Association Between Prostate Magnetic Resonance Imaging and Observation for Low-risk Prostate Cancer

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OBJECTIVE To evaluate the association between prostate magnetic resonance imaging (MRI) and the use of observation for men with low-risk prostate cancer (PCa).

MATERIALS AND METHODS We used the Surveillance, Epidemiology, and End Results-Medicare database to identify men diagnosed with low-risk PCa during 2010-2013. We assessed the use of prostate MRI and management using claims in period surrounding PCa diagnosis. The relation of clinical and demographic factors to receipt of MRI was evaluated with multivariable logistic regression analysis. Following propensity score matching, we fit conditional logistic regression models to examine the association between prostate MRI and initial management, ie, observation or definitive treatment.

RESULTS Of 8144 patients with low-risk PCa, 495 (6.1%) received MRI. Use of MRI increased from 3.4% in 2010 to 10.5% in 2013. A total of 3060 (37.6%) patients received observation. MRI was performed in 265 (8.7%) of patients receiving observation, and 230 (4.5%) who were treated ($P < .0001$). In multivariable analysis, measures of socioeconomic status were significantly associated with the use of prostate MRI. Following propensity score matching, receipt of prostate MRI surrounding the diagnosis of PCa was associated with a significantly higher likelihood of observation (odds ratio = 1.90, 95% confidence interval: 1.56-2.32). This effect persisted in sensitivity analyses attempting to exclude treatment-planning MRIs.

CONCLUSION Receipt of prostate MRI surrounding PCa diagnosis was associated with a nearly 2-fold greater odds of receiving observation vs definitive treatment. UROLOGY 124: 98–106, 2019. Elsevier Inc.

Despite national declines in screening, prostate cancer (PCa) remains the most commonly diagnosed noncutaneous cancer among men in the United States.[1] For those with low-risk features, immediate treatment has not been shown to improve cancer-specific survival, and frequently impacts health-related quality of life including urinary, bowel, and sexual function.[2-5] Active surveillance (AS), a period of close disease observation, has emerged as a strategy to defer or avoid definitive treatment for low-risk patients, and is now regarded as the standard of care by major cancer guideline-issuing bodies.[6] Despite increases in the utilization of AS, recent estimates available through 2013 indicate that the majority of patients with low-risk PCa continue to receive definitive treatment.[7,8] Although longitudinal studies support the safety of AS, uncertainty about the possibility of underestimating an indvidual's risk of harboring aggressive disease remains a strong motivator to treat. As a result, efforts to improve the initial characterization of the disease have been advocated as a means to enhance confidence with observational management.[9]

In the past few years there has been a dramatic expansion in the support for MRI in the evaluation of men with known or suspected PCa.[10] Recent studies have underscored the ability of contemporary prostate MRI to offer high resolution anatomical assessment of the prostate including improved prediction of high-grade or high-stage disease.[11] Moreover, MRI facilitates the performance of targeted MRI-guided in-bore, cognitive, or MR-ultrasound fusion biopsies, which improve detection yields for occult higher-grade cancer that would be missed on

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systematic transrectal ultrasound guided biopsy alone. On the basis of encouraging single and multi-institutional controlled studies, prostate MRI is increasingly recommended as an important staging tool that can identify occult aggressive disease and facilitate enrollment in AS.[12]

Despite growing enthusiasm, there is a lack of population-level evidence that addresses national utilization trends, or practical impact of prostate MRI on disease management. Therefore, we assessed the use of prostate MRI in a population-based, nationally representative cohort of Medicare beneficiaires with low-risk PCa, evaluated patient and healthcare level factors predictive of MRI use, and examined the association between prostate MRI and initial management with observation or definitive therapy. We tested the hypotheses that early MRI use was variable across socio-demographic and provider-level factors, and that use of MRI was associated with greater likelihood of observation as initial management.

MATERIALS AND METHODS

Cohort Identification

We used Surveillance, Epidemiology, and End-Results (SEER) records linked with individual level Medicare claims to identify men with PCa. The SEER-Medicare linkage provides a high level of detail regarding healthcare delivery among older Americans including clinical and demographic characteristics, treatments received, and subsequent outcome.[13] The most recent linkage released in April 2017 includes patients diagnosed through 2013. Patients included in this study were diagnosed with nonmetastatic, lymphnode negative, first primary, low-risk PCa at the age of $\geq$66 years in 2010-2013 according to the D'Amico classification: PSA<10 ng/mL, Gleason score $\leq$3 + 3, and clinical stage $\leq$T2a.[14] Patients were excluded on the basis of absence of Medicare Parts A and/or B, health maintenance organization membership in the 12 month period preceding diagnosis until December 31, 2014, or death, unknown date of diagnosis, incidental detection of PCa on death certificate or at autopsy, missing tumor grade, stage or PSA level. To assure patients received MRI or treatment, we further excluded patients who died within 1 year after diagnosis.

Study Variables

We identified prostate MRI obtained in the period surrounding diagnosis of PCa by common procedural terminology codes (72195, 72196, and 72197). To identify prostate MRI that was performed for the purpose of local staging or risk assessment, we included studies performed in a 19-month window including a 6-month period preceding the month of diagnosis and 12 months following the month of diagnosis. To account for the possibility that MRI studies were obtained during observation to assess for disease progression, rather than for initial staging, we performed sensitivity analyses limiting the time window of interest to 6-9 months after diagnosis, as well as, a window of 3 months preceding until 3 months following the diagnosis of PCa. To account for MRI studies performed for local treatment planning, we regarded prostate MRI studies performed within the 28 days before the initiation of therapy as a component of treatment, and excluded them from analysis. We also performed sensitivity analyses using a period of 14 days prior to treatment start date to distinguish staging MRI from MRI studies performed in the context of treatment planning.

The primary study outcome was initial management for PCa, ie, observation vs definitive therapy. Observation was defined as the absence of definitive cancer-directed therapy within 12 months of diagnosis.[15,16] Consistent with prior work, we identified treatment based on Medicare claims for radical prostatectomy (RP), radiation therapy, androgen deprivation therapy, or ablative therapy. The date of treatment was assigned using inpatient Medicare Provider Analysis and Review files for admissions, outpatient claims, and Medicare Part D files. We compiled relevant sociodemographic, clinical and healthcare-related characteristics, including race, age at diagnosis, year of diagnosis, marital status, comorbidity (measured with Elixhauser score, using Medicare claims in the 12 months prior to PCa diagnosis), SEER region, metropolitan or rural status based on rural-urban continuum codes specified in SEER in 2013, state buy-in and/or low income subsidy for insurance, median household income at the zip code level, and urologist density divided into tertiles (based on 2011 hospital referral region capacity measures, Dartmouth Atlas).[17,18] The clinical factors considered included clinical stage (T1 vs T2), prostate-specific antigen level, and Gleason score.

Statistical Analysis

The primary study objective was to examine the potential association between prostate MRI and observation among men newly diagnosed with low-risk PCa. We described patient characteristics using frequency tables, means, standard deviations, and chi-square tests as appropriate. To identify factors associated with use of prostate MRI in the study cohort, we fit multivariable logistic regression models examining clinical, sociodemographic, and healthcare-related factors. We used propensity score matching to control for confounding associated with the preferential use of MRI.[19] Specifically, we computed propensity scores using logistic regression models including all available clinical, sociodemographic, provider, facility, and cancer-related variables. We used 1:4 greedy matching to pair patients with a similar propensity for exposure (ie, receipt of MRI) within a specific limited range or caliper.[20] We confirmed that the group of patients who underwent MRI and the comparison group of patients who did not receive MRI were balanced across multiple covariates based on standardized differences less than 0.1. Using propensity weighted data, we then constructed conditional logistic regression models to examine the associations between prostate MRI and type of initial treatment (observation vs definitive treatment) for low-risk PCa.

RESULTS

We identified 8144 men with clinical low-risk PCa. A total of 495 (6.1%) underwent MRI either in the period preceding (n = 60, 12.1%) or following (n = 435, 87.9%) diagnosis. The proportion of patients receiving MRI increased in the study period from 3.4% in 2010-10.5% in 2013 (Fig. 1), while the number of patients diagnosed with PCa annually decreased during the same period. A total of 3060 (37.6%) patients received observation within 12 months of diagnosis. Rates of immediate treatment decreased from 69.3% in 2010 to 52.0% in 2013. The common management strategies received included radiation monotherapy in 2895 (35.6%) and RP in 1481 (18.2%). Patient

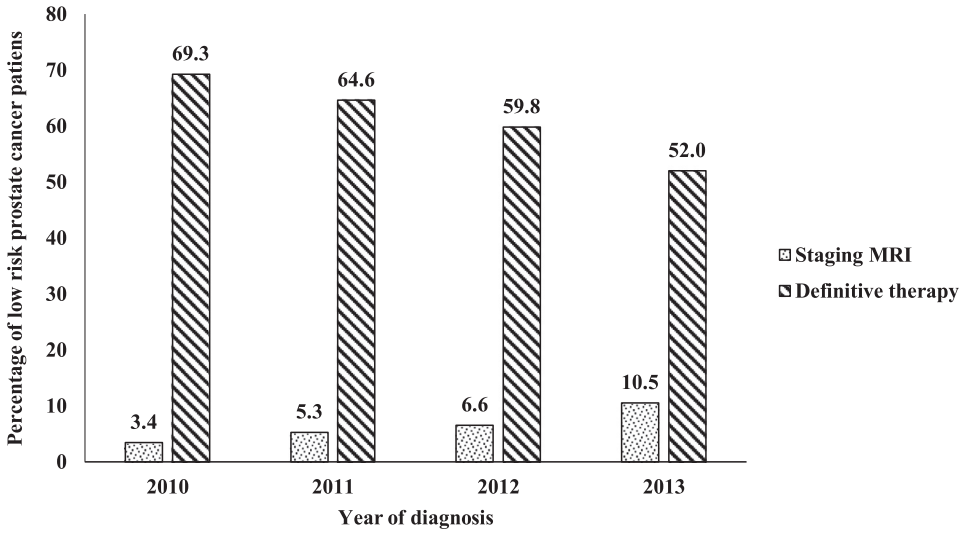

Figure 1. Percentage of patient received prostate MRI and definitive therapy among 8144 low-risk prostate cancer patients by year of diagnosis, 2010–2013.

clinical, sociodemographic, and treatment related characteristics are detailed in Table 1.

We identified significant associations of patient and provider-level factors with the use of prostate MRI surrounding the diagnosis of PCa. In multivariable logistic regression analysis, non-white race, age older than 75 years, residence outside of the northeast, higher urologist density, were associated with lower likelihood of receiving prostate MRI. Diagnosis in later years, highest zip code-level median household income, and clinical tumor stage T2 were associated with higher likelihood of receiving prostate MRI (Table 2).

We first examined the association between prostate MRI and initial management for PCa using multivariable logistic regression. Patients who received prostate MRI were significantly more likely to receive observation (OR = 2.01, 95% CI: 1.66-2.44). In addition, non-white race, older age, being unmarried, low clinical stage, and residence in a region with higher urologist density were significantly associated with the likelihood of receiving observation vs definitive treatment (Table 3).

After propensity score matching to balance factors that were associated with the receipt of MRI, standardized differences for all variables were less than 10% between patients who received prostate MRI and their matched counterparts, indicating adequate matching based on the selected characteristics (Supplementary Table 1). In conditional logistic regression analysis, receipt of prostate MRI surrounding diagnosis was associated with a significantly higher likelihood of receiving observation in the first year (OR = 1.90, 95% CI 1.56-2.32).

We performed multiple sensitivity analyses to evaluate whether the association between MRI and observation was robust to the time period that imaging was obtained relative to diagnosis and treatment. Analyses performed using a window of 3 months preceding until 3 months following diagnosis, as well as 6 or 9 months revealed similar results (data not shown). Exclusion of 60 patients who received MRI before diagnosis, and the exclusion of 25 patients who received MRI both prior to and following diagnosis also yielded similar findings. To address potential misclassification of MRI obtained for the purpose of treatment planning for radiation therapy or RP, we also explored another cutoff prior to treatment. The use of a shorter interval from MRI to treatment (14 days) did not meaningfully change the association between MRI and observation for low-risk PCa

DISCUSSION

Examining the association between prostate MRI surrounding the diagnosis of PCa and the use of observation for low-risk PCa in a nationally representative cohort of Medicare beneficiaries, we identified a 3-fold increase in the use of MRI for men with low-risk PCa from 2010-2013, and observed substantial variation in utilization relating to age, race, socioeconomic status, and healthcare factors including urologist density. Compared with matched patients with similar clinical characteristics including diagnosis year, the odds of receiving observation vs definitive treatment were twice as high for patients who received MRI in the period surrounding diagnosis.

As evidence supporting the safety of AS strengthens with the maturation of numerous longitudinal studies, efforts to decrease primary treatment of low-risk disease have been enthusiastically advocated.[3,21-23] Utilizing prostate MRI to improve disease characterization at initial diagnosis has been offered as a means to enhance confidence in AS, yet the viability of this approach has not yet been empirically demonstrated. Over the past decade, technical modifications including the integration of multiple imaging parameters such as diffusion-weighted imaging have improved the diagnostic accuracy of prostate MRI. These improvements have culminated in the refined prediction of tumor stage, presence of occult high-grade disease, both at initial diagnosis and among men enrolled on AS.[24] As a consequence, the use of prostate MRI has been integrated into clinical practice guidelines as a component of the initial staging evaluation prior to enrollment in AS. In addition, a majority of practicing urologists report favorable opinions of the use of prostate MRI in the diagnostic pathway of PCa.[25] From this

Table 1. Characteristics of 8144 patients with low-risk prostate cancer patients by prostate MRI, 2010-2013

	Overall		Prostate MRI				
			Yes		No		
	n	%	n	%	n	%	*P*
Total	8144			495		7649	
Race							
White	6935	85.2	448	90.5	6487	84.8	<.01
Non-white	1209	14.8	47	9.5	1162	15.2	
Age at Diagnosis (in years)							
Median (Inter quartile)	71 (68-74)		70 (67-73)	71 (68-74)			
66-69	3350	41.1	237	47.9	3113	40.7	<.01
70-74	2982	36.6	179	36.2	2803	36.6	
75+	1812	22.2	79	16.0	1733	22.7	
Year of Diagnosis							
2010	2379	29.2	82	16.6	2297	30.0	<.01
2011	2396	29.4	127	25.7	2269	29.7	
2012	1738	21.3	114	23.0	1624	21.2	
2013	1631	20.0	172	34.7	1459	19.1	
Marital Status							
Unmarried	1387	17.0	77	15.6	1310	17.1	.39
Married	5810	71.3	358	72.3	5452	71.3	
Unknown	947	11.6	60	12.1	887	11.6	
Elixhauser Score							
0	2804	34.4	182	36.8	2622	34.3	.52
1-2	3749	46.0	221	44.6	3528	46.1	
3+	1591	19.5	92	18.6	1499	19.6	
Flu Shot Before Diagnosis							
No	3962	48.6	235	47.5	3727	48.7	.59
Yes	4182	51.4	260	52.5	3922	51.3	
SEER Region							
Northeast	2014	24.7	204	41.2	1810	23.7	<.01
Midwest	681	8.4	14	2.8	667	8.7	
South	2352	28.9	61	12.3	2291	30.0	
West	3097	38.0	216	43.6	2881	37.7	
Metro/Rural							
Big metro	4448	54.6	357	72.1	4091	53.5	<.01
Metro	2402	29.5	113	22.8	2289	29.9	
Other	1294	15.9	25	5.1	1269	16.6	
Any State Buy-In During -12 – 12 Months (25 Months)							
No	>7582	>93.1	>484	>97.8	7098	92.8	<.01
Yes	<562	<6.9	<11	<2.2	551	7.2	
Zip Code Median Income							
1st quartile (lowest)	1950	23.9	65	13.1	1885	24.6	<.01
2nd quartile	1966	24.1	66	13.3	1900	24.8	
3rd quartile	1963	24.1	131	26.5	1832	24.0	
4th quartile (highest)	1970	24.2	217	43.8	1753	22.9	
Unknown	295	3.6	16	3.2	279	3.6	
Stage							
T1	7523	92.4	434	87.7	7089	92.7	<.01
T2	621	7.6	61	12.3	560	7.3	
PSA (median, IQR)	5.4 (4.3-6.9)		5.1 (4.1-6.7)	5.4 (4.4-6.9)		0.01	
Gleason Score							
<6	<101	1.2	<11	<2.2	90	1.2	.84
6	>8043	98.8	>484	>97.8	7559	98.8	
Hospital Referral Region Urologist Density (per 100,000)							
<2.45	2774	34.1	199	40.2	2575	33.7	<.01
2.45-2.84	2692	33.1	98	19.8	2594	33.9	
2.85+	2678	32.9	198	40.0	2480	32.4	

SD, standard deviation.

perspective, our findings are novel and impactful in demonstrating a population-level association between MRI imaging and increased use of conservative management. This work can serve to inform efforts to understand the impact of novel technologies on disease management in low-risk PCa.

We observed increasing frequencies of prostate MRI use from 2010 through 2013, in the backdrop of shifting

Table 2. Factors associated with receipt of prostate MRI surrounding diagnosis among 8144 patients with low risk prostate cancer, 2010-2013

	Prostate MRI		Odds Ratio*	95% Confidence Interval
	Yes n (%)	No n (%)		
Race				
White	448 (90.5)	6487 (84.8)	1.00	
Non-white	47 (9.5)	1162 (15.2)	0.64	0.47–0.88
Age at Diagnosis (in years)				
66-69	237 (47.9)	3113 (40.7)	1.00	
70-74	179 (36.2)	2803 (36.6)	0.86	0.70–1.06
75+	79 (16.0)	1733 (22.7)	0.61	0.46–0.80
Year of Diagnosis				
2010	82 (16.6)	2297 (30.0)	1.00	
2011	127 (25.7)	2269 (29.7)	1.59	1.19–2.12
2012	114 (23.0)	1624 (21.2)	1.96	1.45–2.63
2013	172 (34.7)	1459 (19.1)	3.52	2.67–4.64
Marital Status				
Unmarried	77 (15.6)	1310 (17.1)	1.00	0.77–1.30
Married	358 (72.3)	5452 (71.3)	1.00	
Unknown	60 (12.1)	887 (11.6)	1.10	0.82–1.47
Elixhauser Score				
0	182 (36.8)	2622 (34.3)	1.00	
1-2	221 (44.6)	3528 (46.1)	0.95	0.77–1.18
3+	92 (18.6)	1499 (19.6)	1.00	0.76–1.32
Flu Shot Before Diagnosis				
No	235 (47.5)	3727 (48.7)	1.00	
Yes	260 (52.5)	3922 (51.3)	1.01	0.83–1.22
SEER Region				
Northeast	204 (41.2)	1810 (23.7)	1.00	
Midwest	14 (2.8)	667 (8.7)	0.19	0.10–0.34
South	61 (12.3)	2291 (30.0)	0.33	0.22–0.49
West	216 (43.6)	2881 (37.7)	0.41	0.28–0.60
Metro/Rural				
Big metro	357 (72.1)	4091 (53.5)	1.00	
Metro	113 (22.8)	2289 (29.9)	0.73	0.57–0.92
Other	25 (5.1)	1269 (16.6)	0.43	0.27–0.68
Any State Buy-in During -12-12 Months (25 Months)				
No	>484 (97.8)	7098 (92.8)	1.00	
Yes	<11 (<2.2)	551 (7.2)	0.33	0.17–0.64
Zip Code Median House Income				
1st quartile (lowest)	65 (13.1)	1885 (24.6)	1.00	
2nd quartile	66 (13.3)	1900 (24.8)	0.73	0.50–1.04
3rd quartile	131 (26.5)	1832 (24.0)	1.09	0.78–1.53
4th quartile (highest)	217 (43.8)	1753 (22.9)	1.62	1.16–2.26
Unknown	16 (3.2)	279 (3.6)	1.09	0.61–1.95
Stage				
T1	434 (87.7)	7089 (92.7)	1.00	
T2	61 (12.3)	560 (7.3)	1.55	1.15–2.08
PSA (per 0.1) (median, IQR)	5.1 (4.1-6.7)	5.4 (4.4-6.9)	1.00	0.99–1.00
Hospital Referral Region Urologist Density (per 100,000)				
<2.45	199 (40.2)	2575 (33.7)	1.00	
2.45-2.84	98 (19.8)	2594 (33.9)	0.45	0.33–0.62
2.85+	198 (40.0)	2480 (32.4)	0.42	0.28–0.62

* All variables were mutually adjusted in the model.

detection and treatment patterns. Well-reported declines in prostate-specific antigen screening that occurred following recommendations against screening have culminated in lower rates of disease detection across the risk spectrum.[26] Moreover, we observed a nearly 20% reduction in the proportion of patients with low-risk PCa receiving treatment, likely reflecting the growing acceptance of this practice. We anticipate further changes in practice patterns including decreased rates of screening and detection, and precipitous increases in the use of MRI based on the proliferation of literature that appeared in recent years. For example, recent estimates from the United Kingdom indicate that prostate MRI was obtained in 51% of men newly diagnosed with PCa in England from April 2015 through March 2016, with a majority performed prior to diagnosis.[27]

We found considerable sociodemographic variation in the receipt of prostate MRI including racial and

Table 3. Factors associated with observation (versus definitive therapy) among 8144 low-risk prostate cancer patients, 2010-2013

	Observation n (%)	Definitive Therapy n (%)	Odds Ratio*	95% Confidence Interval
Prostate MRI				
No	2795 (91.3)	4854 (95.5)	1.00	
Yes	265 (8.7)	230 (4.5)	2.01	1.66–2.44
Race				
White	2540 (83.0)	4395 (86.4)	1.00	
Non-white	520 (17.0)	689 (13.6)	1.34	1.17–1.53
Age at Diagnosis				
66-69	1095 (35.8)	2255 (44.4)	1.00	
70-74	1117 (36.5)	1865 (36.7)	1.35	1.22–1.51
75+	848 (27.7)	964 (19.0)	2.20	1.94–2.49
Year of Diagnosis				
2010	731 (23.9)	1648 (32.4)	1.00	
2011	848 (27.7)	1548 (30.4)	1.21	1.07–1.37
2012	698 (22.8)	1040 (20.5)	1.53	1.34–1.75
2013	783 (25.6)	848 (16.7)	2.11	1.84–2.41
Marital Status				
Unmarried	591 (19.3)	796 (15.7)	1.42	1.25–1.61
Married	2052 (67.1)	3758 (73.9)	1.00	
Unknown	417 (13.6)	530 (10.4)	1.39	1.21–1.61
Elixhauser Score				
0	1205 (39.4)	1599 (31.5)	1.00	
1-2	1286 (42.0)	2463 (48.4)	0.68	0.62–0.76
3+	569 (18.6)	1022 (20.1)	0.68	0.59–0.78
Flu Shot Before Diagnosis				
No	1590 (52.0)	2372 (46.7)	1.00	
Yes	1470 (48.0)	2712 (53.3)	0.79	0.71–0.87
SEER Region				
Northeast	703 (23.0)	1311 (25.8)	1.00	
Midwest	244 (8.0)	437 (8.6)	1.47	1.19–1.81
South	830 (27.1)	1522 (29.9)	1.09	0.92–1.29
West	1283 (41.9)	1814 (35.7)	1.90	1.60–2.26
Metro/Rural				
Big metro	1714 (56.0)	2734 (53.8)	1.00	
Metro/	903 (29.5)	1499 (29.5)	1.07	0.96–1.20
Other	443 (14.5)	851 (16.7)	1.12	0.96–1.31
Any State Buy-In During -12 – 12 Months (25 Months)				
No	2878 (94.1)	4705 (92.5)	1.00	
Yes	182 (5.9)	379 (7.5)	0.73	0.60–0.88
Zip Code Median Household Income				
1st quartile (lowest)	676 (22.1)	1274 (25.1)	1.00	
2nd quartile	705 (23.0)	1261 (24.8)	1.03	0.89–1.19
3rd quartile	759 (24.8)	1204 (23.7)	1.19	1.02–1.39
4th quartile (highest)	791 (25.8)	1179 (23.2)	1.24	1.05–1.46
Unknown	129 (4.2)	166 (3.3)	1.32	1.01–1.72
Stage				
T1	2855 (93.3)	4668 (91.8)	1.00	
T2	205 (6.7)	416 (8.2)	0.64	0.53–0.77
PSA (median, IQR) (per 0.1)	5.3 (4.2-6.9)	5.4 (4.4-7.0)	0.99	0.99–0.99
Hospital Referral Region Urologist Density (per 100,000)				
<2.45	986 (32.2)	1788 (35.2)	1.00	
2.45-2.84	1096 (35.8)	1596 (31.4)	1.76	1.53–2.02
2.85+	978 (32.0)	1700 (33.4)	1.58	1.34–1.85

* All variables were mutually adjusted in the model.

socioeconomic disparities. Although non-white men were less likely than white men to receive prostate MRI, they were also less likely to receive definitive treatment. This finding is consistent with other reports indicating that non-white patients are less likely to be treated for PCa,[28] and highlights previously unreported racial disparities in the use of advanced imaging for PCa. As racial disparities in gene expression testing for cancer have been observed,[29] additional study is needed to determine whether unequal use of MRI reflects differences in access or acceptance of its use.

There are several limitations of this work that require discussion. Our study included patients diagnosed from 2010-2013, and practice patterns have continued to

evolve since that time. Although the data used represents the most currently available, anticipated increases in the use of MRI and initial observation for men with low-risk PCa might modify the association of imaging and observational management. Patients in the SEER-Medicare database are also older, on average, than men diagnosed in the US with PCa, which may lead to a greater inclination to select observation as management. Further, the observed association between MRI and observation does not imply causality. Therefore, it is possible that MRI did not influence the decision for treatment or observation, but was undertaken as a component of AS. Because we ascertained prostate MRI status based on administrative claims, we are unable to account for the interpretation of the imaging studies themselves. As a result, we do not know whether MRI provided clinically accurate disease predictions, or how clinicians or patients incorporated prostate MRI data into management decisions.

Although, we attempted to control for confounding associated with the decision to perform prostate MRI using propensity score matching, there might still have been residual confounding due to unmeasured factors. However, we suspect that among otherwise low-risk patients, MRI would be more likely to be obtained in equivocal cases favoring a higher-risk profiles, where such misclassification would mask the association of MRI and observation in patients at average or low risk. Additionally, it is possible that a small number of MRIs were performed for the purpose of treatment planning instead of staging. We tried to reduce misclassification by restricting MRIs to be conducted at least 28 days before treatment and by performing sensitivity analyses with different exclusion criteria, which have not significantly changed our results. Even if such a misclassification exists, we expect that this would also bias in favor of underestimating the association of MRI and observation. As a final consideration, we employed a definition of observation as no definitive treatment within 12 months but lack detail regarding the management received, including AS, watchful waiting, or deferred therapy.

A major strength of our study is the large, population-based cohort of patients with low-risk PCa who received clinical care in the real-world setting. The nationwide Medicare claims data covered a wide spectrum of health services, regardless of where the patients sought their care, therefore providing comprehensive information on the care received by patients. Furthermore, the linked SEER-Medicare database also enabled us to control for many other factors that may influence prostate MRI and treatment decisions, such as sociodemographic factors, comorbidity, and urologist density. In addition to adjusting for these factors in a multivariable logistic regression model, we also conducted propensity score matching followed by conditional logistic regression. The similarity between the findings derived from these 2 different analytical strategies was reassuring.

Efforts to facilitate observational approaches for low-risk PCa are highly valuable to improving the quality of cancer care. Because the use of prostate MRI has grown, and is likely to continue expanding, the cost-effectiveness of MRI-driven pathways are increasingly relevant to the sustainability of the practice. Despite initial high costs associated with obtaining and interpreting MRI studies of the prostate, economic modeling studies imply that MRI would be cost-effective if it resulted in increased utilization of AS for low and very-low risk PCa.[30] The association identified in our study between MRI use and initial observation may serve as an informative basis for examining strategies to improve the quality of PCa care with the anticipated growing use of this technology.

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.urology.2018.07.041.

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EDITORIAL COMMENT

Active surveillance and prostate magnetic resonance imaging (MRI) have revolutionized the management of prostate cancer in recent years. This study evaluates the association between the use of prostate MRI and observation for 8144 men with newly diagnosed low-risk prostate cancer using data from the Surveillance, Epidemiology, and End Results-Medicare database. From 2010-2013, the use of MRI increased 3-fold and the use of observation increased from 30.8%-48.1% in these patients. After propensity-score matching to control for potential confounders captured in the data, the authors demonstrate that men who received a prostate MRI surrounding the diagnosis of prostate cancer were significantly more likely to undergo observation. The authors conclude that prostate MRI may increase confidence in the assignment of low-risk classification and thereby facilitate the use of active surveillance for prostate cancer.

This study offers real-world data that may support the beliefs of many urologists: a prostate MRI without suspicious lesions can make a strong case for active surveillance in an otherwise appropriate candidate. However, there are alternative explanations for the association between MRI and observation noted in this study and the authors are appropriately cautious about making an argument for a causal relationship. Prostate MRIs captured in this analysis may have been used in men who were already being managed with active surveillance. In that context, the use of observation "caused" the MRI more than the converse. Alternatively, there may be unmeasured confounders that are associated with both the use of observation and the use of prostate MRI. One such possibility is a characteristic of the treating physician. Physicians who are more likely to order a prostate MRI for their patients may also be more likely to recommend observation for men with low-risk disease. Particularly in the study period (2010-2013), physicians who were earlier adopters of prostate MRI may also have been more likely to recommend active surveillance to their low-risk prostate cancer patients. Propensity-score matching, which the authors used to generate matched cohorts of patients with and without prostate MRI, can only account for covariates that are captured in the data and cannot control for physician- or hospital-factors that are not available in administrative claims.[1]

Understanding the use of active surveillance on a national level is critically important for the field of urology. Despite long-term data from several centers supporting the safety of active surveillance, its use still varies considerably from physician to physician[2] and the optimal protocol remains unknown.[3,4] Innovations such as prostate MRI and biomarker tests offer us the potential to further refine our patient selection, but we do not know exactly how these tools are being used. Analyses such as this one, using nationally representative data, may help us better understand how these pieces fit

together and how we might continue to improve the management of men with prostate cancer.

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AUTHOR REPLY

The ascendance of prostate magnetic resonance imaging (MRI) coincided with a popular reckoning about years of overdiagnosis and overtreatment of low-grade prostate cancer.[1] Prostate MRI has been heralded as a solution to improve accuracy when diagnosing and staging prostate cancer with 2 primary advantages: (1) detecting occult, high-grade cancer in men who would otherwise be missed, allowing timely treatment, and (2) ruling out aggressive disease in men with ostensibly low-risk cancers allowing greater confidence in avoiding treatment. Studies supporting the performance of prostate MRI in identifying clinically significant cancers have been performed under best-case circumstances—largely in high-volume centers of imaging excellence, and by experts using state-of-the-art equipment.[2] Therefore, it is important to begin to evaluate the assumption that MRI will lead to better clinical outcomes in the "real world."

In this context we appreciate the thoughtful editorial addressing our study which examined the association of prostate MRI and initial management among Medicare beneficiaries with low-risk prostate cancer in Surveillance, Epidemiology, and End Results. We found that men who received prostate MRI in the period surrounding their diagnosis were more likely to be initially observed for their disease. As well-stated by the author(s), there are several alternative explanations that are important to consider in the study period where prostate MRI was in its infancy. As a methodological point, we first wish to clarify that patients in this study were included on the basis of a new diagnosis of prostate cancer, limiting the possibility that MRI was undertaken in the setting of prior active surveillance. Nonetheless, it is possible that physicians who used MRI in the early period were more likely to recommend observation as management, particularly in light of known associations of academic institutions and observation for low-risk cancers.[3] Further, we agree with the commentary that administrative claims lack clinical granularity, limiting our understanding of how MRI data was used when making decisions. For these reasons, we took care to not assert a causal relationship between prostate MRI and observation.

Notwithstanding the possibility that the use of prostate MRI is explained by provider-level variation in the use of observational management or other confounders, there are several notable findings from our study.[4] If a causal association is validated in other studies, the utility of MRI in the management of localized prostate cancer will further support its use. In addition, we found regional, racial, and socioeconomic differences in the use of prostate MRI. In light of recent data showing the growing use of MRI in the contemporary period, there is a timely need to determine how new technologies affect entrenched disparities in prostate cancer care and outcome.[5] Continued expansion of prostate MRI into routine care is likely. Anticipating such changes in the use of MRI and other tools, we fully agree that additional study is needed to understand the benefit of these innovations once put into practice.

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