-only cohorts, respectively, as well as biopsy pathology when applicable. Patients with positive MRI results were offered MRI/TRUS fusion-guided biopsy of suspicious lesions in addition to standard 12-core biopsy, performed in the same setting. Fusion biopsy was performed using the UroNav MRI/TRUS (end-fire iU22 ultrasound; Philips Healthcare, Best, the Netherlands) fusion-guided prostate biopsy system (Invivo, Gainesville, FL, USA). Two biopsy cores were obtained from each lesion; one in the axial and the other in the sagittal plane. After targeted biopsy of the suspicious lesion(s) had been performed, the UroNav workstation where the MRI was processed was turned off and a standard 12-core systematic TRUS-guided prostate biopsy was subsequently performed.

Clinically significant PCa was defined as any Gleason score ≥7 tumour on fusion or standard 12-core TRUS biopsies, Gleason 6 with a lesion volume >0.5 cm^3 volume on MRI, or Gleason 6 with >2 cores positive and/or >50% of any core involved with cancer on biopsy, according to Epstein's criteria [9].

Treating providers were the same for patients in each study group. Biopsy was performed based on aggregate analysis of MRI findings (in the MRI cohort) and clinical variables including PSA, DRE, history of biopsy, race and family history, as well as patient desire. A 3-Tesla Verio® MRI (Siemens, Munich, Germany) was performed using a 16-channel cardiac coil (Sense; Invivo) and an endorectal coil (BPX-30; Medrad, Pittsburgh, PA, USA) filled with PFC-770 (3M, St. Paul, MN, USA) [8]. Sequences obtained included tri-planar T2-weighted imaging, axial diffusion-weighted imaging (*b* values 0, 50, 500, 1 000, 1 500 and 2 000) with apparent diffusion coefficient mapping (*b*-values 0, 50, 500, 1 000, 1 500), and dynamic contrast-enhanced imaging. All mpMRI scans were read prospectively by experienced

genitourinary radiologists and scored with a five-point Likert scale (SQS score), with sequence-specific information that could be used to calculate other scoring systems that may arise (PI-RADSv1) [8]. Patients with a negative MRI who did not undergo biopsy were followed up with PSA and/or interval imaging.

Descriptive statistics are presented as counts and percentages for categorical variables and as means and SD values for continuous variables. The association of patient and disease characteristics by study group (i.e. MRI vs PSA-only) was analysed with Student's *t*-test for continuous data and chi-squared test for categorical variables in univariable analysis. Primary outcomes included rate of prostate biopsy in MRI vs PSA-only groups as well as overall PCa detection in the whole cohort and those who had a post-MRI/PSA prostate biopsy. Secondary outcomes included presence of Gleason score 6, 7 and 8–10 cancers, as well as clinically significant PCa among biopsied patients in the MRI vs PSA-only groups. Multivariable analysis of PCa detection variables was conducted using multinomial logistic regressions adjusting for the covariates age, race, family history of PCa, DRE, history of previous negative biopsy and baseline PSA. All analyses were two-tailed and performed using STATA 14.2 (College Station, TX, USA). A P value < 0.05 was considered statistically significant.

Results

Between June 2011 and November 2014, 2 073 patients without history of PCa presented to one of two urology practices for evaluation of elevated PSA. A total of 167 patients evaluated with PSA only during the accrual period underwent subsequent mpMRI during follow-up and were not included in the analysis. A total of 42 patients who had an MRI of the prostate prior to accrual and 56 patients with follow-up <1 year were excluded. The final study cohort consisted of 1 020 and 788 patients in the MRI and PSA-only arms, respectively (Fig. S1). Patient demographics and clinical characteristics are shown in Table 1. Prior negative biopsy (59.9% vs 32.6%; $P < 0.001$) was significantly more frequent among those undergoing MRI. No differences in baseline PSA, DRE, family history and race were observed between cohorts. Of the 1 020 patients undergoing MRI, 452 patients (44.3%) had a positive MRI. The distribution of suspicion scores for observed lesions is shown in Table S2.

Over a median follow-up of 3.1 years, a total of 465 patients (45.6%) in the MRI group and 442 (56.1%) in the PSA-only group underwent biopsy, corresponding to an 18.7% decrease in the proportion of patients undergoing biopsy in the MRI group ($P < 0.001$; Table 2). Biopsy was performed in 378 patients (83.6%) with positive MRI vs 87 (15.3%) with negative MRI results. The median follow-up among patients with a negative MRI result who did not undergo biopsy was 3.6 years. Repeat mpMRI was performed in 35 patients (7.3%), with the study having remained negative in all patients. One patient had undergone biopsy from this cohort and was negative for PCa. The median follow-up for patients in the PSA-only group who did not undergo biopsy or had negative biopsy was 3.4 years.

Among biopsied patients, overall PCa (56.8% vs 40.7%; $P <$ 0.001) and clinically significant PCa detection (47.3% vs

Table 1 Baseline patient characteristics by era.

Variable	All patients		PSA-only programme		MRI programme		*P**
	N	%	*n*	%	*n*	%	
Number of participants	1 808	100	788	43.6	1 020	56.4	–
Race							
African-American	203	11.2	92	11.7	111	10.9	0.17
White	1 111	61.5	477	60.6	634	62.2	
Asian	169	9.4	86	10.9	83	8.1	
Hispanic	44	2.4	16	2.0	28	2.7	
Other/unknown	281	15.5	117	14.8	164	16.1	
Family history							
No	1 452	80.3	642	81.5	810	79.4	0.27
Yes	356	19.7	146	18.5	210	20.6	
DRE							
Normal	1 628	90.0	710	90.1	918	90.0	0.943
Abnormal	180	10.0	78	9.9	102	10.0	
Prior negative biopsy							
No	940	52.0	531	67.4	409	40.1	<0.001
Yes	868	48.0	257	32.6	611	59.9	
Variable	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	***P*†**
Age, years	63.9	7.6	62.7	7.4	64.8	7.7	<0.001
Baseline PSA, ng/dL	7.6	14.9	7.2	21.1	8.0	7.2	0.268
Prostate volume, mL	55.9	32.8	55.3	29.2	56.6	30.1	0.13

**Chi-squared test.* †*Student's t-test.*

Table 2 Prostate cancer characteristics by group.

Variable	All patients		PSA-only programme		MRI programme		*P**
	N	%	*n*	%	*n*	%	
All cancers (biopsied patients)							
No	463	51.0	262	59.3	201	43.2	<0.001
Yes	444	49.0	180	40.7	264	56.8	
Clinically significant[†] (biopsied patients)							
No	554	61.1	305	69.0	249	53.5	<0.001
Yes	353	38.9	137	31.0	216	46.5	
Gleason score (biopsied patients)							
2–6	146	32.9	72	40.0	74	28.0	0.021
7	211	47.5	73	40.6	138	52.3	
8–10	87	19.6	35	19.4	52	19.7	

**Chi-squared test. [†]Gleason score ≥7, Gleason score 6 with MRI-visible lesion volume ≥0.5 mL, or Gleason score 6 with >2 positive cores and/or >50% involvement of any core.*

Table 3 Multivariable analysis of prostate cancer detection comparing MRI programme with PSA-only programme.

PCa	Univariable			Multivariable[‡]		
	OR	95% CI	*P**	OR	95% CI	*P**
All cancers (biopsied patients)	1.84	1.41–2.40	<0.001	1.74	1.29–2.35	<0.001
Clinically significant[§] (biopsied patients)	2.00	1.52–2.62	<0.001	2.04	1.48–2.80	<0.001
PCa[‡]	**RRR**	**95% CI**	***P*[†]**	**RRR**	**95% CI**	***P*[†]**
Gleason score (biopsied patients)						
2–6	*ref.*	–	–	*ref.*	–	–
7	1.86	1.21–2.87	0.005	1.90	1.16–3.11	0.010
8–10	1.47	0.86–2.51	0.164	1.58	0.83–2.99	0.164

*OR, odds ratio; PCa, prostate cancer; RRR, relative risk ratio. *Logistic regression. [†]Multinomial logistic regression. [‡]Analyses adjusted for: age, race, family history of PCa, DRE, history of previous negative prostate biopsy and baseline PSA. [§]Gleason score ≥7, Gleason score 6 with MRI-visible lesion volume ≥0.5 mL, or Gleason score 6 with >2 positive cores and/or >50% involvement of any core.*

31.0%, $P < 0.001$) were significantly higher in the MRI vs the PSA-only group, corresponding to increased detection of Gleason score 7 lesions (52.3% vs 40.6%; $P = 0.018$) and decreased detection of Gleason score 6 disease (27.7% vs 40%; $P = 0.018$ [Table 2]). In multivariable analysis, the odds of overall PCa (odds ratio [OR] 1.74, 95% CI 1.29–2.35; $P < 0.001$) and clinically significant PCa detection (OR 2.04, 95% CI 1.48–2.80; $P < 0.001$) were significantly higher in the MRI than in the PSA-only group (Table 3).

Biopsy rates and pathological findings stratified by MRI results and SQS scores are presented in Table S2. The incidence rates of clinically significant PCa within lesions of SQS scores 3, 4 and 5 were 27.5%, 70.9% and 98.5%, respectively. Among the 87 patients with negative MRI who underwent biopsy, cancer was detected in 15 (17.2%) cases, with eight (9.2%) having qualified as clinically significant disease.

Of 378 patients, 324 (85.7%) with a positive MRI result underwent combined fusion with 12-core systematic TRUS biopsy (Table 4 and Table S3). The overall cancer detection rate in this group was 65.7%, including 54.9% for fusion biopsies and 54.3% for 12-core systematic biopsies. Detection of clinically significant PCa, however, was significantly higher on targeted fusion biopsy than on 12-core systematic TRUS biopsy (50.3% vs 41.4%; $P = 0.022$ [Table 4]), which corresponded to increased detection of Gleason score 7 lesions (60.5% vs 47.7%; $P = 0.009$). Of the 14 clinically significant tumours missed on fusion biopsy, seven were Gleason score 6 tumours and seven were Gleason score 7 tumours.

Discussion

Improved understanding of the biological heterogeneity of PCa has unveiled the gross over-detection and often unnecessary treatment of clinically insignificant cancers through widely used PSA-based screening practices [5,7]. Consensus statements issued by the USPSTF arguing against the universal use of PSA would theoretically diminish morbidity related to diagnosis of low-risk PCa, but also leave vulnerable a population of patients with higher-risk pathologies shown to benefit from primary intervention [5,7,10–14]. This dilemma highlights the need for a more refined approach to the management of patients with elevated PSA levels that selectively identifies patients with clinically significant disease.

The results of the present study offer a real-world interpretation of how integration of MRI technology into the

Table 4 Prostate cancer characteristics by biopsy type in patients who underwent MRI-guided fusion biopsy.

	Combined fusion and 12-core (+MRI)						P*
	All		Fusion target		12-core		
	N	%	n	%	n	%	
N	324	–	324	–	324	–	
All cancers							
No	111	34.3	146	45.1	148	45.7	0.875
Yes	213	65.7	178	54.9	176	54.3	
Clinically significant†							
No	147	45.4	161	49.7	190	58.6	0.022
Yes	177	54.6	163	50.3	134	41.4	
Gleason score							
2–6	52	24.4	36	20.3	61	34.7	0.009
7	118	55.4	107	60.5	84	47.7	
8–10	43	20.2	34	19.2	31	17.6	

**Chi-squared test. †Gleason score ≥ 7, Gleason score 6 with MRI-visible lesion volume ≥0.5 mL, or Gleason score 6 with >2 positive cores and/or >50% involvement of any core.*

triage of patients with elevated PSA influences patterns of prostate biopsy and cancer detection compared with PSA alone. We show in the clinical practice setting that utilization of MRI as a risk assessment tool significantly reduces the use of prostate biopsy when compared with clinical decision-making based on PSA alone. At 3.1-year follow-up, an 18.7% reduction in biopsy rate among men evaluated with MRI was observed in the context of biopsy being performed in only 15.3% of men with negative MRI compared with 83.6% of men with positive MRI. Moreover, despite the reduction in biopsy rate, PCa detection increased by 39.4% in the MRI cohort, which corresponded to a 52.6% increase in detection of clinically significant pathology. Benefit derived from MRI was seen to extend beyond the identification of men with a positive study, but also involved the ability to perform targeted biopsy of suspicious lesions as the incidence of clinically significant PCa was appreciably higher among patients receiving combined fusion with systematic 12-core TRUS biopsy than in patients with positive MRI who only underwent non-targeted 12-core TRUS biopsy.

Several studies lend support to our findings, albeit in the context of highly idealized trial scenarios. In a pilot study nested within the Goteborg randomized screening trial, use of targeted biopsy alone in 124 men with a suspicious lesion on pre-biopsy MRI would reduce biopsy rates by at least 33% while leading to a 48% increase in detection of clinically significant PCa when compared to systematic biopsy based on elevated PSA value alone [15]. Similarly, in a prospective assessment of MRI use in the setting of elevated PSA level, the PROMIS trial presented two hypothetical models for patient evaluation: one based on standard practice of TRUS biopsy in men with elevated PSA levels, and another using MRI as a triage tool, reserving biopsy for men with suspicious imaging lesions. Comparison of both pathways revealed a significantly higher positive predictive value for the MRI-based approach, as the incidence of clinically significant PCa in the standard TRUS biopsy and the MRI biopsy cohort was 19% and 51%, respectively [1]. Most recently, Kasivisvanathan et al. [6] randomized 500 patients at risk of PCa to TRUS biopsy or MRI/ultrasonography-guided fusion biopsy and determined that using MRI prior to biopsy was superior to standard TRUS biopsy with regard to increased detection of clinically significant PCa and reduced detection of clinically insignificant disease.

The present study places the findings of the PROMIS and PRECISION trials into a more practical context, illustrating in a contemporary practice setting how implementation of MRI into the triage algorithm for elevated PSA would indeed facilitate preferential identification of patients with aggressive disease, while mitigating overdiagnosis of insignificant pathology. Fundamental assumptions of both the PROMIS and PRECISION trials predicating the superiority of an MRI-based risk assessment are that, firstly, all patients presenting with elevated PSA level would be candidates for MRI and that, secondly, TRUS biopsy would be performed in all patients with elevated PSA level, both of which are not representative of true clinical practice within the USA; in fact, among 788 patients in the present study's PSA-only group, only 56% went on to receive biopsy at a median 3.1-year follow-up. Nevertheless, despite the selective use of biopsy even in the PSA-only cohort, we still observed a significantly higher positive predictive value for cancer detection with the MRI-based approach, with clinically significant PCa detection having increased by >50% when compared with biopsy based on PSA alone. Also notable is the higher detection rate for clinically significant PCa in the MRI cohort despite greater incidence of prior negative biopsy, further supporting the sensitivity of MRI for aggressive disease phenotypes compared with PSA-driven systematic biopsy.

The benefit we observed to performing targeted biopsy of suspicious lesions is consistent with that reported in the contemporary literature [2,16,17]. A systematic review evaluating the role of MRI with and without fusion technology showed that, while overall PCa diagnosis rates were similar between targeted biopsy and non-targeted 12-core TRUS biopsy, the use of targeted biopsy significantly increased detection of aggressive subtypes [16]. Similarly, the addition of standard TRUS biopsy to targeted biopsy in patients with positive MRI was shown to be of limited utility by Siddiqui et al. [2] in a landmark prospective trial evaluating MRI-fusion biopsy in 1 003 patients with clinical suspicion for PCa. Although the combination of 12-core TRUS biopsy and targeted biopsy increased diagnosis of PCa by 10% in their study cohort, less than half would qualify as clinically significant, with only 3% representing intermediate- or high-risk disease.

A diagnostic platform integrating MRI as a secondary test in men with elevated PSA would be premised on omission of biopsy in the absence of suspicious imaging lesions, a practice which raises concern for the missed detection of clinically significant disease in patients with elevated PSA level but negative MRI. Previous attempts to discern the negative predictive value (NPV) of MRI are limited by selection biases inherent in the study of radical prostatectomy cohorts, largely skewing disease detection rates. A more accurate assessment of MRI sensitivity for clinically significant PCa is provided by the PROMIS trial, as transperineal mapping biopsy of men with elevated PSA level without a diagnosis of PCa represents a more balanced pathological reference standard. Using Gleason score ≥4 + 3 as a primary definition for clinically significant PCa, Ahmed et al. [1] observed that 89% of men with negative MRI had absent or indolent pathology on transperineal biopsy, translating to a NPV significantly higher than that seen after standard 12-core TRUS biopsy when performed for elevated PSA level. Even when considering a more inclusive definition for clinically significant PCa (GS ≥ 3 + 4 or cancer core length ≥4 mm), which is more in line with our study criteria, the NPV of MRI (72%) remained significantly greater than 12-core TRUS biopsy (65%), indicating that while MRI is not perfect at excluding the presence of clinically significant disease, it does demonstrate incremental benefit over the current standard practice of non-targeted systematic TRUS biopsy [1].

Although our series may underestimate the risk of missed detection of clinically significant PCa in the MRI cohort, given that biopsy was not performed in all patients with negative MRI, there are several factors that allow us to infer a relatively favourable NPV from the current literature [1,17]. All patients in the present series received high-quality imaging using a 3-Tesla magnet with an endorectal coil, meeting the standards of the American College of Radiology as outlined in the PI-RADS V2 module [18]. Furthermore, biopsy was only performed by experienced providers well beyond their initial learning curve. This is in contrast to the PROMIS and PRECISION trials, in which a favourable NPV and a high level of confidence in a negative MRI result were achieved despite use of 1.5-Tesla magnet without endorectal coil and despite biopsy being performed by providers with varying level of experience [1,6]. Thus, the high quality of MRI performed in the present study would lead us to believe that our rate of missed clinically significant PCa in patients with negative MRI is not significantly different from what is established in the current literature. Nevertheless, as biopsy was not performed in all patients with negative MRI, broader conclusions regarding the NPV of MRI in men with elevated PSA cannot be drawn from the present study.

Several limitations of the present study should be noted. Biopsy in both study cohorts was performed at the discretion of individual practitioners after evaluation of imaging and patient-specific clinical characteristics rather than based on set criteria, potentially contributing to differences in biopsy rates and PCa detection. However, the study objective was to capture this variability that often exists in true clinical practice and demonstrate the utility of mpMRI as a risk assessment tool within this framework. Reasons for MRI having not been performed were multifactorial and included lack of insurance approval as well as patient refusal. Inability to obtain insurance approval for MRI may have been a reflection of underlying socio-economic differences between the PSA-only and MRI groups, which may have, in turn, influenced observed differences in biopsy and cancer detection rates between groups. Similarly, patients who refused MRI may have done so because of an inherent inclination to proceed with biopsy in the setting of elevated PSA; this may have contributed to increased biopsy rates in the PSA-only group. A higher prior negative biopsy rate was observed in the MRI arm, which was not entirely unexpected given its current use primarily in this setting. Although this may have influenced biopsy practice patterns, higher cancer detection rates in this cohort indicate a strength of MRI as a tool to capture disease which may have otherwise been missed using conventional PSA-based screening. Furthermore, the present study offers a real-world perspective on the feasibility of integrating MRI technology into the contemporary clinical practice setting, where the universal use of MRI in the evaluation of patients with elevated PSA is currently not standard practice.

The negative stigma associated with PSA screening based on the USPSTF recommendations may have also influenced the decision to pursue biopsy among patients presenting with elevated PSA and explain, in part, the differences between study groups. Nevertheless, any impact of the USPSTF guidelines on subsequent decision for biopsy would probably have been distributed equally among PSA-only and MRI groups given the temporal overlap of both cohorts as well as the focus of these recommendations having been on the role of PSA screening rather than the decision for biopsy among those with elevated PSA. Furthermore, several factors mitigate the impact of this policy shift on observed differences between groups, including study of the same providers prior to and after 2012 as well as the lack of corresponding changes in PSA-testing and biopsy guidelines set forth by the American Urological Association or the American Cancer Society. The use of the endorectal coil in our series may not be representative of current practice given improvements in mpMRI technology; however, its use in the present study was based on limitations in the amount of signal needed to obtain high-quality prostate imaging in the early phase of our MRI programme [19]. The short follow-up of our study cohort is a limitation, particularly with respect to the consequences of missing clinically significant PCa in patients with negative

MRI. All patients in our study, however, would reenter a PSA screening protocol and undergo repeat evaluation in the context of concerning PSA change with repeat MRI or standardized biopsy. This practice may mitigate, but not entirely eliminate, the risks of missed detection of clinically significant PCa in patients for whom initial biopsy was deferred because of a negative MRI result. Lastly, patients were from two independent but regionally confined academic community practices. Studies from centres across the country are needed to confirm generalizability.

In conclusion, with the growing body of level 1 evidence supporting mpMRI in the assessment of a man's risk of PCa [1,2,6], we have shown that, when implemented in clinical practice, the use of mpMRI to triage patients with elevated PSA does indeed increase detection of clinically significant PCa in the context of a reduced number of prostate biopsies. Although these improvements support a possible paradigm shift in the evaluation of patients with elevated PSA, we also recognize that the full impact of MRI to guide biopsy decision is not currently understood and will probably require a decade of follow-up to understand its clinical relevance. As such, our study results support the notion that in the short-term, use of MRI as a triage tool in men with elevated PSA offers opportunity to better diagnose and risk-stratify PCa compared with the status quo.

Conflict of Interest

None declared.

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Abbreviations: OR, odds ratio; mpMRI, multiparametric MRI; PCa, prostate cancer; USPSTF, US Preventative Services Task Force; SQS, Simplified Qualitative System; PI-RADS, Prostate Imaging Reporting and Data System; NPV, negative predictive value.

Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Diagram of study population distribution.
Table S1. Reasons for deferred MRI in the PSA-only cohort.
Table S2. Prostate cancer detection in the MRI programme.
Table S3. Prostate cancer characteristics by biopsy type in patients who underwent MRI-guided fusion biopsy.