CANADIAN JOURNAL OF UROLOGY

Tech Science Press

Doi:10.32604/cju.2026.074677
ARTICLE

Clinical and racial predictors of adverse pathology at radical prostatectomy: implications for undertreatment among patients receiving radiation and hormonal therapy

Mutlay Sayan,[1*] Yetkin Tuac,[2] Zhiyu Qian,[3,4] Alexander P. Cole,[3,4] Jonathan E. Leeman,[1] Martin T. King,[1] Paul L. Nguyen,[1] Anthony V. D'Amico,[1]

[1]Department of Radiation Oncology, Brigham and Women's Hospital and Dana Farber Cancer Institute, Boston, MA, USA
[2]Department of Statistics, Ankara University, Ankara, Türkiye
[3]Department of Urology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA
[4]Center for Surgery and Publlic Health, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

SAYAN M, TUAC Y, QIAN Z, COLE AP, LEEMAN JE, KING MT, NGUYEN PL, D'AMICO AV. Clinical and racial predictors of adverse pathology at radical prostatectomy: implications for undertreatment among patients receiving radiation and hormonal therapy. *Can J Urol* 2026;33(3):583–591.

Objectives: *Under-grading exists in up to 7% of patients undergoing radical prostatectomy (RP) for prostate cancer (PC). We assessed whether underrepresented race and ethnicity disproportionately increased the odds of adverse pathology at RP in patients with biopsy Gleason score 6 or 7 PC at high-risk for upgrading and/or upstaging at RP based on age and PC indices at presentation.*

Methods: *This retrospective cohort study analyzed 76,474 patients in the National Cancer Database (2015–2021) with biopsy Gleason score 6 or 7 N0M0 PC. Odds ratio (OR) at RP of adverse pathology defined as prostatectomy (p) Gleason score 9–10, node-positive disease, or pT3b-T4 PC in patients at high- or highest-risk for upgrading at RP. The highest-risk group comprised age > 70 years, PSA > 10 ng/mL, cT2 or higher, ≥50% positive biopsy cores, and Black or other non-White race and/or Hispanic ethnicity versus the same clinical factors and White race and non-Hispanic ethnicity for high-risk. Others were classified as low-risk.*

Results: *The adverse pathology OR was 4.36 (95% CI, 3.10–6.89), and 2.64 (95% CI, 2.25–3.08) for patients in the high-risk and highest-risk groups respectively compared to low-risk. Highest-risk patients had a significantly higher adverse pathology OR [1.70 (95% CI, 1.11–2.60); p = 0.015] when compared to high-risk patients.*

Conclusions: *Disproportionate under-grading and under-staging observed in under-represented minorities can lead to under-treatment in the highest-risk patients electing to undergo radiation and androgen deprivation therapy (ADT), given ADT duration could be based on under-graded PC, highlighting the urgent need to improve the detection strategy in these patients.*

Key Words: prostatic neoplasms, prostatectomy, Gleason score, staging, health status disparities

Received date 15 October 2025
Accepted for publication 09 January 2026
Published online 26 June 2026

*Corresponding Author: Mutlay Sayan.
Email: msayan@bwh.harvard.edu

Introduction

The standard of care (SOC) for detecting prostate cancer (PC) has evolved to include both a 12-core transrectal ultrasonography–guided systematic biopsy and targeted biopsies of PIRADS 3, 4 and 5 lesions identified on multiparametric magnetic resonance imaging (mpMRI).[1,2] Despite this advance, the biopsy Gleason score is upgraded to Grade Group ≥2 in approximately 7% of patients at radical prostatectomy (RP).[3] Because this estimate reflects a best-case scenario in an expert-center setting, real-world upgrading rates are likely higher, especially in community practice where imaging and biopsy approaches are more variable. Therefore, studies are needed to elucidate the optimal image-guided paradigm to better classify Gleason score in this important group of under-graded patients. In addition, due to limited and conflicting data,[4–6] it remains unknown whether patients from under-represented backgrounds at high-risk for upgrading and upstaging based on clinical factors at diagnosis have a disproportionately higher risk of upgrading and upstaging at RP when compared with all other patients.

Recent findings from a randomized comparison of fluorine-18 prostate-specific membrane antigen–1007 positron emission tomography/computed tomography (^{18}F-PSMA-1007 PET/CT) with mpMRI demonstrated the superiority of PSMA PET in identifying the dominant intra-prostatic lesion and correctly identifying extracapsular extension using the RP specimen as the gold standard for comparison.[7] Although PSMA PET was not evaluated in our study, these data suggest that PSMA PET may help identify subsets of patients who are under-graded or under-staged by current SOC biopsy approaches. While our analytic cohort consists of patients who underwent RP, RP pathology provides the only definitive assessment of upgrading and upstaging and therefore serves as the reference standard for identifying patients who would be at risk for undertreatment had they instead elected radiation and hormonal therapy.

In the current study, we assessed whether under-represented race and ethnicity disproportionately increased the risk of adverse pathology at RP in patients with biopsy Gleason score 6 or 7 PC known to be at higher risk for under-grading and under-staging based on age and PC indices at presentation in order to understand how best to design a prospective randomized detection study assessing the impact of adding PSMA PET imaging to the SOC approach for PC detection on upgrading or upstaging at RP in under-represented and all other patient cohorts.

Methods

Data source

We performed a retrospective cohort analysis of data from 2004 to 2021 using the PC Participant User File from the National Cancer Database (NCDB). The NCDB is a nationwide hospital-based cancer registry co-sponsored by the American Cancer Society and the American College of Surgeons, capturing approximately 70% of new cancer diagnoses in the United States. The study has been reported in line with the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guideline.[8] An institutional review board waiver was obtained from Brigham and Women's Hospital for the use of de-identified administrative data.

Study cohorts

Patients were included if they met all of the following criteria:

1. Biopsy-confirmed prostate cancer with a biopsy Gleason score of 6 (3 + 3) or 7 (3 + 4 or 4 + 3).
2. Clinically localized disease (N0M0) at diagnosis.
3. Definitive treatment with RP.
4. Preoperative clinical staging with both transrectal ultrasound (TRUS) and endorectal coil magnetic resonance imaging (erMRI), as documented in the NCDB Site-Specific Factor 15 (codes 020 and 030). While the dataset codes the MRI exam as endorectal, many of these patients may have also had an mpMRI, given that mpMRI has been available since 1982.[9]
5. Year of diagnosis 2015 or later, corresponding to implementation of the revised Gleason grading system following the 2014 International Society of Urological Pathology (ISUP) Consensus Conference.[10]

Patients were excluded if they met any of the following criteria:

1. Diagnosis prior to 2015.
2. Biopsy Gleason score other than 6 or 7, including Gleason score ≥8 or missing biopsy grade information.
3. Node-positive (N1) or metastatic (M1) disease at diagnosis.
4. No record of radical prostatectomy as definitive treatment.
5. Absence of documented TRUS or erMRI for clinical staging.

Outcomes and measures

Odds ratio (OR) at RP of adverse pathology defined as prostatectomy (p) Gleason score of 9–10, node-positive disease, or pT3b-T4 PC for patients at high or highest-risk for upgrading at RP based on age at diagnosis and PC indices. Highest-risk comprised age >70 years, PSA >10 ng/mL, clinical stage T2 or higher, ≥50% positive biopsy cores and Black or other non-white race and/or Hispanic ethnicity versus the same clinical factors and White race and non-Hispanic ethnicity for High-risk. All remaining patients were classified as low-risk. These thresholds were selected because age, PSA level, clinical tumor stage, and percent of biopsy cores positive are well-established predictors of upgrading, upstaging, and adverse pathology at RP[11–14] and are incorporated into widely used risk assessment frameworks such as NCCN and CAPRA.[2,15] The risk of all-cause mortality (ACM) was a secondary end point.

Pre-specific statistical analysis plan

Distribution of baseline clinical characteristics

For descriptive analyses, continuous variables such as age, baseline PSA, and the percentage of positive biopsy cores were summarized using medians and interquartile ranges (IQRs) to reflect their non-normal distributions. However, in the multivariable models, these variables were incorporated in categorical form using clinically established cutpoints to facilitate interpretability and to align with standard prostate cancer risk stratification. Specifically, age was grouped into <50, 50–70, and >70 years; baseline PSA was categorized as <4, 4–<10, 10–20, and >20 ng/mL; and the percentage of positive biopsy cores was modeled as <50% vs. ≥50%.

Adverse pathology odds ratio

To validate the factors associated with adverse pathology at RP that we used to define our high and highest risk groups we performed a multivariable logistic regression analysis.[16] Independent variables included age, baseline PSA levels, clinical tumor stage, percentage of positive biopsy cores, Charlson Deyo Comorbidity Index, income level, insurance, location, race, and ethnicity. Race data included White and Black or other non-White race including American Indian, Aleutian, Eskimo, Chinese, Japanese, Filipino, Hawaiian, Korean, Vietnamese, Laotian, Kampuchean, Thai, Asian Indian or Pakistani, Tahitian, Samoan, Tongan, Melanesian, New Guinean, Pacific Islander, or Other. Race was defined according to self-reported race categories as recorded in the NCDB.

Ethnicity data included Mexican, Puerto Rican, Cuban, South or Central American, Spanish, Latino, Dominican Republic, or other specified Spanish/Hispanic origin and these ethnicities were categorized as Hispanic ethnicity. Adjusted odds ratios (aORs) and 95% confidence intervals (CIs) were calculated to quantify the strength of associations and determine significant predictors.

Odds ratios were calculated for 2 high-risk categories compared to low-risk that were pre-specified based on the factors known to be significantly associated with an increased risk of upgrading or upstaging at RP,[2] including age >70 years at diagnosis, PSA >10 ng/mL, clinical T2 stage or higher, ≥50% positive biopsy cores, Black or other under-represented race, or Hispanic ethnicity. The two high-risk categories were called highest and high and were defined as (1) Highest: Black or other non-White race or Hispanic ethnicity, with age >70 years at diagnosis, PSA >10 ng/mL, clinical stage T2 or higher, and ≥50% positive biopsy cores where other non-White race included American Indian, Aleutian, Eskimo, Chinese, Japanese, Filipino, Hawaiian, Korean, Vietnamese, Laotian, Kampuchean, Thai, Asian Indian or Pakistani, Tahitian, Samoan, Tongan, Melanesian, New Guinean, Pacific Islander, or Other Asian; and (2) High: White race and non-Hispanic ethnicity, with age > 70 years at diagnosis, PSA > 10 ng/mL, clinical stage T2 or higher, and ≥50% positive biopsy cores. All other patients not included in these two groups were classified as low risk.

Estimates of ACM and ACM-risk

Cox regression analyses were performed to evaluate the risk of ACM within each pre-defined high-risk group where the low-risk group served as the baseline. We also compared the highest risk group to high-risk. Hazard ratios (HRs) with 95% CIs and corresponding *p*-values were reported for each high-risk group.

For illustrative purposes, estimates of ACM, stratified by risk group, were calculated and compared. ACM estimates were calculated using a 1- Kaplan Meier estimator of overall survival[17] and a log-rank *p*-value was used to compare these estimates in the two high-risk groups compared to low-risk and in addition to one another. An adjustment for 3 comparisons in the ACM estimate calculation were made using a Bonferroni correction[18] such that statistical significance was defined as $p > 0.05/3$ or <0.0167 for these comparisons. For all other analyses, statistical significance was defined as a p-value < 0.05. All statistical analyses were conducted using the Statistical

Package for the Social Sciences (SPSS) software, version 30 (IBM Corporation, Armonk, NY, USA), with the exception of the ACM estimates and 95% CIs with covariates, which were calculated using R (version 4.2.3) with the *survival* package (version 3.6.4). ACM figure was generated using the *survminer* package (version 0.5.0) in R.

Results

Description of patient baseline characteristics

Of the 2,161,253 patients initially analyzed, 76,474 (3.5%) met the study inclusion criteria. The median age was 62 years (IQR, 57–67). Most patients were White (81.4%, n = 62,255), followed by Black (14.3%, n = 10,934), and Hispanic (4.7%, n = 3623). The distribution of pre-specified risk categories among patients was 98.9% (n = 75,499) low-risk, 1.1% (n = 863) high-risk, and 0.01% (n = 107) highest-risk as summarized in Table 1.

TABLE 1. **Baseline clinical characteristic of 76,474 study patients in the study cohort**

Clinical characteristic	Values
Age, years, median (IQR)	62 (57–67)
Race, No. (%)	
White	62,255 (81.4%)
Black	10,934 (14.3%)
Other	3285 (4.3%)
Ethnicity, No. (%)	
Hispanic	3623 (4.7%)
Non-Hispanic	71,337 (93.3%)
Unknown	1514 (2.0%)
Year of diagnosis, No. (%)	
2014–2015	37,424 (49.0%)
2016–2017	39,050 (51.0%)
Baseline PSA, ng/mL, No. (%)	
<4	210 (0.3%)
4 to <10	1003 (1.3%)
10 to 20	1445 (1.9%)
>20	73,816 (96.5%)
Percentage of positive biopsy cores, median (IQR)	41.66 (0–100)
Clinical T Stage, No. (%)	
T1a-b	383 (0.5%)
T1c	56,778 (74.2%)
T2a-c	16,041 (21.0%)
T3a-b	1258 (1.6%)
T4	17 (0.02%)
Not Available	1997 (2.6%)
Biopsy Gleason score, No. (%)	
3 + 3	20,988 (27.4%)
3 + 4	36,320 (47.5%)
4 + 3	19,166 (25.1%)
Charlson-Deyo comorbidity index, No. (%)	
0	62,738 (82.0%)
1	10,704 (14.0%)
2	2063 (2.7%)
≥3	969 (1.3%)
Type of insurance coverage, No. (%)	
Private	45,159 (59.1%)
Medicare, Medicaid, or other government	30,480 (39.8%)
Uninsured	835 (1.1%)
Income quartile, No. (%)	
<$46,277	9864 (12.9%)
$46,277–$57,856	14,131 (18.5%)
$57,857–$74,062	17,461 (22.8%)
≥$74,063	35,018 (45.8%)
Location type, No. (%)	
Metropolitan	64,930 (84.9%)
Urban	8239 (10.8%)
Rural	3305 (4.3%)
Pre-specified Risk Groups (%)	
Low risk	75,499 (98.9%)
High risk	863 (1.1%)
Highest risk	107 (0.01%)

Note. Abbreviations: PSA, prostate-specific antigen; IQR, interquartile range; No, number; T, tumor.

Adjusted odds ratios of adverse pathology and comparison of ACM-risk and estimates by risk categories

Adverse pathology at RP was identified in 8679 of 76,474 patients (11.3%). Of patients in highest, high, and low risk groups, adverse pathology was observed in 39/107 (36.4%), 222/863(25.7%), and 8418/75,499 (11.1%), respectively. The adverse pathology OR was 4.355 (95% CI, 3.104–6.891), and 2.635 (95% CI, 2.252–3.083) for patients in the high- and highest-risk groups respectively compared to low-risk. Highest risk patients had a significantly higher adverse

pathology OR [1.704 (95% CI, 1.112–2.603; $p = 0.015$)] when compared to high-risk patients (Table 2). When restricting the endpoint to Gleason upgrading alone, both high-risk (OR 1.929; 95% CI 1.542–2.421; $p < 0.001$) and highest-risk patients (OR 2.626; 95% CI 1.501–4.609; $p < 0.001$) had significantly greater odds of upgrading compared with the low-risk group.

At a median follow-up of 5.93 years (IQR, 4.89–7.07), 3771 patients (5.10%) had died, of these deaths, 16/107 (14.95%), 95/863 (11.01%) and 3660/75,499 (4.85%) were in the highest-, high- and low-risk groups, respectively. ACM-risk was significantly higher in the highest- and high-risk groups compared to the low-risk group, with a HRs of 3.137 (95% CI, 1.920–5.127; $p < 0.001$) and 2.252 (95% CI, 1.837–2.761; $p < 0.001$), respectively. When comparing ACM-risk between highest- and high-risk groups, the HR was 1.378 (95% CI, 0.811–2.349; $p = 0.23$). As shown in Figure. 1, after adjusting for multiple comparisons, the adjusted estimates of ACM were significantly higher in patients in the highest- and high-risk categories compared to those in the low-risk category ($p < 0.001$) but not highest compared to high risk ($p = 0.23$). Specifically, the 6-year adjusted estimates of ACM were 4.70% (95% CI 4.60–4.90) in the low-risk category, 10.22% (95% CI 7.92–12.45) in the high-risk category, and 13.95% (95% CI 6.13–21.11) in the highest-risk categories category.

Discussion

In this study, we found that underrepresented minorities who presented with clinical factors are associated with an increased risk of upgrading or upstaging at RP had a significantly higher odds of adverse pathology at RP and a numerically greater risk of ACM compared to all other patients. The clinical relevance of this finding is that race and ethnicity associated with higher odds of upgrading at RP, predisposing the highest risk patients, as defined in this study, to under-treatment who elect to undergo radiation therapy, given the duration and type of androgen deprivation[19–21] used would be based on an under-graded and/or under-staged PC. Over time, under-treatment could lead to an increased risk of both prostate cancer-specific mortality (PCSM) and ACM. These findings provide evidence to conduct a detection trial to evaluate whether there is an added benefit when adding PSMA PET scans to SOC detection to identify undersampled higher-grade or higher-stage disease. Such a trial would enroll patients of all races and ethnicities with biopsy Gleason score 6 or 7 PC who have the high-risk clinical factors associated with upgrading and upstaging at RP. These patients would be randomized to either (1) undergo a biopsy of any suspicious areas detected on the PSMA PET in addition to those visualized and sampled on the mpMRI and a 12-core systematic TRUS-guided biopsy, and then proceed to RP, or (2) proceed directly to RP after mpMRI-targeted and 12-core systematic TRUS guided biopsy. Patients would be stratified prior to randomization by the two high-risk groups defined in this study. The primary endpoints would be the rates of upgrading or upstaging at RP in each high-risk group. This study design will enable an assessment of whether a biopsy guided by PSMA PET lowers the rate of upgrading and upstaging at RP compared to the SOC detection approach across all patients at high-risk for upgrading or upstaging or only within a specific patient cohort defined by race/ethnicity.

Several limitations deserve further discussion. First, in the NCDB database, patients are coded as having undergone an erMRI. However, it is unclear whether all patients underwent both systematic TRUS- and MRI-targeted biopsies or only a TRUS-guided systematic biopsy. Therefore, our results provide an upper estimate of the increased odds of adverse pathology at RP and elevated risk of mortality within each high-risk group given some patients with adverse pathology who did not undergo a targeted biopsy based on the mpMRI findings may have been removed from our study cohort if targeted biopsies of suspicious areas on mpMRI were performed and revealed a Gleason score of 9 or 10. In addition, the database does not distinguish between MRI-cognitive and MRI-fusion biopsy techniques, nor does it provide information on the biopsy platforms used, limiting our ability to evaluate how specific biopsy approaches may have contributed to upgrading or upstaging. The NCDB also does not include lesion-level detail, so we could not determine whether sites of pathologic upstaging corresponded to the preoperative MRI-targeted regions. Second, while there was a significant increase in the odds of adverse pathology in the highest compared to the high-risk group, this did not translate into a significant increase in ACM-risk during the median follow-up of 5.93 years. Although the highest-risk group had a higher point estimate for ACM (HR 1.38), this difference was not statistically significant, and therefore no conclusions can be made regarding long-term mortality differences between these groups. Third, PCSM data was not available in the NCDB database. Therefore, a future study

TABLE 2. **Adverse pathology odds and all-cause mortality hazard ratios**

Characteristics	Patients, No.	Events, No.	Estimate	aOR (95% CI)	*p* value
Age, years					
<50	3162	62	−0.335	0.715 (0.622, 0.823)	<0.001
50–70	66,142	2083	Reference		
>70	7170	383	0.362	1.435 (1.331, 1.548)	<0.001
Race					
White	62,255	2039	Reference		
Black	10,934	358	0.264	1.302 (1.218, 1.390)	<0.001
Other	3285	131	0.202	1.224 (1.089, 1.376)	<0.001
Ethnicity					
Non-Hispanic	71,337	2327	Reference		
Hispanic	3623	143	0.219	1.245 (1.117, 1.387)	<0.001
Baseline PSA, ng/mL					
<4	210	5	−0.202	0.817 (0.428, 1.560)	0.540
4 to <10	1003	17	Reference		
10 to 20	1445	57	0.431	1.539 (1.129, 2.100)	0.006
>20	73,816	2449	0.589	1.801 (1.388, 2.339)	<0.001
Clinical T Stage					
T1a-b	383	13	−0.171	0.843 (0.584, 1.217)	0.362
T1c	56,778	1419	Reference		
T2a-c	16,041	598	0.436	1.547 (1.466, 1.633)	<0.001
T3a-b	1258	401	1.797	6.031 (5.353, 6.795)	<0.001
T4	17	17	4.101	60.393 (13.617, 267.85)	<0.001
Charlson-Deyo comorbidity index, No. (%)					
0	62,738	2603	Reference		
1	10,704	781	0.049	1.051 (0.979, 1.128)	0.170
2	2063	246	−0.055	0.946 (0.818, 1.094)	0.456
≥3	969	141	−0.132	0.877 (0.701, 1.096)	0.248
Type of insurance coverage, No. (%)					
Private	45,159	1524	Reference		
Medicare, Medicaid, or other government	30,480	2199	0.175	1.191 (1.131, 1.254)	<0.001
Uninsured	835	48	0.188	1.206 (0.971, 1.498)	0.100
Income quartile, No. (%)					
<$46,277	9864	663	Reference		
$46,277–$57,856	14,131	851	0.005	1.005 (0.922, 1.095)	0.909
$57,857–$74,062	17,461	882	−0.047	0.954 (0.859, 1.060)	0.371
≥$74,063	35,018	1375	0.000	1.000 (0.917, 1.091)	0.995
Location type, No. (%)					
Metropolitan	64,930	3099	Reference		
Urban	8239	494	0.049	1.051 (0.972, 1.136)	0.214
Rural	3305	178	0.017	1.017 (0.904, 1.143)	0.782
Percentage of positive biopsy cores					
<50%	42,931	1049	Reference		
≥50%	33,542	1479	0.793	2.211 (2.106, 2.321)	<0.001
Pre-specified Risk Groups					
Low risk	75,499	8418	Reference	OR (95% CI)	
High risk	863	222	1.001	2.635 (2.252–3.083)	<0.001
Highest risk*	107	39	1.531	4.355 (3.104–6.891)	<0.001
All-Cause Mortality by Pre-specified Risk Groups				**HR (95% CI)**	***p* value**
Low risk	75,499	3660	Reference		
High risk	863	95	0.812	2.252 (1.837–2.761)	<0.001
Highest risk*	107	16	1.143	3.137 (1.920–5.127)	<0.001

Note. Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; PSA, prostate-specific antigen; HR, hazard ratio; T, tumor. *Patients in the highest-risk category had aOR for adverse pathology of 1.704 (95% CI, 1.112–2.603; $p = 0.015$) and an all-cause mortality HR of 1.378 (95% CI, 0.811–2.349; $p = 0.23$) compared with those in high-risk.

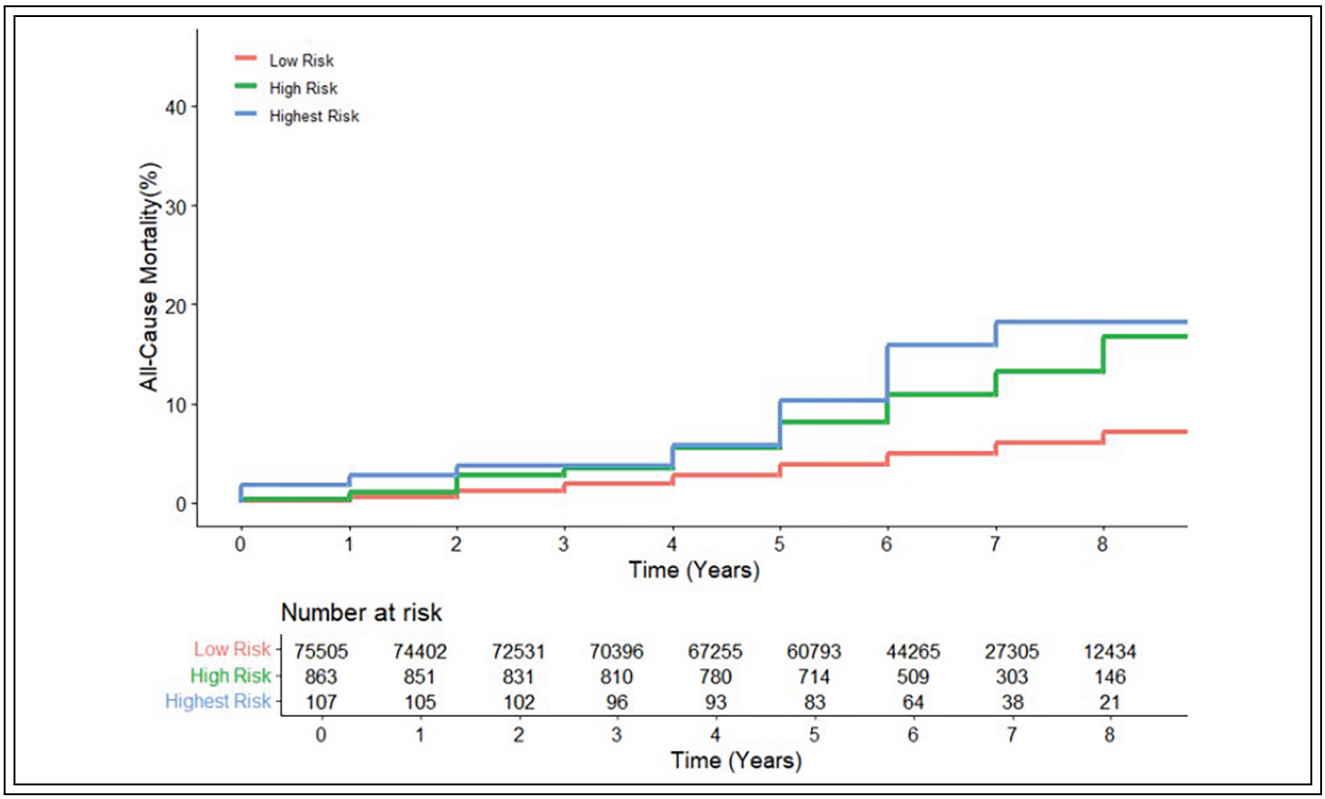

FIGURE 1. All-cause mortality estimates for the pre-specified risk groups for upgrading and upstaging at radical prostatectomy, *p*-values of <0.001 for the Highest- and High- vs. Low-risk and 0.23 for Highest- vs. High-risk

where this data is available will be needed to determine the specific contribution of PC-specific versus other causes of death to ACM, stratified by race and ethnicity, given these proportions may differ by race/ethnicity in that under-represented minorities are at a higher risk for death from non-PC causes such as long-term sequala of the metabolic syndrome[22–24] compared to all others. Nevertheless, given the significantly higher OR of adverse pathology among underrepresented minorities relative to their non-underrepresented counterparts, it is likely that PCSM will remain a significant component of ACM in this population. Additionally, further stratification of ACM was not feasible because the number of deaths was small, especially in the highest-risk subgroup, making further ACM stratification unreliable. Fourth, the highest-risk subgroup was relatively small (n = 107), which limits the precision of the estimated ORs and may reduce the stability of model-based comparisons; therefore, findings for this subgroup should be interpreted with appropriate caution. Fifth, as our cohort consists exclusively of patients undergoing RP, our assessment regarding undertreatment among patients receiving radiation and hormonal therapy is necessarily indirect; RP pathology serves as the reference standard for identifying occult high-risk disease that may lead to undertreatment when biopsy risk alone guides radiation and ADT decisions. Finally, genomic classifiers[25] and artificial intelligence platforms[26] deserve future study to determine whether they are able to add to clinical factors in more accurately defining who is at risk for having adverse pathology to RP.

Conclusion

The disproportionate under-grading and under-staging observed in the current study in under-represented minorities can lead to under-treatment in the highest risk patients electing to undergo radiation therapy and ADT, given that the ADT duration could be based on an under-graded Gleason score. Over time, under-treatment can translate into an increased mortality risk, highlighting the urgent need to improve the detection strategy in these patients.

Acknowledgement

We thank the patients and their families, as well as the institutions and clinicians contributing to the National Cancer Database for their dedication to cancer research and data collection.

Funding Statement

This research did not receive any funding.

Author Contributions

The authors confirm contribution to the paper as follows: Conceptualization, Mutlay Sayan and Anthony V. D'Amico; methodology, Mutlay Sayan and Anthony V. D'Amico; formal analysis, Yetkin Tuac; data curation, Zhiyu Qian; writing—original draft preparation, Mutlay Sayan and Anthony V. D'Amico; writing—review and editing, Mutlay Sayan, Yetkin Tuac, Zhiyu Qian, Alexander P. Cole, Jonathan E. Leeman, Martin T. King, Paul L. Nguyen, and Anthony V. D'Amico; supervision, Mutlay Sayan and Anthony V. D'Amico. All authors reviewed and approved the final version of the manuscript.

Availablility of Data and Materials

The authors confirm that the data supporting the findings of this study are available within the article.

Ethics Approval

An institutional review board waiver was obtained from Brigham and Women's Hospital for the use of de-identified administrative data.

Informed Consent

Informed consent was waived for this study due to its retrospective design and the use of anonymized data.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. Bekelman JE, Rumble RB, Freedland SJ. Clinically localized prostate cancer: ASCO clinical practice guideline endorsement of an AUA/ASTRO/SUO guideline summary. *J Oncol Pract* 2018;14(10):618–624. doi:10.1200/jop.18.00434.
2. Schaeffer EM, Srinivas S, Adra N et al. NCCN guidelines® insights: prostate cancer, version 3.2024: featured updates to the NCCN guidelines. *J Natl Compr Cancer Netw* 2024;22(3):140–150. doi:10.6004/jnccn.2024.0019.
3. Ahdoot M, Wilbur AR, Reese SE et al. MRI-targeted, systematic, and combined biopsy for prostate cancer diagnosis. *N Engl J Med* 2020;382(10):917–928. doi:10.1056/NEJMoa1910038.
4. Sundi D, Ross AE, Humphreys EB et al. African American men with very low-risk prostate cancer exhibit adverse oncologic outcomes after radical prostatectomy: should active surveillance still be an option for them? *J Clin Oncol* 2013;31(24):2991–2997. doi:10.1200/jco.2012.47.0302.
5. Faisal FA, Sundi D, Cooper JL et al. Racial disparities in oncologic outcomes after radical prostatectomy: long-term follow-up. *Urology* 2014;84(6):1434–1441. doi:10.1016/j.urology.2014.08.039.
6. Jalloh M, Myers F, Cowan JE, Carroll PR, Cooperberg MR. Racial variation in prostate cancer upgrading and upstaging among men with low-risk clinical characteristics. *Eur Urol* 2015;67(3):451–457. doi:10.1016/j.eururo.2014.03.026.
7. Mookerji N, Pfanner T, Hui A et al. Fluorine-18 prostate-specific membrane antigen-1007 PET/CT vs. multiparametric MRI for locoregional staging of prostate cancer. *JAMA Oncol* 2024;10(8):1097–1103. doi:10.1001/jamaoncol.2024.3196.
8. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol* 2008;61(4):344–349. doi:10.1016/j.jclinepi.2007.11.008.
9. Giganti F, Rosenkrantz AB, Villeirs G et al. The evolution of MRI of the prostate: the past, the present, and the future. *Am J Roentgenol* 2019;213(2):384–396. doi:10.2214/ajr.18.20796.
10. Epstein JI, Egevad L, Amin MB et al. The 2014 international society of urological pathology (ISUP) Consensus conference on gleason grading of prostatic carcinoma: definition of grading patterns and proposal for a new grading system. *Am J Surg Pathol* 2016;40(2):244–252. doi:10.1097/pas.0000000000000530.
11. Epstein JI, Feng Z, Trock BJ, Pierorazio PM. Upgrading and downgrading of prostate cancer from biopsy to radical prostatectomy: incidence and predictive factors using the modified Gleason grading system and factoring in tertiary grades. *Eur Urol May* 2012;61(5):1019–1024. doi:10.1016/j.eururo.2012.01.050.
12. Leeman JE, Chen MH, Huland H, Graefen M, D'Amico AV, Tilki D. Advancing age and the odds of upgrading and upstaging at radical prostatectomy in men with gleason score 6 prostate cancer. *Clin Genitourin Cancer* 2019;17(6):e1116–e1121. doi:10.1016/j.clgc.2019.07.018.
13. Yang DD, Mahal BA, Muralidhar V et al. Risk of upgrading and upstaging among 10 000 patients with gleason 3+4 favorable intermediate-risk prostate cancer. *Eur Urol Focus* 2019;5(1):69–76. doi:10.1016/j.euf.2017.05.011.
14. Lotan Y, Shariat SF, Khoddami SM et al. The percent of biopsy cores positive for cancer is a predictor of advanced pathological stage and poor clinical outcomes in patients treated

with radical prostatectomy. *J Urol* 2004;171(6 Pt 1):2209–2214. doi:10.1097/01.ju.0000127730.78973.fe.
15. Cooperberg MR, Pasta DJ, Elkin EP et al. The university of california, san francisco cancer of the prostate risk assessment score: a straightforward and reliable preoperative predictor of disease recurrence after radical prostatectomy. *J Urol* 2005;173(6):1938–1942. doi:10.1097/01.ju.0000158155.33890.e7.
16. Agresti A. *Categorical data analysis*. Hoboken, NJ, USA: John Wiley & Sons, Inc.; 2012.
17. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 1958;53(282):457–481. doi:10.1080/01621459.1958.10501452.
18. Shi Q, Pavey ES, Carter RE. Bonferroni-based correction factor for multiple, correlated endpoints. *Pharm Stat* 2012;11(4):300–309. doi:10.1002/pst.1514.
19. Bolla M, De Reijke TM, Van Tienhoven G et al. Duration of androgen suppression in the treatment of prostate cancer. *N Engl J Med* 2009;360(24):2516–2527. doi:10.1056/NEJMoa0810095.
20. Horwitz EM, Bae K, Hanks GE et al. Ten-year follow-up of radiation therapy oncology group protocol 92-02: a phase III trial of the duration of elective androgen deprivation in locally advanced prostate cancer. *J Clin Oncol* 2008;26(15):2497–2504. doi:10.1200/jco.2007.14.9021.
21. Zapatero A, Guerrero A, Maldonado X et al. High-dose radiotherapy and risk-adapted androgen deprivation in localised prostate cancer (DART 01/05): 10-year results of a phase 3 randomised, controlled trial. *Lancet Oncol* 2022;23(5):671–681. doi:10.1016/S1470-2045(22)00190-5.
22. Falkner B, Cossrow ND. Prevalence of metabolic syndrome and obesity-associated hypertension in the racial ethnic minorities of the United States. *Curr Hypertens Rep* 2014;16(7):449. doi:10.1007/s11906-014-0449-5.
23. Cossrow N, Falkner B. Race/ethnic issues in obesity and obesity-related comorbidities. *J Clin Endocrinol Metab* 2004;89(6):2590–2594. doi:10.1210/jc.2004-0339.
24. Javed Z, Haisum Maqsood M, Yahya T et al. Race, racism, and cardiovascular health: applying a social determinants of health framework to racial/ethnic disparities in cardiovascular disease. *Circ Cardiovasc Qual Outcomes* 2022;15(1):e007917. doi:10.1161/CIRCOUTCOMES.121.007917.
25. Spratt DE, Zhang J, Santiago-Jiménez M et al. Development and validation of a novel integrated clinical-genomic risk group classification for localized prostate cancer. *J Clin Oncol* 2018;36(6):581–590. doi:10.1200/jco.2017.74.2940.
26. Esteva A, Feng J, Van Der Wal D et al. Prostate cancer therapy personalization via multi-modal deep learning on randomized phase III clinical trials. *npj Digit Med* 2022;5(1):71. doi:10.1038/s41746-022-00613-w.

