Letters

RESEARCH LETTER

Use of Active Surveillance or Watchful Waiting for Low-Risk Prostate Cancer and Management Trends Across Risk Groups in the United States, 2010-2015

Historically, most patients with low-risk prostate cancer (clinical category T1c-T2a, prostate-specific antigen level <10 ng/mL, and Gleason 6 disease) were treated with radical prostatectomy, while radiotherapy-based treatment was the favored approach for high-risk localized prostate cancer.[1] However, conservative management of low-risk prostate cancer with active surveillance or watchful waiting (AS/WW) offers an alternative to radical prostatectomy or radiotherapy,[2] and national guidelines began advocating its use in 2010.[3,4] Nevertheless, current AS/WW rates across the United States are not well established, and it is unclear if increasing acceptance of AS/WW for low-risk prostate cancer might be associated with changes in management patterns in higher-risk prostate cancer. Therefore, we examined US trends in management patterns for localized prostate cancer across risk groups.

Methods | The custom Surveillance, Epidemiology, and End Results (SEER) Prostate Active Surveillance/Watchful Waiting database, unlike other databases, includes a quality-assured AS/WW variable.[5] The proposal for this study was approved by the SEER custom data group. All men with localized prostate cancer diagnosed between 2010 and 2015 and known management type were included.

Patients designated by treating facilities as receiving AS or WW as management without any receipt of definitive therapy were coded by SEER as AS/WW.[5] If changes from AS/WW to definitive therapy occurred within 1 year of diagnosis for reasons other than disease progression, the cases were coded as the definitive therapy used. Definitive therapy types were defined by SEER as either definitive radical prostatectomy or radiotherapy (including external-beam radiotherapy, brachytherapy, or any combination thereof); the positive predictive value and specificity of both variables are high.

Baseline characteristics, stratified by year of diagnosis, were summarized by descriptive statistics. Use of initial

Table. Baseline Characteristics by Year of Diagnosis Among Men Diagnosed as Having Localized Prostate Cancer in the United States From 2010 to 2015 in the SEER Prostate Active Surveillance/Watchful Waiting Database[a]

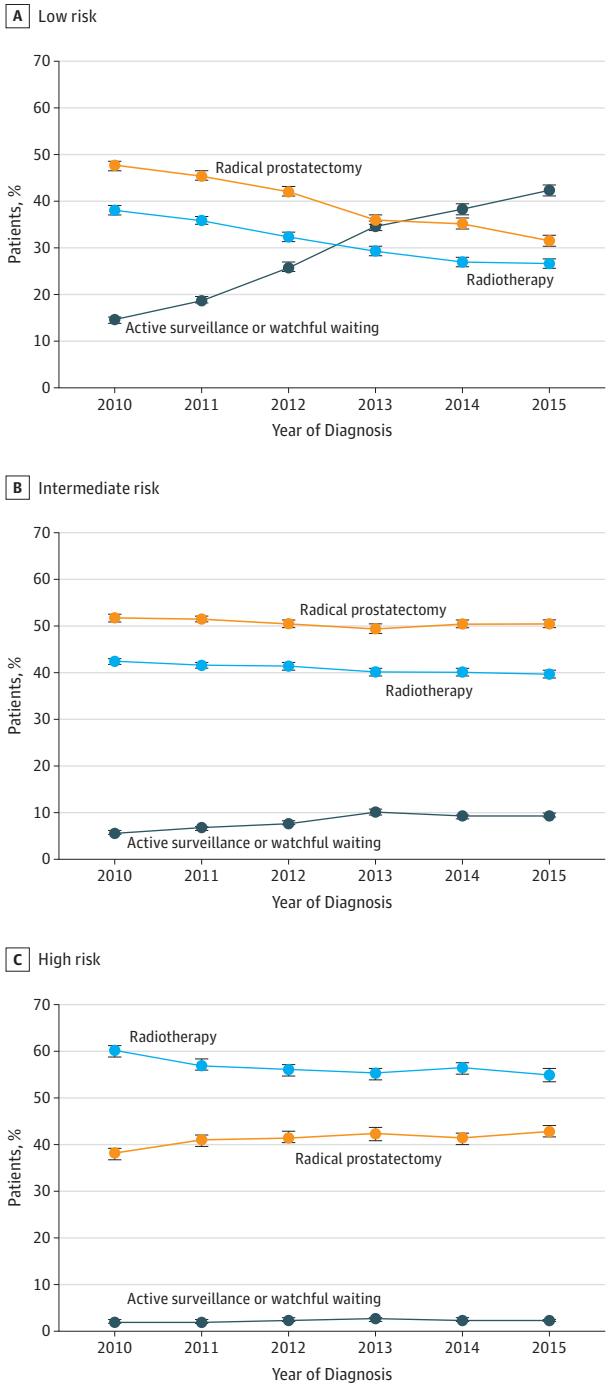
Characteristics	Overall (N = 164 760)	Year					
		2010 (n = 31 355)	2011 (n = 31 916)	2012 (n = 26 653)	2013 (n = 25 802)	2014 (n = 23 894)	2015 (n = 25 140)
Initial management type, No. (%)							
Active surveillance or watchful waiting	20 879 (12.7)	2542 (8.11)	3187 (10.0)	3362 (12.6)	4139 (16.0)	3684 (15.4)	3965 (15.8)
Radical prostatectomy	75 531 (45.8)	15 031 (47.9)	15 205 (47.6)	12 300 (46.2)	11 343 (44.0)	10 591 (44.3)	11 061 (44.0)
Radiotherapy	68 350 (41.5)	13 782 (44.0)	13 524 (42.4)	10 991 (41.2)	10 320 (40.0)	9619 (40.3)	10 114 (40.2)
NCCN risk category, No. (%)							
Low risk	50 302 (30.5)	10 724 (34.2)	10 791 (33.8)	8491 (31.9)	7737 (30.0)	6400 (26.8)	6159 (24.5)
Intermediate risk	81 836 (49.7)	15 241 (48.6)	15 620 (48.9)	13 164 (49.4)	12 889 (50.0)	12 076 (50.5)	12 846 (51.1)
High risk	32 622 (19.8)	5390 (17.2)	5505 (17.2)	4998 (18.8)	5176 (20.1)	5418 (22.7)	6135 (24.4)
Prostate-specific antigen level, median (IQR), ng/mL	6.2 (4.7-9.2)	6.0 (4.6-8.8)	6.0 (4.6-8.6)	6.1 (4.7-9.0)	6.3 (4.8-9.3)	6.5 (4.8-9.7)	6.7 (5.0-10.1)
Positive cores, No. (%)							
≥3	79 184 (48.1)	13 475 (43.0)	12 740 (39.9)	12 973 (48.7)	12 753 (49.4)	12 873 (53.9)	14 370 (57.2)
≤2	47 812 (29.0)	9215 (29.4)	8767 (27.5)	8154 (30.6)	7930 (30.7)	6834 (28.6)	6912 (27.5)
Unknown	37 764 (22.9)	8665 (27.6)	10 409 (32.6)	5526 (20.7)	5119 (19.8)	4187 (17.5)	3858 (15.4)
Age, median (IQR), y	64 (59-70)	64 (58-70)	64 (58-69)	64 (58-69)	65 (59-69)	65 (59-70)	65 (59-70)
Race, No. (%)[b]							
Black	26 616 (16.2)	4856 (15.5)	4863 (15.2)	4363 (16.4)	4318 (16.7)	4013 (16.8)	4203 (16.7)
Other	138 144 (83.8)	26 499 (84.5)	27 053 (84.8)	22 290 (83.6)	21 484 (83.3)	19 881 (83.2)	20 937 (83.3)

Abbreviations: IQR, interquartile range; NCCN, National Comprehensive Cancer Network; SEER, Surveillance, Epidemiology, and End Results.

[a] $P < .05$ for all patient characteristics across years 2010-2015. Percentages may not add to 100% because of rounding.

[b] Race was defined via the SEER race recode variable as black vs other (including white, other, and unknown race) for the purposes of this study. Race was collected and documented by SEER registries via information from medical records, face sheets (patients' 1-page clinical information summary), clinician notes, photographs, and any other medical record sources available to registries.

Figure. Initial Management Trends Among Patients Diagnosed as Having Low-, Intermediate-, and High-Risk Prostate Cancer in the United States From 2010 to 2015 in the Surveillance, Epidemiology, and End Results Prostate Active Surveillance/Watchful Waiting Database



Stratified by National Comprehensive Cancer Network risk category (low risk: n=50 302; intermediate risk: n=81 836; high risk: n=32 622). Error bars indicate 95% confidence intervals.

management or therapy type (AS/WW, radical prostatectomy, or radiotherapy), stratified by National Comprehensive Cancer Network risk category (low, intermediate, or high),[3] was determined from 2010 to 2015, with the Cochran-Armitage test used to test for trends.

Two-sided *P* values were applied with an α = .05. Analyses were performed with Stata/SE version 15.1 (StataCorp). The Dana-Farber/Harvard Cancer Center institutional review board granted a waiver of informed consent.

Results | Among 164 760 men, 20 879 (12.7%) had AS/WW management, 68 350 (41.5%) had radiotherapy, and 75 531 (45.8%) had radical prostatectomy. Men with diagnoses in 2015 (n = 25 140) compared with 2010 (n = 31 355) had significantly lower rates of low-risk disease (24.5% vs 34.2%), a higher median age (65 vs 64 years), and a higher median prostate-specific antigen level (6.7 vs 6.0 ng/mL) (all *P* < .05) (**Table**).

In men with low-risk disease (n = 50 302), AS/WW use increased from 14.5% to 42.1% from 2010 to 2015 (*P* < .001 for trend), while radical prostatectomy decreased from 47.4% to 31.3% (*P* < .001 for trend) and radiotherapy from 38.0% to 26.6% (*P* < .001 for trend) (**Figure**, A). In men with intermediate-risk disease (n = 81 836), AS/WW use increased from 5.8% to 9.6% from 2010 to 2015 (*P* < .001 for trend), while radical prostatectomy decreased from 51.8% to 50.6% (*P* = .004 for trend) and radiotherapy from 42.4% to 39.8% (*P* < .001 for trend) (Figure, B). In men with high-risk disease (n = 32 622), AS/WW use remained stable (1.9% to 2.2%) from 2010 to 2015 (*P* = .08 for trend), while radical prostatectomy use increased from 38.0% to 42.8% (*P* < .001 for trend) and radiotherapy use decreased from 60.1% to 55.0% (*P* < .001 for trend) (Figure, C).

Discussion | Use of AS/WW for men with low-risk localized prostate cancer increased from 2010 to 2015, becoming the most common management approach. Radical prostatectomy use declined among men with low-risk disease but increased among patients with higher-risk disease. Although increasing use of AS/WW for low-risk disease has been supported by high-level evidence and guidelines since 2010,[2,3] shifting management patterns toward more radical prostatectomy in higher-risk disease and away from radiotherapy does not coincide with any new level 1 evidence or guideline changes.[6] The potential downstream effects of efforts to increase AS/WW for men with low-risk disease on management of other risk groups requires further examination.

Strengths of this study include the large, diverse population representative of the US population and high-quality AS/WW data, providing an accurate and contemporary metric of AS/WW use and management trends in the United States. Limitations include lack of data on AS/WW compliance and lack of information regarding neoadjuvant androgen deprivation therapy use. Also, the study only investigated management patterns; how the trends will translate into clinical outcomes is unknown.

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COMMENT & RESPONSE

Long-term Follow-up of Antibiotics vs Surgery for Appendicitis

To the Editor The study by Dr Salminen and colleagues[1] compared antibiotic therapy alone vs appendectomy to treat uncomplicated acute appendicitis. The cumulative incidence of appendicitis recurrence after 5 years was 39.1% in the antibiotic group. The complication rate was 6.5% in the antibiotic group and 24.4% in the surgical group. We have several concerns about these results.

First, the calculation of the complication rate in the antibiotic group appears inaccurate. More than one-third of patients in the antibiotic group had recurrent appendicitis, but recurrent appendicitis was not considered to be a complication. In our opinion, the failure of antibiotic therapy should be considered a type of complication. Adding recurrent appendicitis would increase the complication rate in the antibiotic group to approximately 45%. In addition, the complication rate in the appendectomy group was extremely high. Zhu et al[2] reported a 14.7% complication rate in lengthened-incision open appendectomy to treat complicated appendicitis. The complication rate in surgically treated uncomplicated acute appendicitis should be lower.

Second, with a recurrence rate of appendicitis of 39.1% over 5 years, patients who received antibiotics would always be concerned about its recurrence and potential complicated appendicitis in the future.[3] On the contrary, appendectomy showed a 99.6% success rate.[4] Similar results of appendectomy have also been reported in other research.[5] From the perspective of patients, antibiotic therapy might be considered inferior.

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To the Editor Dr Salminen et al[1] reported 5-year follow-up results from a clinical trial that randomized patients with acute