Active surveillance in favorable intermediate-risk prostate cancer patients: Predictors of deferred intervention and treatment choice

Rashid K. Sayyid, MD, MSc[1]; Laurence Klotz, MD, FRCSC[2]; John Z. Benton, BS[3]; Merry Ma, MD, PhD[1]; Phillip Woodruff, RN, BIS[1]; Raj Satkunasivam, MD, MS[4]; Martha K. Terris, MD[1,5]; Christopher J.D. Wallis, MD, PhD, FRCSC[*6]; Zachary Klaassen, MD, MSc[1,5*]

[1]Section of Urology, Department of Surgery, Medical College of Georgia-Augusta University, Augusta, GA, United States; [2]Division of Urology, Department of Surgery, Sunnybrook Health Sciences Centre, Toronto, ON, Canada; [3]Medical College of Georgia, Augusta, GA, United States; [4]Department of Urology and Center for Outcomes Research, Houston Methodist Hospital, Houston, TX, United States; [5]Georgia Cancer Center, Augusta, GA, United States; [6]Department of Urology, Vanderbilt University Medical Center, Nashville, TN, United States

[*]*Co-senior authors*

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Corresponding author: Dr. Zachary Klaassen, Medical College of Georgia at Augusta University, Georgia Cancer Center. Augusta, GA, United States; zklaassen19@gmail.com

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Abstract

Introduction: Active surveillance (AS) is increasingly used for favorable intermediate-risk (FIR) prostate cancer (PCa). Our objective was to determine oncological and sociodemographic predictors of deferred definitive therapy and decision for radical prostatectomy (RP) vs. radiotherapy (XRT).

Methods: The Surveillance, Epidemiology, and End Results Prostate with Watchful Waiting database was used to identify all FIR PCa diagnosed between 2010 and 2015 opting for AS for at least one year following diagnosis. We sought to determine predictors of treatment and treatment type using multivariable logistic regression.

Results: A total of 20 334 patients were identified. An annual decrease in incident FIR patients managed initially with AS between 2010 (4061) and 2015 (2947) was noted (p for trend <0.001); 17 895 (88.0%) patients underwent deferred RP and/or XRT. Patients with higher baseline cancer volume and clinical stage were significantly more likely to discontinue AS. Patients of higher socioeconomic status were more likely to undergo deferred therapy, with increased odds

for XRT over RP. African American patients had lower odds of undergoing definitive intervention (odds ratio 0.83, p=0.030) and were significantly more likely to opt for XRT. Oncological characteristics leading to FIR classification influenced treatment choice at the time of deferred intervention: XRT was treatment of choice in 86.3% and 86.0% of Gleason group 2 and PSA 10–20 FIR patients, respectively; 96.1% of treated cT2b-c FIR patients opted for RP. **Conclusions:** Most FIR PCa patients initially managed with AS eventually undergo deferred definitive therapy, with choice of treatment significantly influenced by patients' baseline oncological and sociodemographic characteristics.

Introduction

Active surveillance (AS) is currently the standard of care for very low- and low-risk prostate cancer (PCa).[1,2] This management strategy has proven its long-term oncologic safety in these cohorts and simultaneously maintains patient quality of life,[3,4] and thus there has been increased interest in expanding the indications for AS to the intermediate risk cohort. This is supported by results from the Prostate Testing for Cancer and Treatment (ProtecT) trial demonstrating that low- and intermediate-risk PCa patients managed conservatively with active monitoring had long-term PCa-mortality outcomes similar to those managed with radical prostatectomy (RP) or radiotherapy (XRT).[5] Furthermore, a large, multinational autopsy study demonstrated that more than half of Asian men with incidental PCa at autopsy harbored evidence of Grade Group (GG) two disease or worse, confirming the indolent nature of a subset of this risk group.[6] These findings have contributed to multiple governing bodies supporting AS use for patients with favorable intermediate risk (FIR) PCa,[1,2] defined per the National Comprehensive Cancer Network (NCCN) as predominant GG1 disease, percentage of positive biopsy cores <50%, and a single NCCN intermediate risk factor.[7] These recommendations have been reflected in an increased uptake of AS for patients with intermediate-risk disease, with a recent analysis of the Surveillance, Epidemiology, and End Results (SEER) Prostate with Watchful Waiting (WW) database demonstrating that use of AS for such patients has significantly increased over time, from 3.7% in 2010 to 7.3% in 2015.[8]

With the increased uptake of AS for FIR PCa patients, understanding the factors influencing the decision to discontinue AS in favor of deferred definitive intervention, as part of a shared decision-making process between the patient and physician, becomes important. Our objective was thus to evaluate both oncologic and sociodemographic predictors of undergoing deferred definitive intervention after a period of AS, and in patients undergoing deferred intervention, choice of RP versus XRT.

Methods

Patient population

Men with NCCN FIR PCa were identified using the SEER WW database, which is a nationally representative database supported by the National Cancer Institute that captures patients with incident PCa from 18 population-based registries, accounting for approximately 30% of the US population. Study patients were diagnosed with PCa between 2010 and 2015 and all underwent documented AS or WW for a period of at least one year as per records from the treating institutions.[9] Such patients thus did not receive definitive therapy for at least one year following diagnosis and were managed with AS or WW for at least one year following diagnosis. Thus, patients initially managed with AS or WW but subsequently opted for definitive therapy within one year of diagnosis and those that simply deferred treatment by one year were not included in the cohort. Patients older than 80 years at time of diagnosis were excluded from our cohort, as the majority of such patients would be expected to fall under the WW category.[10] Patients were not excluded if they had a prior diagnosis of another non-PCa related malignancy and were noted as such.

FIR patients were subdivided into one of three groups based on which risk factor categorized them as having intermediate risk disease, per NCCN criteria: GG2, PSA 10-20 ng/ml and cT2b-c. Each patient thus had only one intermediate risk factor and the three FIR groups were mutually exclusive.

Given the deidentified and public availability of the dataset, research ethics board approval for this study was not required by the participating institutions.

Study outcomes

The two primary study outcomes were: (i) a definitive intervention event (defined as RP or definitive XRT) and (ii) choice of RP versus definitive XRT among those who opted for intervention. Definitive XRT includes both external beam radiotherapy and/or brachytherapy treatment. These two outcomes were each operationalized as a binary variable (yes versus no), with time to intervention not available from this dataset.

Study variables

Patient oncologic and sociodemographic variables were available at time of PCa diagnosis only. Oncologic variables included: clinical T, N, and M stages, serum prostate-specific antigen (PSA) level, Gleason Score on prostate biopsy or transurethral resection of the prostate specimens, and number of positive and sampled biopsy cores/specimens. The percent positive cores variable was calculated from the number of positive and sampled cores/specimens for each patient. Follow-up serum PSA levels, clinical exam and imaging findings, and repeat biopsy results were not available, and thus the trigger for discontinuing AS in favor of deferred therapy was not available.

Baseline patient-level sociodemographic variables included: year of diagnosis, age at diagnosis, race, insurance status, marital status, and SEER registry. Individual socioeconomic

status (SES) was derived from the following five county-level variables: percentage of individuals (i) below the poverty line, (ii) unemployed, (iii) median household income, (iv) foreign born, and (v) with less than a high school education.[11-13]

Statistical analysis

Continuous variables were reported using medians and interquartile ranges (IQR). Categorical variables were reported using frequency counts and proportions and were compared using the Chi-square test. Predictors of deferred therapy and decision for RP versus definitive XRT were each evaluated using univariable and multivariable logistic regression analyses. All of the aforementioned oncologic and sociodemographic variables, operationalized as categorical variables, were included *a priori* in the multivariable analyses to control for potential sources of confounding. The variance inflation factor test was used to test for variable multicollinearity. A cut off value of five was used to exclude variables on the basis of a high degree of multicollinearity. The Cuzick's test for trend, an extension of the Wilcoxon rank-sum test,[14] was used to evaluate trends in AS uptake by year for each FIR group. A p-value of <0.05 denoted statistical significance. R version 4.0.3 (The R Foundation for Statistical Computing, Vienna, Austria) was used to perform all statistical analyses.

Results

Of 357,140 men with PCa in the SEER WW database, we identified 20,334 men with NCCN FIR PCa who were managed with AS for at least one year following diagnosis. Of these 20,334 men, 9,224 (45.4%), 2,552 (12.6%), and 8,558 (42.1%) were in the GG2, PSA 10-20 ng/ml, and cT2b-c groups, respectively (Figure 1). Baseline sociodemographic and oncologic characteristics for the overall cohort and by FIR group are presented in Table 1. Median age at diagnosis was 64.0 years (IQR 58.0-69.0). Caucasian and African American patients accounted for 14,182 (69.7%) and 3,344 (16.4%) patients, respectively. Median serum PSA level at diagnosis 5.60 ng/ml and median percent positive cores was 21.4% (IQR 12.5-33.3%, Table 1).

Four thousand sixty-one patients (20.0% of all patients in the study cohort) were diagnosed in 2010 and this figure decreased to 2,947 (14.55%) in 2015 (p for trend <0.001). Of the 20,334 patients in the cohort, 17,895 (88.0%) eventually underwent deferred definitive therapy with either RP and/or XRT. The corresponding figures in the GG2, PSA 10-20 ng/ml and cT2b-c groups were 7,666 (83.1%), 1,710 (67.0%), and 8,519 (99.5%), respectively ($p<0.001$). Of the 7,666 and 1,710 patients in the GG2 and PSA 10-20 ng/ml groups, respectively, definitive XRT was the treatment of choice in 6,616 (86.3%) and 1,470 (86.0%) patients, respectively. Conversely, 8,186 patients (96.1% of treated patients) in the cT2b-c group opted for RP (p across FIR groups <0.001).

Predictors of undergoing deferred therapy on univariable logistic regression analyses are presented in Supplementary Table 1. On multivariable analysis, baseline oncologic variables predicting increased odds of deferred intervention included higher volume disease on

biopsy/TURP specimens in the GG2 and PSA 10-20 ng/ml groups (odds ratio [OR] for 37.6-49.9% versus 0-12.5%: 1.33 and 2.10, p=0.008 and p<0.001, respectively) and more advanced clinical stage in all three FIR groups (OR: 3.00 and 5.26 for cT2a versus cT1, p<0.001 in the GG2 and PSA 10-20 ng/ml groups respectively, and OR: 15.5 for cT2c versus cT2b in the cT2b-c group, p<0.001).

With regards to baseline sociodemographic variables, patients of higher SES were significantly more likely to undergo definitive therapy in all three FIR groups (ORs for highest versus lowest quartiles: 1.72, 1.50, and 1.60, p<0.001, 0.013, and 0.03 for the GG2, PSA 10-20 ng/ml and cT2b-c groups, respectively). In the GG2 group, African American patients (versus Caucasian OR: 0.83, p=0.03) and those diagnosed in a Western region (versus Northeastern OR: 0.81, p=0.014) had significantly lower odds of undergoing definitive therapy, whereas patients who were not married were significantly more likely to opt for definitive therapy (OR: 1.43, p<0.001). In the cT2b-c group, older patients (OR for 70-79 versus 30-49: 0.16, p=0.004), those who were uninsured (versus insured OR: 0.18, p=0.009), and those diagnosed in a Southeastern region (versus Northeastern OR: 0.42, p=0.022) all had significantly lower odds of undergoing definitive therapy (Table 2).

Among patients who underwent deferred definitive therapy, patients with larger tumor volume at time of diagnosis were significantly more likely to opt for definitive XRT over RP in all FIR groups (OR for 37.6-49.9% versus 0-12.5%: 0.34, 0.21, and 0.33, p<0.001, p=0.014, and p<0.001 for the GG2, PSA 10-20 ng/ml and cT2b-c groups, respectively). Conversely, patients with a more advanced clinical stage were significantly more likely to opt for RP (OR: 167.2 and 239.8 for cT2a versus cT1, p<0.001 in the GG2 and PSA 10-20 ng/ml groups respectively, and OR: 38.6 for cT2c versus cT2b in the cT2b-c group, p<0.001). In the GG2 group, patients with a PSA of 5-10 ng/ml (OR 1.60, p=0.033) and no prior non-PCa malignancy (OR 1.60, p=0.033) were both significantly more likely to opt for RP over definitive XRT. With regards to sociodemographic variables, older patients (ORs for 70-79 versus 30-49: 0.034 and 0.027, p<0.001 for the GG2 and cT2b-c groups, respectively) and those of higher SES in the GG2 (OR for 2nd versus lowest: 0.63, p=0.013) and cT2b-c groups (OR for 3rd versus lowest:0.32, p =0.034) were significantly more likely to choose XRT over RP. Similarly, African American patients in the GG2 and PSA 10-20 ng/ml groups were significantly more likely to undergo XRT (OR versus Caucasian: 0.58 and 0.34, p=0.003 and 0.012, respectively). Conversely, patients who were not married were significantly more likely to undergo RP versus XRT in the GG2 (OR: 1.39, p=0.016) and cT2b-c groups (OR: 2.45, p<0.001, Table 3, Supplementary Table 2).

Discussion

In this population-based analysis of 20,334 men with FIR PCa managed with AS for at least one year following diagnosis, we determined that most (88.0%) patients eventually discontinued AS in favor of deferred definitive therapy. This figure is significantly higher than that previously

reported for low risk PCa patients from the SEER WW database (65.7%). [15] It is also higher than the proportion treated in a recent single center experience of AS in intermediate risk cancer, where it was 49% at 10 years.[16] Notably, choice of deferred definitive therapy differed by FIR risk group in our cohort. XRT was the treatment of choice for patients with GG2 and PSA 10-20 ng/ml FIR PCa (86.3% and 86.0%, respectively), whereas RP was the treatment of choice for 96.1% of patients with cT2b-c FIR PCa.

A significant annual decrease in number of FIR PCa patients managed with AS was observed for the overall cohort, which was secondary to an absolute decrease in number of PSA 10-20 ng/ml and cT2b-c FIR patients managed with AS. There was a concurrent increase in the number of GG2 FIR patients managed with AS. Despite this overall decrease, it is not possible to infer that there has been a decreased uptake of AS for FIR patients without considering the number of such patients managed with definitive therapy during the same timeframe. This decrease may in part reflect the overall decrease in PCa incidence following the 2012 United States Preventive Services Task Force recommendations.[17]

Advanced clinical stage was consistently found to be strongly associated with increased odds of undergoing deferred definitive intervention, and among those who underwent intervention, RP over XRT (ORs of 38.6-239.8 across all three FIR groups). These findings may be related to the increased uptake of multiparametric magnetic resonance imaging (mp-MRI) in the follow up of AS patients since 2010, resulting in increased detection of extraprostatic extension.[18] This would plausibly trigger discontinuation of AS and may also explain the decrease in numbers of cT2b-c FIR patients managed with AS between 2010 and 2015 in our cohort.

Patients of higher SES were significantly more likely to undergo deferred definitive therapy across FIR subgroups. Patients of higher SES are known to be more likely to follow up with their physicians,[19,20] and thus be more compliant with repeat PSA, clinical exam and biopsy protocols. This increases the likelihood of detecting signs of disease progression/understaging, which act as triggers for intervention. Interestingly, such patients were also more likely to opt for definitive XRT over RP in two of the FIR groups. Similarly, FIR African American patients with GG2 or PSA 10-20 ng/ml were more likely to opt definitive XRT over RP even after controlling for baseline oncologic and sociodemographic variables such as SES and insurance status. These findings may reflect African American patients' known distrust of the medical system[21-23] and their desire to avoid invasive interventions. This is further reflected in GG2 FIR African American patients being 17% less likely to undergo definitive intervention.

This is the first population-based study evaluating sociodemographic and oncologic predictors of deferred definitive therapy in AS FIR PCa patients. Our study is strengthened by our use of a large, validated,[24,25] nationally representative dataset.[9] It is important to note however that our deferred intervention rate of 88.0% is significantly higher than those previously reported in other series, which have ranged between 31 and 49% over a five to ten year follow up

period.[16,26-28] This difference is likely related in part to differences in cohort eligibility criteria with previously reported series applying stricter eligibility criteria. In these series, AS was often restricted to FIR patients older than 65 years[26,28] or a life expectancy less than ten years.[28] Furthermore, these series originated in academic tertiary centers where practice patterns are likely to differ from those seen in population-based settings. However, without follow up oncologic data (e.g. PSA changes, mp-MRI findings, GS upgrading or increased PCa volume on repeat biopsies), exact triggers for intervention, and information regarding patients' medical comorbidities it is not possible to discern the exact reasons for these disparities. AS protocols (i.e. timing of confirmatory biopsy, frequency of PSA measurements, etc.) were not available for these patients. Practice patterns have also evolved since the study time period of 2010 to 2015. There has been an increased uptake of mp-MRI[29] and prognostic genetic biomarkers[30] in the AS setting, as well as changes to the GS scoring system.[31] Thus, the results of this study must interpreted in light of these recent advances. Further limitations to this study include the absence of timing of interventions, which precluded us from performing time-to-event analyses with Cox proportional hazard modeling, and inability to differentiate patients initially managed with AS or WW. However, by excluding patients older than 80 years at time of diagnosis, we attempted to minimize the number of patients in the WW group.[10] Similar to other studies originating from population-based registries, this analysis is subject to the limitations and inherent biases characteristic of population-based registries, particularly with regards to missing data which has been found to be as high as 46% in validation studies of this dataset.[24,25] Patients in the SEER database are from population-based cancer registries covering approximately 35 percent of the US population, and thus results from this dataset may not be generalizable to the entire US population.[9]

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Figures and Tables

Fig.1. Study flow chart. SEER: Surveillance, Epidemiology, and End Results.

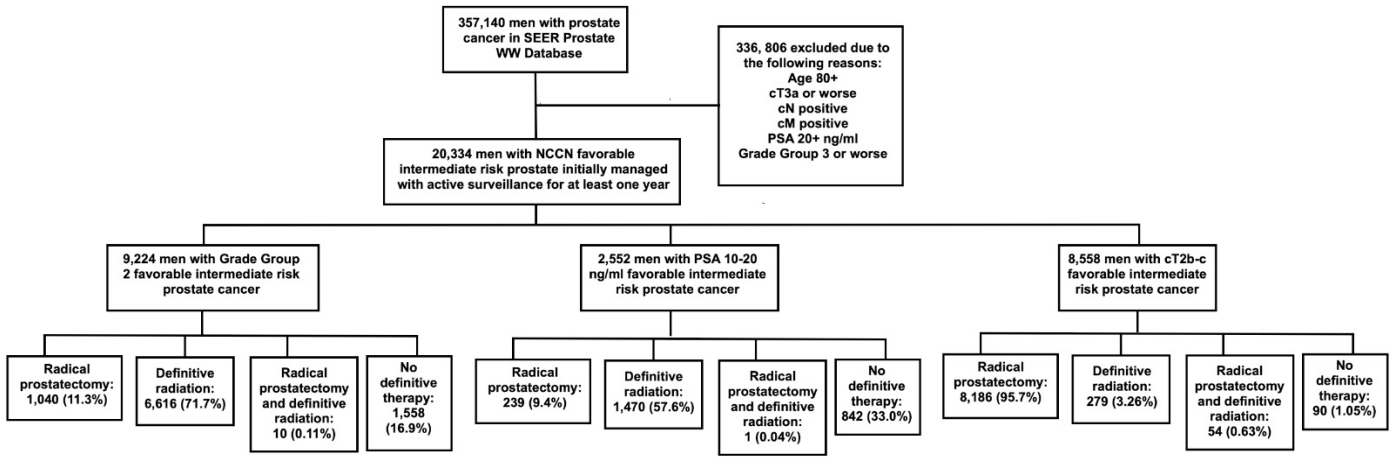

Table 1. Baseline demographic and oncologic characteristics for overall cohort and by risk group				
Variable	**Overall favorable intermediate-risk cohort (n=20 334)**	**GG2 favorable intermediate-risk cohort (n=9224)**	**PSA 10–20 ng/ml favorable intermediate-risk cohort (n=2552)**	**cT2b-c favorable intermediate-risk cohort (n=8558)**
Year of diagnosis				
2010	4061 (20.0%)	1454 (15.8%)	502 (19.7%)	2105 (24.6%)
2011	3707 (18.2%)	1438 (15.6%)	466 (18.3%)	1803 (21.1%)
2012	3603 (17.7%)	1651 (17.9%)	435 (17.0%)	1517 (17.7%)
2013	3163 (15.6%)	1547 (16.8%)	409 (16.0%)	1207 (14.1%)
2014	2853 (14.0%)	1459 (15.8%)	379 (14.9%)	1015 (11.9%)
2015	2947 (14.55%)	1675 (18.2%)	361 (14.1%)	911 (10.6%)
Age at diagnosis, median (IQR)	64.0 (58.0–69.0)	66.0 (61.0–71.0)	67.0 (61.0–72.0)	60.0 (55.0–65.0)
Race				
Caucasian	14 182 (69.7%)	6302 (68.3%)	1590 (52.3%)	6290 (73.5%)
African American	3344 (16.4%)	1772 (19.2%)	473 (18.5%)	1099 (12.8%)
Hispanic	1567 (7.71%)	590 (6.40%)	252 (9.87%)	725 (8.47%)
Asia/Pacific Islander	864 (4.25%)	367 (3.98%)	166 (6.50%)	331 (3.87%)
American Indian/Alaska Native	68 (0.33%)	31 (0.34%)	8 (0.31%)	29 (0.34%)
Unknown	309 (1.52%)	162 (1.76%)	63 (2.47%)	84 (0.98%)
Marital status				
Married	14 173 (69.7%)	6046 (65.5%)	1548 (60.7%)	6579 (76.9%)
Not married	4144 (20.4%)	2105 (22.8%)	631 (24.7%)	1408 (16.5%)
Unknown	2017 (9.9%)	1073 (11.6%)	373 (14.6%)	571 (6.67%)
SEER registry				
New Jersey	2816 (13.8%)	1361 (14.7%)	295 (11.6%)	1160 (13.6%)
San Francisco-Oakland	1123 (5.52%)	559 (6.06%)	196 (7.68%)	368 (4.30%)
Los Angeles	1142 (5.62%)	374 (4.05%)	146 (5.72%)	622 (7.27%)
Louisiana	1106 (5.44%)	503 (5.45%)	139 (5.45%)	464 (5.42%)
Connecticut	982 (4.83%)	506 (5.49%)	102 (4.00%)	374 (4.37%)

Detroit (metropolitan)	1709 (8.40%)	1044 (11.3%)	119 (4.66%)	546 (6.38%)
Seattle (Puget Sound)	1071 (5.27%)	470 (5.10%)	98 (3.84%)	503 (5.88%)
Rural Georgia	53 (0.26%)	30 (0.33%)	12 (0.47%)	11 (0.13%)
Atlanta (metropolitan)	801 (3.94%)	504 (5.46%)	101 (4.0%)	196 (2.29%)
California (excluding SF/SJM/LA)	4052 (19.9%)	1556 (16.9%)	650 (25.5%)	1846 (21.6%)
Greater Georgia	1828 (9.0%)	963 (10.4%)	237 (9.29%)	628 (7.34%)
Kentucky	1235 (6.07%)	398 (4.31%)	140 (5.49%)	697 (8.14%)
San Jose-Monterey	725 (3.57%)	327 (3.55%)	123 (4.82%)	275 (3.21%)
Utah	511 (2.51%)	189 (2.05%)	36 (1.41%)	286 (3.34%)
Hawaii	271 (1.33%)	107 (1.16%)	41 (1.61%)	123 (1.44%)
Iowa	584 (2.87%)	233 (2.53%)	62 (2.43%)	289 (3.38%)
New Mexico	321 (1.58%)	100 (1.08%)	54 (2.12%)	167 (1.95%)
Alaska Natives	4 (0.02%)	0 (0.0%)	1 (0.04%)	3 (0.035%)
Insurance status				
Insured	18 239 (89.7%)	8074 (87.5)	2106 (82.5%)	8059 (94.2%)
Uninsured	212 (1.04%)	86 (0.93%)	52 (2.04%)	74 (0.86%)
Medicaid	681 (3.35%)	318 (3.45%)	150 (5.88%)	213 (2.49%)
Unknown	1202 (5.91%)	746 (8.09%)	244 (9.56%)	212 (2.48%)
Socioeconomic status				
1 (Lowest)	4620 (22.7%)	1991 (21.6%)	664 (26.0%)	1965 (23.0%)
2	4580 (22.5%)	2055 (22.3%)	656 (25.7%)	1869 (21.8%)
3	5724 (28.1%)	2674 (29.0%)	691 (27.1%)	2359 (27.6%)
4 (Highest)	5410 (26.6%)	2504 (27.1%)	541 (21.2%)	2365 (27.6%)
PSA at diagnosis, median (IQR)	5.60 (4.40–7.70)	5.60 (4.50–7.10)	12.30 (10.90–14.60)	5.00 (4.10–6.30)
Percent cores positive, median (IQR)	21.4 (12.5–33.3)	25.0 (16.7–33.3)	16.7 (8.33–25.0)	18.8 (11.1–33.3)
cT Stage				
cT1	9603 (47.2%)	7383 (80.0%)	2220 (87.0%)	0 (0.0%)
cT2a	2173 (10.7%)	1841 (20.0%)	332 (13.0%)	0 (0.0%)
cT2b	373 (1.83%)	0 (0.0%)	0	373 (4.36%)
cT2c	8185 (40.3%)	0 (0.0%)	0	8185 (95.6%)
Prostate cancer as first diagnosed malignancy				

Yes	19 046 (93.7%)	8543 (92.6%)	2364 (92.6%)	8139 (95.1%)
No (i.e., previous, non-prostate cancer diagnosis)	1288 (6.33%)	681 (7.38%)	188 (7.37%)	419 (4.90%)

GG: grade group; IQR: interquartile range; PSA: prostate-specific antigen; SF/SJM/LA: San Francisco, San Jose-Monterey, Los Angeles.

Table 2. Predictors of receiving deferred therapy (radical prostatectomy or radiation therapy) on multivariable logistic regression analysis for favorable intermediate prostate cancer patients by group

	GG2 favorable intermediate-risk cohort (n=9224)			**PSA 10–20 ng/ml favorable intermediate-risk cohort (n=2552)**			**cT2b-c favorable intermediate-risk cohort (n=8558)**		
Variable	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**P-value**	**OR**	**95% CI**	**p**
Year of diagnosis (Reference: 2010–11)									
2012–13	0.88	0.75–1.03	0.12	0.80	0.64–1.02	0.071	0.45	0.25–0.78	**0.005**
2014–15	0.89	0.75–1.04	0.14	0.76	0.59–0.97	**0.028**	0.64	0.33–1.22	0.17
Age at diagnosis (Reference: 30–49 years)									
50–59	1.22	0.75–1.91	0.40	0.91	0.27–2.66	0.87	1.17	0.26–3.68	0.81
60–69	1.43	0.89–2.20	0.12	1.08	0.33–3.10	0.90	0.44	0.10–1.25	0.18
70–79	1.30	0.81–2.03	0.26	0.88	0.27–2.54	0.82	0.16	0.036–0.50	**0.004**
Race (Reference: Caucasian)									
African American	0.83	0.70–0.98	**0.03**	0.85	0.65–1.13	0.27	0.69	0.36–1.43	0.29
Hispanic	0.97	0.75–1.28	0.85	0.96	0.68–1.36	0.83	0.61	0.29–1.38	0.20
Asia/Pacific Islander/American Indian/Alaska Native	0.94	0.69–1.30	0.69	0.95	0.64–1.43	0.81	2.86	0.57–52.2	0.31

Insurance status (Reference: Insured)									
Uninsured	0.58	0.39–1.11	0.096	0.59	0.32–1.12	0.10	0.18	0.058–0.82	**0.009**
Medicaid	0.88	0.65–1.20	0.40	0.78	0.53–1.17	0.23	0.72	0.27–2.52	0.55
Marital status (Reference: Married)									
Not married	1.43	1.24–1.65	**<0.001**	1.17	0.94–1.46	0.16	1.61	0.91–2.76	0.087
SEER registry region (Reference: Northeast)									
Southeast	1.10	0.91–1.34	0.31	1.15	0.82–1.60	0.43	0.42	0.20–0.87	**0.022**
Midwest	1.21	0.86–1.73	0.28	1.00	0.62–1.63	1.00	0.79	0.28–2.56	0.66
West	0.81	0.68–0.96	**0.014**	0.76	0.57–1.02	0.068	0.79	0.38–1.60	0.53
SES quartiles *(*Reference: 1 [lowest])									
2	1.30	1.08–1.57	**<0.001**	1.26	0.95–1.67	0.11	1.78	0.89–3.68	0.11
3	1.11	0.93–1.32	0.24	1.07	0.81–1.41	0.64	0.93	0.50–1.72	0.83
4 (Highest)	1.72	1.41–2.10	**<0.001**	1.50	1.09–2.08	**0.013**	1.60	1.12–3.52	0.03
PCa as first cancer diagnosis (Reference: Previously diagnosed with other cancer)	1.20	0.95–1.52	0.12	1.46	1.01–2.09	**0.042**	0.50	0.12–1.45	0.27
PSA (References: 0–5 ng/ml for groups 1 and 3; 10–15 ng/ml for group 2)									
5–10 ng/ml	1.20	0.99–1.45	0.053				1.17	0.65–2.00	0.59
10–20 ng/ml				1.13	0.69–1.81	0.62			
Percent cores positive (Reference: 0–12.5%)									

12.6–25.0%	1.06	0.88–1.28	0.51	1.22	0.96–1.55	0,10	0.92	0.42–1.94	0.83
25.1–37.5%	1.44	1.20–1.72	**<0.001**	1.58	1.22-2.07	**<0.001**	0.67	0.23–0.10	**0.13**
37.6–49.9%	1.33	1.08–1.65	**0.008**	2.10	1.34–3.25	**<0.001**	0.76	0.32–1.82	0.53
cT Stage (cT1 as reference for groups 1 and; cT2b for group 3)									
cT2a	3.00	2.44–3.72	**<0.001**	5.26	3.49–8.29	**<0.001**			
cT2c							15.5	9.40–25.2	**<0.001**

CI: confidence interval; NA: not available; OR: odds ratio; PSA: prostate-specific antigen; SEER: Surveillance, Epidemiology, and End Results; SES: socioeconomic status.

Table 3. Predictors of receiving radical prostatectomy versus radiation therapy on multivariable logistic regression analysis for favorable intermediate prostate cancer patients by group

	GG2 favorable intermediate-risk cohort (n=9224)			PSA 10–20 ng/ml favorable intermediate-risk cohort (n=2552)			cT2b-c favorable intermediate-risk cohort (n=8558)		
Variable	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**P-value**	**OR**	**95% CI**	**p**
Year of diagnosis (Reference: 2010–11)									
2012–13	0.96	0.74–1.25	0.75	1.47	0.79–2.75	0.23	1.05	0.72–1.54	0.80
2014–15	1.03	0.79–1.34	0.83	1.46	0.76–2.86	0.26	1.29	0.84–2.03	0.25
Age at diagnosis (Reference: 30–49 years)									
50–59	0.42	0.20–0.88	**0.025**	0.46	0.04–5.34	0.56	0.48	0.11–1.45	0.25
60–69	0.12	0.059–0.25	**<0.001**	0.40	0.040–4.50	0.49	0.12	0.028–0.34	**<0.001**
70–79	0.034	0.015–0.071	**<0.001**	0.12	0.010–1.37	0.11	0.027	0.006–0.082	**<0.001**
Race (Reference: Caucasian)									
African American	0.58	0.41–0.83	**0.003**	0.34	0.14–0.78	**0.012**	0.69	0.41–1.19	0.16
Hispanic	1.15	0.75–1.77	0.54	0.76	0.33–1.75	0.51	0.96	0.49–2.02	0.90
Asia/Pacific Islander/American Indian/Alaska Native	0.96	0.59–1.57	0.88	0.62	0.23–1.72	0.36	0.54	0.27–1.19	0.10
Insurance status (Reference: Insured)									
Uninsured	1.50	0.45–4.83	0.51	1.37	0.16–9.18	0.77	0.87	0.18–15.6	0.89
Medicaid	0.56	0.28–1.08	0.087	0.62	0.18–2.11	0.44	0.78	0.36–1.88	0.56

Marital status (Reference: Married)									
Not married	1.39	1.06–1.81	**0.016**	0.84	0.46–1.53	0.57	2.45	1.67–3.57	**<0.001**
SEER registry region (Reference: Northeast)									
Southeast	1.38	0.98–1.94	0.069	1.16	0.46–2.94	0.76	0.71	0.42–1.17	0.18
Midwest	1.36	0.91–2.03	0.14	1.33	0.42–4.17	0.63	0.81	0.42–1.63	0.54
West	1.09	0.82–1.45	0.54	0.82	0.37–1.80	0.62	1.07	0.66–1.71	0.79
SES quartiles (Reference: 1 [lowest])									
2	0.63	0.44–0.91	**0.013**	0.81	0.37–1.78	0.60	1.11	0.66–1.89	0.70
3	0.78	0.57–1.08	0.13	0.68	0.32–1.44	0.32	0.61	0.38–0.96	**0.034**
4 (Highest)	0.74	0.53–1.04	0.084	0.46	0.20–1.00	0.052	1.00	0.59–1.69	1.00
PCa as first cancer diagnosis (Reference: Previously diagnosed with other cancer)	1.60	1.04–2.46	**0.033**	0.97	0.33–2.90	0.96	1.61	0.88–2.79	0.10
PSA (References: 0–5 ng/ml for groups 1 and 3; 10–15 ng/ml for group 2)									
5–10 ng/ml	1.35	1.04–1.74	**0.023**				1.29	0.87–1.89	0.20
10–20 ng/ml				1.41	0.35–5.76	0.63			
Percent cores positive (Reference: 0–12.5%)									

12.6–25.0%	0.77	0.57–1.05	0.10	0.69	0.37–1.29	0.25	0.74	0.42–1.26	0.27
25.1–37.5%	0.51	0.38–0.69	**<0.001**	0.42	0.20–0.85	**0.017**	0.33	0.20–0.54	**<0.001**
37.6–49.9%	0.34	0.23–0.48	**<0.001**	0.21	0.058–0.70	**0.014**	0.33	0.18–0.58	**<0.001**
cT Stage (cT1 as reference for groups 1 and; cT2b for group 3)									
cT2a	167.2	122.65–233.09	**<0.001**	239.8	133.8–459.3	**<0.001**			
cT2c							38.6	26.9–55.6	**<0.001**

CI: confidence interval; NA: not available; OR: odds ratio; PSA: prostate-specific antigen; SEER: Surveillance, Epidemiology, and End Results; SES: socioeconomic status