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Original Article

Impact of United States Preventive Services Task Force recommendations on prostate biopsy characteristics and disease presentation at a tertiary-care medical center

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ABSTRACT

Background: To evaluate early consequences of 2012 United States Preventive Services Task Force (USPSTF) recommendations for decreased prostate-specific antigen (PSA) screening on prostate biopsy characteristics and prostate cancer presentation.

Materials and methods: A single tertiary-care institution, multisurgeon, prospectively maintained database was queried for patients undergoing prostate biopsy from October 2005 to September 2016. Patient demographics, biopsy characteristics, and extent of disease were reported. Patient cohorts before and after USPSTF recommendations were compared using two-sample *t* test, Chi-square test, and Wilcoxon rank sum test with significance at $P < 0.05$.

Results: A total of 2,000 patients were analyzed, including 1,440 patients before and 560 patients after USPSTF recommendations. Following the recommendations, patients had higher prebiopsy PSA (5.90 vs. 6.70, $P < 0.001$). Overall, 817 (40.9%) patients had prostate cancer detected at biopsy with an increase from 37.0% before to 50.8% after ($P < 0.001$). Biopsies detected less low-risk Gleason $\leq$6 prostate cancer (47.4% vs. 41.1%) and more intermediate-risk Gleason 7 cancer (30.9% vs. 39.7%), with comparable findings of high-risk Gleason $\geq$8 cancer (21.7% vs. 19.2%), $P = 0.042$. In addition, greater percentage of core involvement ($P < 0.001$) was seen. At the time of diagnosis, extraprostatic extension identified by pelvic imaging increased from 12.6% to 18.9%, $P = 0.039$, with a trend toward lymph node positivity (1.1% vs. 2.2%, $P = 0.078$). Of those with metastatic disease, bony involvement occurred more often (1.7% vs. 3.2%, $P = 0.041$).

Conclusions: After 2012 USPSTF guidelines, patients presented with higher PSA with prostate cancer were detected more frequently. More adverse, pathologic prostate cancer features were found on biopsy with the extent of disease implicating locally advanced/metastatic disease. These findings should be considered when counseling patients about prostate cancer screening importance.

1. Introduction

Prostate cancer is the most commonly diagnosed non-dermatologic malignancy and third leading cause of cancer-related death in men in the United States. The American Cancer Society in 2017 estimated that 161,360 new cases would be diagnosed with 26,730 deaths directly attributable to prostate cancer.[1,2] Screening for prostate cancer through prostate-specific antigen (PSA) and digital rectal examination (DRE) has reduced prostate cancer mortality by 50% over the past 20 years.[3] However, PSA screening for the early diagnosis and treatment of prostate cancer has recently been called into question.

The efficacy of PSA screening was examined through two large-scale randomized control trials, namely the European Randomized Study of Screening for Prostate Cancer and the U.S. Prostate, Lung, Colorectal, and Ovarian trial.[4,5] Largely based on these two studies, the United States Preventive Services Task Force (USPSTF) in May

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2012 formally recommended against the use of population-based PSA screening for prostate cancer, issuing a Grade D recommendation discouraging the practice altogether.[6] In the years since the 2012 USPSTF recommendation against PSA screening, PSA testing and DRE have decreased substantially leading to a decline in the incidence of prostate cancer.[7–9] The unintended consequence of this pendulous decision away from prostate cancer screening is the possibility for increases in prostate cancer mortality and an excess of adverse cancer-specific outcomes.[10–12]

Reductions in the detection of early-stage prostate cancer incidence and PSA-based prostate cancer screening rates in men aged 50 years and older have been reported in the literature, coinciding with the 2012 USPSTF recommendations.[8] It remains speculative, however, whether this decrease will ultimately affect the overall course of disease and if patients will present with more advanced or metastatic prostate cancer. In this study, we evaluated the early consequences of decreased PSA screening on prostate biopsy characteristics and presentation of prostate cancer. Our aim was to determine if in our clinical practice patients presented with more advanced prostate cancer at the time of diagnosis and with higher rates of metastatic disease since widespread implementation of the 2012 USPSTF guidelines.

2. Methods

Institutional review board approval was obtained for a retrospective review of a single tertiary-care institution, multisurgeon, prospectively maintained database for all patients undergoing prostate needle biopsy (PNB) between October 2005 and September 2016. Patients were excluded if complete records were not available for analysis. Those with evidence of prostate cancer on PNB were defined as having histologic evidence of prostatic adenocarcinoma on at least one core of tissue. Prostatic intraepithelial neoplasia and atypical small acinar proliferation (ASAP) in the absence of any prostatic adenocarcinoma were considered premalignant and thus benign. Rare nonadenocarcinoma histologies arising from the prostate were excluded.

Prostate biopsies were performed using the BK Medical Falcon 2101 and the BK Flex Focus 300 from BK Ultrasound North America, Peabody, MA. No MRI (magnetic resonance imaging)/US (ultrasound) fusion biopsies were included in these data as this technology was not available at our institution during the time period of the study. A Prostate Biplane 8808e simultaneous biplane transducer was used for real-time imaging during biopsy. An average of 13 prostate biopsy cores were obtained for each patient in our study population.

The population was subdivided into two cohorts. Patients comprising the pre-2012 USPSTF recommendation cohort were analyzed from October 2005 to May 2012, and patients post-2012 USPSTF recommendation were analyzed from June 2012 to September 2016. Patient demographics (age, ethnicity, DRE, and prebiopsy PSA), biopsy characteristics (prostate volume determined by transrectal ultrasound, number of biopsy cores, presence of prostate cancer, Gleason score, and percentage core involvement), and extent of disease (extraprostatic extension on either MRI or computed tomography imaging of the pelvis, lymph node positivity on imaging, and presence of bony metastatic disease) were reported. Gleason scores of each patient were further categorized as low-risk (Gleason $\leq$ 6), intermediate-risk (Gleason 7), and high-risk (Gleason $\geq$ 8) prostate cancer.

Patient cohorts before and after USPSTF recommendations were compared using two-sample *t* test, Chi-square test, and Wilcoxon rank sum test, where appropriate, with significance set at $P < 0.05$. All analyses were performed using SAS 9.4 (SAS Institute Inc., NC, USA).

3. Results

A total of 2,000 patients were analyzed, including 1,440 patients before and 560 patients after the 2012 USPSTF recommendations were published. Average age between the two groups was nearly equivalent (64.0 years vs. 64.1 years, $P = 0.712$). Most patients were Caucasian, 89.8% and 85.2% between the prerecommendation and postrecommendation cohorts, respectively, with African American, Hispanic/Latino, Asian, and Native American ethnicities also represented. There was statistical significance seen in patients having abnormal DRE (49.5% vs. 42.5%, $P = 0.007$) although these abnormalities were not further stratified to determine if this was merely prostatic enlargement or examination findings concerning malignancy. Following the recommendations, patients presented with a higher prebiopsy PSA of 6.70 [95% confidence interval (CI): 4.73–10.00] than that reported before recommendations were published, which was 5.90 (95% CI: 4.13–8.70), $P < 0.001$ (Table 1).

Prostate size was similar between both the groups, 40.1 cc vs. 39.7 cc, with a median of 13 biopsy cores taken in each group. Overall, 817 (40.9%) patients had prostate cancer detected at biopsy with an increase from 37.0% before to 50.8% after USPSTF recommendations were published ($P < 0.001$). Biopsies detected less low-risk Gleason $\leq$6 prostate cancer (47.4% vs. 41.1%) and more intermediate-risk Gleason 7 cancer (30.9% vs. 39.7%), with comparable findings of high-risk Gleason $\geq$8 cancer (21.7% vs. 19.2%), $P = 0.042$. In addition, greater percentage of core involvement ($P < 0.001$) was seen (Table 2).

At the time of diagnosis, extraprostatic cancer extension identified by either computed tomography or MRI pelvic imaging increased from 12.6% to 18.9%, $P = 0.039$. Pelvic imaging also detected a trend toward lymph node positivity defined as lymph nodes >1 cm in size within the pelvis (1.1% vs. 2.2%, $P = 0.078$). Of those with metastatic disease at the time of diagnosis, bony involvement occurred more often (1.7% vs. 3.2%, $P = 0.041$) (Table 3).

A total of 363 patients were elected to undergo radical prostatectomy for treatment of prostate cancer. Radical prostatectomy comprised 42.0% (n = 139) in the earlier cohort compared with 48.9% (n = 224) in the later cohort, $P = 0.065$. Alternative therapies included patients undergoing active surveillance (17.4% vs. 19.0%, n = 147 patients; $P = 0.633$), external beam radiation therapy alone (16.1% vs. 11.3%, n = 118 patients; $P = 0.061$), androgen deprivation therapy alone (6.2% vs. 5.6%, n = 49 patients; $P = 0.877$), and external beam radiation therapy plus androgen deprivation therapy (12.2% vs. 7.4%, n = 85 patients; $P = 0.041$) (Table 4). For patients who underwent radical prostatectomy, final pathology comparing the two groups showed Gleason $\leq$6 prostate cancer in 22.8% vs. 19.4% ($P = 0.512$), Gleason 7 prostate cancer in 52.7% vs. 60.4% ($P = 0.159$), and Gleason $\geq$ 8 prostate cancer in 8.9% vs. 16.5% ($P = 0.044$) (Table 5).

4. Discussion

The USPSTF in 2008 changed the recommendation for PSA screening to a D grade (recommending against screening) in men $\geq$ 75 years of age, stating that there was not enough evidence that screening in this age group and ultimately active treatment for prostate cancer resulted in greater benefit than watchful waiting alone.[13] This statement was then further expanded in May 2012, when the USPSTF updated their recommendation to a D grade for PSA screening in all men regardless of age citing that the benefits of PSA screening do not outweigh the harms, including the high false-positive rate, negative psychological effects, complications of PNB, and the risk for overdiagnosis and overtreatment of the patient.[6] The effects of these recommendations have been widespread,

Table 1
Patient demographics.

Variable	Before May 2012 USPSTF recommendations (n = 1,440)	After May 2012 USPSTF recommendations (n = 560)	*P*
Age (y)	64.0	64.1	0.712
Ethnicity			0.005
Caucasian	1,291 (89.8%)	476 (85.2%)	
African American	70 (4.9%)	40 (7.2%)	
Hispanic/Latino	46 (3.2%)	33 (5.9%)	
Asian	20 (1.4%)	3 (0.5%)	
Native American	1 (0.1%)	1 (0.2%)	
Other	9 (0.6%)	6 (1.1%)	
Abnormal DRE	685 (49.5%)	225 (42.5%)	0.007
Prebiopsy PSA (ng/mL)	5.90 (4.13–8.70)	6.70 (4.73–10.00)	<0.001
Prior biopsy	470 (32.6%)	170 (30.4%)	0.326

DRE, digital rectal examination; PSA, prostate-specific antigen; USPSTF, United States Preventive Services Task Force.

affecting prostate cancer screening both locally in the United States and internationally.[14] Subsequent to the 2012 USPSTF recommendations, Shoag et al reported a 64% decrease in DRE screening and a 39% decrease in PSA screening,[9] and McGinley et al demonstrated a 21.4% decrease in PNB for prostate cancer diagnosis in the 2 years following the USPSTF official statement.[15] Banerji et al found an even greater decline in PNB. The number of biopsies performed during the 30-month period before and after USPSTF recommendations was analyzed, with a 31% decrease in biopsies performed.[16] This has translated into a 16.2% decrease in radical prostatectomy volume when operative case logs available from the American Board of Urology were studied from a nationally representative sample of urologists.[17]

The present study reviewed the early effects of the 2012 USPSTF recommendations at a tertiary-care academic institution on PNB characteristics and prostate cancer presentation. Higher rates of prostate cancer diagnosis were seen following the 2012 statement, with the rate of positive biopsy increasing from 37.0% to 50.8% ($P < 0.001$). With this, there was a shift toward higher PSA at initial presentation from 5.90 to 6.70 ($P < 0.001$), suggesting the possibility of more advanced prostate cancer histology and burden. We saw a decrease of 6.3% in low-risk Gleason ≤6 prostate cancer, whereas intermediate-risk cases increased by 8.8%, and high-risk cases were nearly equivalent ($P = 0.042$). In addition, on

Table 2
Prostate biopsy characteristics.

Variable	Before May 2012 USPSTF recommendations (*n* = 1,440)	After May 2012 USPSTF recommendations (*n* = 560)	*P*
Prostate volume (cc) determined on TRUS	40.1 (30.0, 60.0)	39.7 (29.0, 59.0)	0.240
Number of biopsy cores	13 (12, 17)	13 (13, 14)	0.341
Prostate cancer on biopsy	533 (37.0%)	284 (50.8%)	<0.001
Gleason scores			0.042
Low risk (Gleason ≤ 6)	251 (47.4%)	116 (41.1%)	
Intermediate risk (Gleason 7)	164 (30.9%)	112 (39.7%)	
High risk (Gleason ≥ 8)	115 (21.7%)	54 (19.2%)	
Core involvement (%)	2.0 (0, 30)	13.0 (0, 60)	<0.001

TRUS, transreectal ultrasound; USPSTF, United States Preventive Services Task Force.

Table 3
Extent of disease at time of diagnosis.

Variable	Before May 2012 USPSTF recommendations (*n* = 1,440)	After May 2012 USPSTF recommendations (*n* = 560)	*P*
Extraprostatic extension (EPE) on imaging (MRI or CT pelvis)	181 (12.6%)	106 (18.9%)	0.039
Lymph node (LN) positivity on imaging (MRI or CT pelvis)	16 (1.1%)	12 (2.1%)	0.078
Presence of bony metastatic disease	25 (1.7%)	18 (3.2%)	0.041

CT, computed tomography; MRI, magnetic resonance imaging; USPSTF, United States Preventive Services Task Force.

inspecting radical prostatectomy specimens, there was a clinically significant increase in high-risk Gleason 8–10 disease ($P = 0.044$) seen in the cohort of patients following the recommendations. These findings may represent an early shift toward more adverse, pathologic prostate cancer as patients present later due to decreased PSA testing. Furthermore, when we analyzed patients for signs of locally advanced and metastatic disease before active treatment, patients were found to be 6.3% ($P = 0.039$) more likely to have extraprostatic extension, which is a known predictor of biochemical recurrence following radical prostatectomy.[18] Markers for extent of disease were studied, and a modest trend toward an increase in clinically significant pelvic lymph nodes on imaging (1.1% vs. 2.2%, $P = 0.078$) was found, along with an increase in bony metastases in those patients presenting with metastatic prostate cancer at time of diagnosis (1.7% vs. 3.2%, $P = 0.041$).

Several studies have reported an increase in positive biopsy rates since implementation of the USPSTF recommendations. Olsson et al reported annual increases in positive PNB rates, from 39% in 2010–2011 to 41.4% in 2013, 42.6% in 2014, and 46% in 2015 ($P < 0.001$).[19] Gaylis et al documented an increase in prostate cancer on PNB from 46% to 50% ($P = 0.0001$),[20] and Porter et al similarly found a 36% decrease in biopsies containing no cancer and 15% decrease in biopsies with Gleason 6 prostate cancer in the 2 years and 6 months after USPSTF recommendations, suggesting a trend toward more positive biopsies and those with higher grade cancers.[16]

Examination of the literature corroborates this concerning trend in migration toward more advanced prostate cancer at time of initial presentation. Data extracted from the National Oncology Data Alliance on 87,562 men revealed a rise in the percentage of men with intermediate-risk or high-risk prostate cancer by 2.9% per year after 2011 ($P < 0.003$).[21] Evaluation of the National Cancer Database by Dalela et al noted in the time frame immediately surrounding the release of the 2012 USPSTF recommendations a decrease in low-risk prostate cancer at diagnosis from 31.9% in 2011 to 25.9% in 2013, a corresponding increase in intermediate-risk cancer from 43.5% to 45.1%, and high-risk cancer from 24.5% to 29.0% (all $P < 0.001$).[22] In addition, Shah et al reported data from patients diagnosed with prostate cancer by PNB between 2010 and 2013 and compared these with those of patients diagnosed between 2015 and 2016. They discovered a 5.4% higher incidence of Gleason 7–10 prostate cancer in the post-USPSTF recommendations period.[23]

These trends have raised concern on increased incidence of metastatic prostate cancer at time of diagnosis. Hu et al found that in men <75 years between 2011 and 2013, there was an increase in the proportion of men with distant metastases at initial presentation from 2.7% (95% CI: 2.5–2.9%) to 4.0% (95% CI: 3.8–4.2%) that coincided with an increase in intermediate- and high-risk prostate

Table 4
Therapy after prostate cancer diagnosis.

Variable	Before May 2012 USPSTF recommendations (n = 533)	After May 2012 USPSTF recommendations (n = 284)	*P*
Radical prostatectomy	224 (42.0%)	139 (48.9%)	0.065
Active surveillance	93 (17.4%)	54 (19.0%)	0.633
EBRT	86 (16.1%)	32 (11.3%)	0.061
ADT	33 (6.2%)	16 (5.6%)	0.877
EBRT + ADT	65 (12.2%)	21 (7.4%)	0.041

ADT, androgen deprivation therapy; EBRT, external beam radiation therapy; USPSTF, United States Preventive Services Task Force.

Table 5
Radical prostatectomy outcomes.

Variable	Before May 2012 USPSTF recommendations (n = 224)	After May 2012 USPSTF recommendations (n = 139)	*P*
Gleason ≤ 6	51 (22.8%)	27 (19.4%)	0.512
Gleason 7	118 (52.7%)	84 (60.4%)	0.159
Gleason ≥ 8	20 (8.9%)	23 (16.5%)	0.044

USPSTF, United States Preventive Services Task Force.

cancer from 46.3% (95% CI: 45.9–46.9%) to 56.4% (95% CI: 55.9–56.9%) ($P < 0.01$).[24] Dalela et al in a population-based data review from 18 SEER (surveillance epidemiology and end results) registries noted that the incidence of metastatic prostate cancer increased significantly between 2009 and 2013 at a rate of 3.1% per year ($P < 0.05$). On age stratification, men aged 45–54 years and 55–64 years experienced a continuous increase of 1.77% and 1.45% per year ($P < 0.05$), respectively, in metastatic prostate cancer.[25]

Limitations of this study include its retrospective design and the biases inherent to this. In addition, this was a study analyzing patients at a tertiary-care academic institution. The generalizability of this patient population may be limited due to the complexity of patients seen within this setting. Finally, it is difficult to know whether the effects seen in this study are due to decreased PSA screening as a result of the 2012 USPSTF recommendations or if improved patient selection has led to greater yield in diagnosing patients and thus should be interpreted within this context.

5. Conclusion

As public health policy regarding PSA screening is revised over the coming years, it is important to analyze the downstream effects of reduced screening guidelines and its sequelae. It has been estimated that abandonment of PSA screening would lead to a 13–20% increase in prostate cancer mortality, and the incidence of metastatic disease would more than double.[26,27] There is an urgent need to provide uniform guidelines to reduce the discrepancies seen in prostate cancer screening for both urologists and general practitioners alike.[28,29] As such, the USPSTF recently released a draft statement on prostate cancer screening, changing the recommendation to a Grade C for men aged 55–69 years but maintaining the Grade D recommendation for men ≥70 years. This study demonstrated an increase in PSA at presentation, a greater incidence of PNB positivity, biopsy results with less Gleason ≤6 and more Gleason 7–10 prostate cancer at diagnosis, radical prostatectomy specimens with more high-risk disease, and extent of disease implicating higher rates of locally advanced or metastatic prostate cancer. These findings should be considered when counseling patients about the importance of prostate cancer screening.

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Conflicts of interest

None of the authors have any conflicts of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.prnil.2018.03.001.

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