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Clinical-Prostate cancer

A propensity score matched analysis of the effects of African American race on the characteristics of regions of interests detected by magnetic resonance imaging of the prostate

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Abstract

Objectives: To evaluate the effects of African American (AA) race on the number, location, Prostate Imaging Reporting and Data System (PI-RADS) score, cancer detection rate, and cancer upgrade rate of the regions of interest (ROI) discovered on mltiparametric magnetic resonance imaging (mp-MRI) of the prostate.

Methods: We performed an institutional retrospective study of 592 patients who received a prostate mp-MRI. Number of ROI (1−4), their location, and PI-RADS score v2 were evaluated in a matched cohort of Caucasian and AA males. Propensity score matching was performed using the variables of age, prostate specific antigen (PSA) level, and prostate volume. Comparisons utilized chi-square tests and $P < 0.05$ was considered significant.

Results: One hundred and twenty three AA patients were matched with an equal number of Caucasian men of similar characteristics. The AA population's median age was 63 years (57.3−69.3), median PSA 6.6 (4.6−12.1), and median prostate volume 55 ml (33−90.8). The Caucasian population's median age was 66.3 years (60.9−71.1), median PSA 5.4 (3.8−8), and median prostate volume 52.5 ml (33.2−83). The number of ROI was 2 or more in 24% of AA men and 12% of Caucasian men ($P = 0.035$), and 3 or more in 10% of AA and 2% of Caucasian men ($P = 0.034$). There was no significant difference in location, PI-RADS scores, cancer detection rate, and cancer upgrade rate of the ROI between the 2 groups.

Conclusions: AA patients, as compared to Caucasian counterparts, have a higher number of ROI detected on prostate mp-MRI.

Keywords: Prostate cancer; Prostate MRI; Regions of interest; Black race; Number; Location; PIRADS

1. Introduction

Prostate cancer is the most common cancer diagnosis affecting men in the United States with an estimate of 164,690 new cases of prostate cancer that will be diagnosed in 2018 according to the American Cancer Society [1]. For decades, when a patient is suspected of having prostate cancer, a tissue biopsy is offered to achieve a diagnosis. However, the identification and characterization of the disease has needed more precision with increasing interest in nerve sparing surgery, active surveillance (AS), and focal therapy. Advances in magnetic resonance imaging have played a significant role in satisfying this increased need for precision and risk stratification [2]. Multiparametric magnetic resonance imaging (mp-MRI) is now being used for serial monitoring of disease progression in patients during AS for

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Table 1.
Descriptive statistics of the study patients before and after 1:1 matching.

	Overall	White	African American	*P* value	Matched cohort	White	African American	Standardized mean difference
Age	65.5 (59.7−70.7)	66.3 (60.9−71.1)	63 (57.3−69.3)	0.0107	63.1 (57.7−69.1)	63.3 (58.1−68.7)	63.1 (57.5−69.3)	0.527
PSA	5.7 (4.1−8.7)	5.4 (3.8−8)	6.6 (4.6−12.1)	0.0002	6.2 (4.5−10.3)	6.2 (4.4−10)	6.3 (4.6−10.3)	0.095
Prostate volume	52 (33−85)	52.5 (33.2−83)	55 (33−90.8)	0.6332	53.7 (33−89.5)	50 (33−84)	57 (33−91)	0.185

prostate cancer, to guide focal therapy, and to plan surgery high-risk disease [3,4]. It is therefore becoming imperative that we understand the performance of this imaging modality in different patient populations.

This study aimed to review the findings of mp-MRI in AA men and compare their regions of interest regarding the number, location, and Prostate Imaging Reporting and Data System (PI-RADS) characteristics to Caucasian men of matched age, prostate volume, and PSA levels.

2. Methods

We performed a retrospective review of 592 mp-MRI studies of the prostate carried out at our institution between October of 2015 and October of 2017 under an institutional review board approved protocol. Patients included in this study were only individuals who underwent imaging in the course of being considered candidates for AS. Patients undergoing mp-MRI for rising PSA with previous negative biopsies, patients with history of undergoing pre-MRI biopsy outside our system, or for surgical planning were excluded to decrease heterogeneity of the population. Our protocol for imaging the prostate was deployed through a Philips Ingenia 3.0 T MRI system using a 32-element anterior torso phased array coil coupled with an integrated posterior 20 element array in the tabletop. The protocol itself consisted of large field of view (FOV) (32 cm or greater) 2D fast spin-echo T2-weighted images with fat suppression and 3D T1 gradient-echo (GRE) with Dixon fat-water separation (fat, water, in-phase, out-of-phase reconstructions); small FOV (18 cm) fast spin-echo T2 images of the prostate in the axial, sagittal, and coronal planes; axial diffusion weighted images in small FOV (Philips, 18 cm) and larger FOV (GE, 30 cm); small (22 cm) FOV bolus IV gadolinium chelate dynamic contrast enhanced T1 GRE series (20 serial postcontrast phases, temporal resolution <10 seconds); and a final large FOV pelvic postcontrast T1 GRE Dixon (water reconstruction) series. Examinations were interpreted and analyzed using DynaCAD (Invivo, Gainesville, FL). All of the studies were read by fellowship-trained radiologists. All of the biopsies examined in the study were magnetic resonance imaging targeted biopsies performed by 1 urologist at our institution using the UroNav machine (Invivo, Gainesville, FL). The procedure was performed with the assistant of local injectable anesthesia and under informed consent. The targeted biopsy was performed first (2−4 cores) followed by 12 systemic biopsies distributed throughout the 6 areas of the prostate (right base, right mid, right apex, left base, left mid, and left apex). The tissue was examined by genitourinary trained pathologists, and the results reported according to the International Society of Urological Pathology recommendations for reporting prostate cancer biopsy results. Tissue obtained from the targeted biopsy was sent separately for pathologic examination.

Cancer detection rate (CDR) was defined as identifying any Gleason 3+3 (Grade Group 1) prostate cancer or higher. Cancer upgrade rate (CUR) was defined as identifying any new cancer Gleason 3+4 (Grade Group 2) or higher. In this study, we used propensity-matching (1:1 Greedy nearest neighbor matching with a caliper of 0.1) of our selected AA patients with Caucasian patients to control for confounders using the variables of age, PSA level, and prostate volume (Table 1). Propensity score matching is a statistical matching technique that attempts to reduce the bias due to confounding variables that could be found in an estimate of the outcome of interest obtained from merely comparing subjects who had the exposure (in this case AA race) to those who did not. We made sure that our covariates are balanced across the racial groups within strata of the propensity score. We then compared the characteristics of the ROI found on mp-MRI (number, location, and PI-RADS score) between AA and Caucasian patients using univariate analysis. Categorical variables were compared using a chi-square test, while numeric variables were analyzed using a *t* test when assumptions were met. The final pathology results of patients in this study who were treated with radical prostatectomy were also included for completeness and analyzed using simple univariate analysis. Only ROIs with PI-RADS score above 2 were included in this report.

3. Results

One hundred and twenty three AA patients were matched with an equal number of Caucasian patients. The AA population's median age was 63 years (57.3−69.3), median PSA 6.6 (4.6−12.1), and median prostate volume 55 ml (33−90.8). The Caucasian population's median age was 66.3 years (60.9−71.1), median PSA 5.4 (3.8−8), and median prostate volume 52.5 ml (33.2−83). No significant differences were identified in age, PSA level, or prostate volume stratified by race in the matched cohort ($P > 0.05$). The

Table 2.
Number of the regions of interest detected on multiparametric magnetic resonance imaging of the prostate stratified by patients' race.

Population	No significant lesion (no lesion or PIRADS 2)	1 lesion	2 or more lesions	3 or more lesions	Overall *P* value	Total
African American	50%	26%	24%	10%	0.025	123
Caucasian	60%	28%	12%	2%		123

number of ROI was 2 or more in 24% of AA men and 12% of Caucasian men ($P = 0.035$), and 3 or more in 10% of AA and 2% of Caucasian men ($P = 0.340$) (Table 2). The position of the ROI in the peripheral zone vs. transition zone, right side vs. left side, prostate apex vs. middle vs. base is described using percentages in Fig. 1. The location of the ROI was not affected by race in any of these comparisons (Table 3).

Finally, AA patients were not significantly different from Caucasian patients when comparing proportions of ROI with PI-RADS 3, 4, or 5.

3.1. Targeted biopsy results

The overall CDR was 50%, and the CUR was 41%. CDR and CUR differed significantly with PI-RADS v2 score. Higher PI-RADS v2 score was associated with higher CDR ($P < 0.0001$) and CUR ($P < 0.0001$). CDR and CUR among African American patients were 56 and 42%, respectively, vs. 45% and 30% for Caucasian patients. Although higher in African American patients, neither CDR ($P = 0.3294$) nor CUR ($P = 0.3465$) were significantly different between the 2 groups.

3.2. Postprostatectomy pathology results

Twenty AA patients and 25 Caucasian patients were treated with radical prostatectomy. The number of patients treated with surgery was too small for meaningful comparison, but adverse pathologic features did not predominate in either of the 2 racial groups.

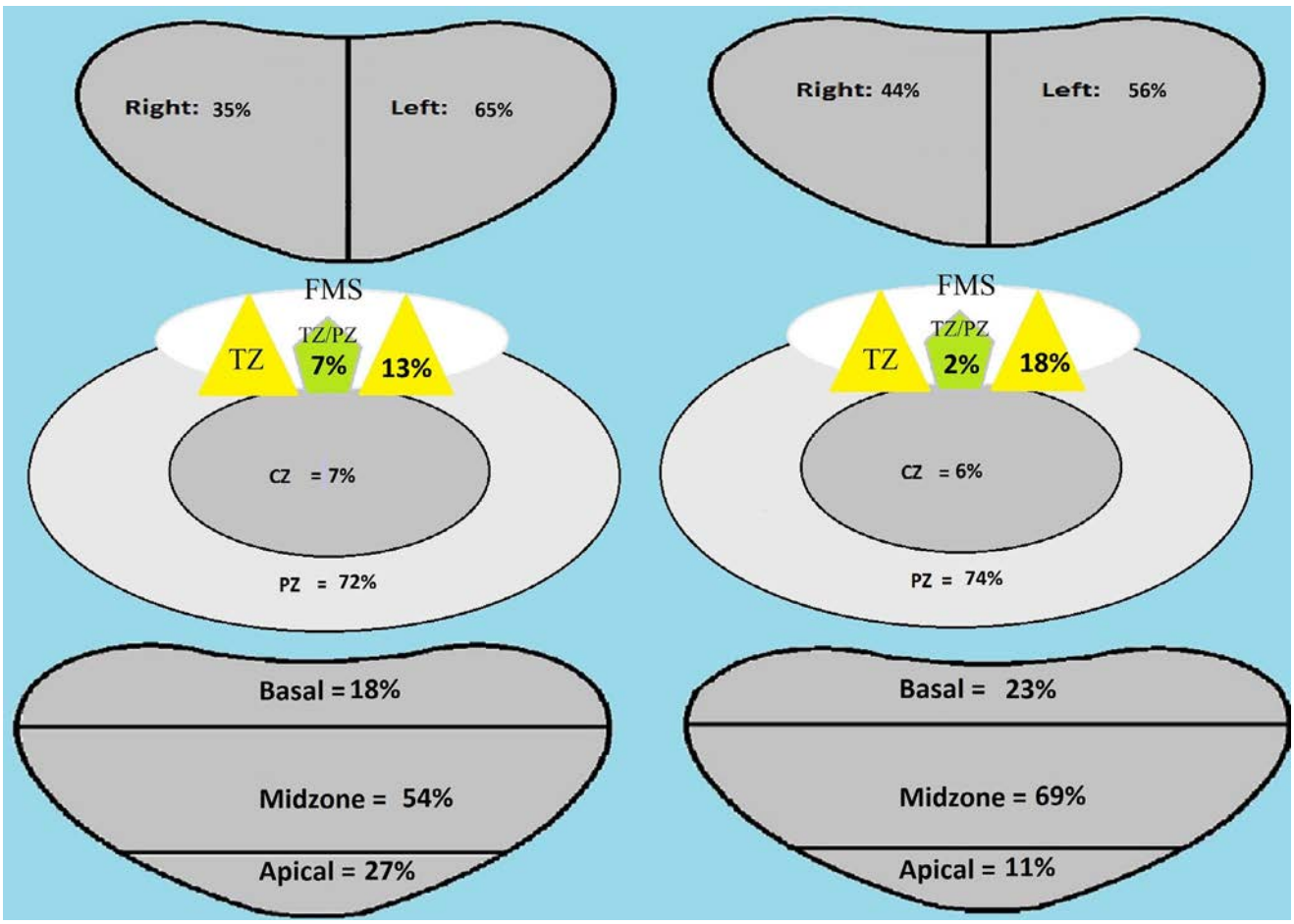

Fig. 1. Distribution of the regions of interest seen on magnetic resonance imaging of the prostate in African American (left) and Caucasian patients (right) treated at Henry Ford Health System in Detroit.

Table 3.
Results of the analysis of the association of race with the location of region of interest on multiparametric magnetic resonance imaging of the prostate.

	CZ	TZ	PZ	*P* value	R	L	*P* value	APEX	MID	BASE	*P* value
African American	7%	20%	72%	0.615	35%	65%	0.164	27%	54%	18%	0.321
Caucasian	6%	20%	74%		44%	56%		11%	69%	23%	

CZ = central zone; L = left side; PZ = peripheral zone; R = right side; TZ = transition zone.

4. Discussion

In this study, through a propensity score-matched analysis, we found that AA patients have more ROI when compared to Caucasian patients of the same age, PSA level, and prostate size. We also found that ROI are generally similar in location and PI-RADS score in AA and Caucasian patients. The results of our study have clinical implications. First, our results help validate PI-RADS v2 for use in AA patients. By showing that PI-RADS v2 assigned an equal proportion of significant [3–5] ROI to AA and Caucasian patients, one can conclude that it is safe to assume that v2 is not leading to an increased rate of prostate biopsy in AA patients by disproportionately assigning high PI-RADS scores to their lesions [5]. Second, we show that prostate nomograms that control for the number of lesions seen on MRI may want to consider taking the race of the patients into account. Stamatakis et al. demonstrated in their institutional retrospective study that 29% of the patients in their cohort who were initially on AS based on mp-MRI were later reclassified as not meeting criteria to be on AS after confirmatory biopsy [6]. In this study, reclassification was strongly associated with the number of lesions, lesion density, and highest MRI lesion score. Without taking race into account, AA patients will be predicted to have a higher chance of going off AS, based on their higher number of ROI, when their likelihood of being diagnosed with significant cancer may not have been higher than their Caucasian counterparts. In fact, Shin et al. retrospectively analyzed 661 patients (117 AA) who had mp-MRI before biopsy and then underwent MRI/US image fusion targeted biopsy and did not find significant differences between AA and Caucasian men in the detection rate of overall cancer (35.0% vs. 34.2%, $P = 0.9$) and clinically significant prostate cancer (Gleason ≥ 7) (18.8% vs. 21.7%, $P = 0.3$) with fusion biopsy [7]. This study also validates our findings of no significant differences between the races in the location of dominant lesions on mp-MRI, and in the proportion of PI-RADS scoring. Finally, our results may help counsel AA patients on the possibility and benefit of focal therapy of prostate cancer. Mouraviev et al. studied the rationale of focal ablative treatment for localized prostate cancer based on the laterality of tumors in paraffin-embedded radical prostatectomy specimens and concluded that AA men may not be the best candidates for focal therapy because their prostate cancer was more likely to involve both sides of the prostate when compared with Caucasian patients [8]. We show that, based on magnetic resonance imaging, AA patients are not different from Caucasian patients when it comes to the laterality of ROI. Therefore, since MRI is the guiding technology for many of the focal therapy platforms, and since lesions not seen on MRI are significant in a limited number of patients, AA males should not be excluded from future studies assessing the safety and efficacy of focal treatment of prostate cancer.

The higher number of PI-RADS 2 lesions in AA patients deserves an explanation. We hypothesize that many of these PI-RADS 2 areas are related to inflammation or benign prostatic hyperplasia, both are more prevalent in AAs. The prevalence of prostatitis has been shown previously to be higher in AA men compared to Caucasian men, 40.7% vs. 28.7%, respectively. [9]. This higher prevalence of prostatitis in AAs may, in turn, lead to a higher number of lesions detected by prostate MRI since prostatitis shows early enhancement with heterogeneous appearance and patchy pattern and may mimic prostate cancer [10]. There is also a possible field change-related explanation to the higher number of lesions in AA patients.

Devaney et al. recently reported that genome-wide methylation patterns differed by ethnic/racial groups [11], which suggests distinct differences in the field development of prostate cancer in AA vs. Caucasian men.

There are several limitations to the present study. First, our database is retrospective. Second, the study MRIs were reviewed independently by multiple fellowship-trained radiologists who may have different levels of experience with prostate MRI reading and interpretation, however, these radiologists are exposed to a high volume of mp-MRI of the prostate at our institution and are likely to have reached a point in the their learning curve to provide accurate readings that can be validated by an external reviewer. Third, with the high volume of pathology samples examined by our pathologists, it was not logistically feasible to ask for a consensus pathology examination for each sample included in this study. However, since all prostate samples are examined by a small group of specialized genitourinary pathologists with frequent intradepartmental consultation for challenging cases, we believe that discrepancies in diagnosis and grading would be minimal. Fourth, we acknowledge the limitations that come with the small number of patients in the study like the possibility of not having enough power to detect small differences. Fifth, we performed the matching as a way to control for

confounders and thus allow us to present our univariable results after matching, but multivariable analysis with a larger number of patients could have produced different results. Finally, many of our patients did not undergo radical prostatectomy to further correlate with distribution of lesions. We are thus unable to verify the impact of the additional lesions in AA men on their postprostatectomy CUR.

5. Conclusions

AA patients, as compared to Caucasian counterparts, have a higher number of lesions detected on prostate mp-MRI. The other characteristics of ROI suspicious for prostate cancer on MRI were similar between the 2 groups.

Conflicts of interest

None.

References

[1] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin 2018;68:7–30.

[2] Reva S, Nosov A, Novikov R, Petrov S. Imaging and markers as novel diagnostic tools in detecting insignificant prostate cancer: a critical overview. Int Sch Res Notices 2014;2014:243080.

[3] Kasivisvanathan V, Rannikko AS, Borghi M, Panebianco V, Mynderse LA, Vaarala MH, et al. MRI-targeted or standard biopsy for prostate-cancer diagnosis. N Engl J Med 2018;378:1767–77. https://doi.org/10.1056/NEJMoa1801993:Epub 2018 Mar 18.

[4] Mehralivand S, Shih JH, Rais-Bahrami S, Oto A, Bednarova S, Nix JW, et al. A magnetic resonance imaging-based prediction model for prostate biopsy risk stratification. JAMA Oncol 2018;4:678–85. https://doi.org/10.1001/jamaoncol.2017.5667.

[5] Weinreb JC, Barentsz JO, Choyke PL, Cornud F, Haider MA, Macura KJ, et al. PI-RADS prostate imaging—reporting and data system: 2015, version 2. Eur Urol 2016;69:16–40.

[6] Stamatakis L, Siddiqui MM, Nix JW, Logan J, Rais-Bahrami S, Walton-Diaz A, et al. Accuracy of multiparametric magnetic resonance imaging in confirming eligibility for active surveillance for men with prostate cancer. Cancer 2013;119:3359–66.

[7] Shin T, Smyth TB, Ukimura O, Ahmadi N, de Castro Abreu AL, Oishi M, et al. Detection of prostate cancer using magnetic resonance imaging/ultrasonography image-fusion targeted biopsy in African-American men. BJU Int 2017;120:233–8.

[8] Mouraviev V, Sun L, Madden JF, Mayes JM, Moul JW, Polascik TJ. Prostate cancer laterality does not predict prostate-specific antigen recurrence after radical prostatectomy. Urology 2007;70:1141–5.

[9] Carver BS, Bozeman CB, Williams BJ, Venable DD. The prevalence of men with National Institutes of Health category IV prostatitis and association with serum prostate specific antigen. J Urol 2003;169:589–91.

[10] Shenoy D, Packianathan S, Chen AM, Vijayakumar S. Do African-American men need separate prostate cancer screening guidelines? BMC Urol 2016;16:19.

[11] Devaney JM, Wang S, Furbert-Harris P, Apprey V, Ittmann M, Wang BD, et al. Genome-wide differentially methylated genes in prostate cancer tissues from African-American and Caucasian men. Epigenetics 2015;10:319–28.