2020

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Cite as: Rasul R, Golden A, Feuerstein MA. Prostate cancer risk group is associated with other-cause mortality in men with localized prostate cancer. *Can Urol Assoc J* 2020;14(10):E507-13. http://dx.doi.org/10.5489/cuaj.6324

Published online May 12, 2020

Abstract

Introduction: Informed decision-making in localized prostate cancer must consider the natural history of the disease, risks of treatment, and the competing risks from other causes. Other-cause mortality has often been associated with comorbidity or treatment-related side effects. We aimed to examine the association between prostate cancer aggressiveness and other-cause mortality.

Methods: Using the Surveillance, Epidemiology, and End Results (SEER)18 registries, patients diagnosed with localized prostate cancer between 2004 and 2015 were identified. Patients were categorized into low-, intermediate- and high-risk groups. Vital status, death due to prostate cancer, and death due to other causes were based on death certificate information. Survival analyses were performed to assess the association between prostate cancer risk group and mortality while adjusting for demographic variables, year of diagnosis, and initial therapy.

Results: A total of 464 653 patients were identified with a median followup of 5.4 years. Cardiovascular disease was the most common cause of mortality during the study period. Compared to low-risk patients, intermediate- and high-risk patients had a higher risk of mortality from other cancers, cardiovascular disease, and other causes of death regardless of initial treatment. Men who underwent surgery as initial therapy had lower cumulative mortality rates compared to those with radiation as their initial therapy.

Conclusions: Intermediate- and high-risk prostate cancers are associated with higher risk of other-cause mortality. This appears to be independent of treatment type and may not be solely explained by comorbidity status. Further studies controlling for comorbidity and treatment burden should be explored.

Introduction

In 2019, there will be an estimated 174 000 new cases of prostate cancer diagnosed in the U.S.[1] Approximately 80% of these patients will be diagnosed with localized disease, with a five-year prostate cancer relative survival rate of greater than 99%. However, prostate cancer remains the second leading cause of cancer-related death. For predicting prostate cancer mortality (PCM) and guiding treatment decisions, risk classifications using stage, grade, and prostate-specific antigen (PSA) have been established and routinely integrated into clinical practice.[2] There is a clear and definite association between higher risk disease and PCM.

Predicting other-cause mortality (OCM) in men with prostate cancer has been more elusive. Currently, the National Comprehensive Cancer Network (NCCN) guidelines recommend predicting individual life expectancy based on life insurance tables and adding or subtracting 50% if the patient is estimated to be in the highest or lowest quartile of health status.[3] Previous authors have devised nomograms and other tools using patient comorbidities to more accurately predict OCM.[4,5] Other research has focused on the relationship between prostate cancer treatment and OCM, demonstrating that perhaps there is a treatment-related effect on OCM.[6]

To our knowledge, there has been a paucity of research examining the association between prostate cancer risk classification and OCM. This could aid pre-treatment nomograms to guide treatment decisions or further elucidate risks of treatment. The objective of this study was to report the association between prostate cancer risk classification and OCM using a nationwide cancer database.

Methods

Data source

Data were extracted from the Surveillance, Epidemiology, and End Results (SEER) 18 Registries Custom Data Release, April 2018, that included supplemental data fields for radiation therapy and chemotherapy for the November 2017 submission, using SEER Stat 8.3.5 software. SEER is sponsored by the National Cancer Institute to maintain and distribute cancer incidence and survival data from population-based

cancer registries representing approximately 34% of the U.S. population. The SEER registries collect information on site and extent of disease, first course of cancer-directed therapy, and socio-demographic characteristics, with active followup for date and cause of death.[7]

Cohort

All primary prostate cancer patients diagnosed from 2004–2015 with neither known regional lymph node involvement nor distant site(s) of metastatic involvement at time of diagnosis were identified, and vital status was determined through December 2015. Cases were excluded if they had unknown previous cancer history or unknown cause of death, a diagnosis determined from autopsy or death, survival time less than a month after diagnosis, prostate cancer with stage IV or unknown, or whose prostate cancer risk group could not be classified.

Outcomes

Clinical collaborative staging (CS) characteristics related to the prostate cancer diagnosis were extracted from SEER data, including the American Joint Committee on Cancer (AJCC) 6-7th Edition TNM staging, tumor grade, Gleason score (SEER CS site-specific factors 8 and 10), and PSA at diagnosis (Supplementary Table 1). SEER assigns PSA a value of 0.1 for measurements 0.1 or less and a value of 98.0 for measurements 98.0 or greater. To be consistent with the 2004–2009 SEER Gleason score definition, cases diagnosed from 2010–2015 were assigned the Gleason score from pathology samples from prostatectomy if both surgical and biopsy or transurethral resection of the prostate (TURP) samples were scored. TNM staging was classified as T0-T2/N0/M0 or T3/N0/M0. For men with stage T2 NOS, Gleason score and PSA were used to classify risk group. Prostate cancer risk group was defined using the D'Amico classification system[2]: high-risk (PSA >20 ng/ml or Gleason >7 or T3); intermediate-risk (PSA 10–≤20 ng/ml or Gleason 7 or T2b/T2c); low-risk (PSA <10 ng/ml and Gleason <7 and T1-T2a); or unknown (none of the previous).[3] Men whose risk group was unknown due to missing PSA and Gleason score values were excluded (n=38 069; 7.6% of 502 722 men with primary localized prostate cancer).

Other study variables were extracted from SEER, including age at diagnosis, race, marital status, census tract poverty indicator, geographic region of SEER registry and initial prostate cancer therapy (radiation or surgery). In SEER, radiation and surgery variables are under-reported and no indication of therapy should be interpreted as no/unknown. In SEER, a variable for chemotherapy as initial therapy is limited to yes or no/unknown, therefore, important treatment information, such as use of concurrent androgen deprivation therapy (ADT) with radiation, is not available.

Survival time was defined as the difference in months between the date of diagnosis of prostate cancer and the date of death reported to SEER, the date last known to be alive, or December 2015, whichever was earliest. Vital status (categorized as alive or dead), death due to a specific cancer, and death due to other non-cancer cause were based on death certificate information reported to SEER and SEER's definition of cause of death. Deaths were categorized as PCM and OCM. The latter was further subdivided into other non-prostate cancer mortality (non-PCM), cardiovascular mortality (CVM) or other causes.

Statistical analysis

The frequency and percent of categorical study variables were compared by prostate cancer risk group using Chi-squared tests. For continuous variables, mean and standard deviation (SD) or median and interquartile range (IQR) were reported, and differences were assessed using Kruskal-Wallis tests.

Survival analyses were performed to assess the association between prostate cancer risk group and mortality outcomes (overall mortality, PCM, non-PCM, CVM, and other causes), while adjusting for confounders (demographic variables, year of prostate cancer diagnosis, and initial therapy). Men alive at time of last followup or December 2015 were censored. For the outcome of overall mortality, a Cox proportional hazards model was used. For cause-specific mortality, separate Fine and Gray competing risks models were used, which account for the potential for death due to other causes. Models were stratified by initial therapy because this variable did not exhibit proportional hazards over time. For the Cox and Fine and Gray models, adjusted hazard ratios and adjusted sub-distribution hazard ratios were reported, respectively. Given the large sample size, results should be interpreted using confidence intervals (CI) and effect sizes to evaluate clinical relevance. Analyses were conducted using SAS software, version 9.4 (SAS Institute, Cary, NC, U.S.).

Results

The study cohort consisted of 464 653 men diagnosed with localized prostate cancer from 2004–2015. Median followup after prostate cancer diagnosis was 5.4 years (IQR 2.9–8.3). Patient characteristics are shown in Table 1. Patients with high-risk prostate cancer were older than intermediate- and low-risk patients. Intermediate-risk patients were more likely to have prostatectomy as their initial therapy compared to high-risk patients. Low-risk patients were more likely to be treated with radiation compared to intermediate- and high-risk patients.

By the end of the study period, the cumulative mortality rate from any cause, adjusted for the population at risk at each time point, was 31.2% (95% CI 30.8–31.5%). Table

Table 1. Patient characteristics

Characteristic	Overall (N=464 653)		Low-risk (n=122 398, 26.3%)		Intermediate-risk (n=229 996, 49.5%)		High-risk (n=112 259, 24.2%)	
	n	%	n	%	n	%	n	%
Age group (years)								
<55	52 020	11.1	13 526	11.1	29 341	12.8	9153	8.2
55–64	163 020	34.7	45 100	36.9	84 096	36.6	33 824	30.1
65–74	174 975	37.3	48 749	39.8	83 688	36.4	42 538	37.9
75–84	65 980	14.1	14 240	11.6	29 741	12.9	21 999	19.6
≥85	8658	1.8	783	0.6	3130	1.4	4745	4.2
Race								
White	360 800	76.8	96 580	78.9	179 012	77.8	85 208	75.9
Black	71 301	15.2	17 155	14.0	35 976	15.6	18 170	16.2
American Indian/AK native, Asian/ Pacific Islander	23 682	5.0	5598	4.6	10 950	4.8	7134	6.4
Unknown	8870	1.9	3065	2.5	4058	1.8	1747	1.6
Poverty level								
Q1	124 276	26.5	33 670	27.5	61 624	26.8	28 982	25.8
Q2	114 703	24.4	29 821	24.4	56 769	24.7	28 113	25.0
Q3	117 071	24.9	30 842	25.2	58 344	25.4	27 885	24.8
Q4	108 603	23.1	28 065	22.9	53 259	23.2	27 279	24.3
Marital status								
Married	319 352	68.0	83 172	68.0	160 848	69.9	75 332	67.1
Unmarried	94 483	20.1	23 619	19.3	45 495	19.8	25 369	22.6
Unknown	50 818	10.8	15 607	12.8	23 653	10.3	11 558	10.3
Geographic region of SEER cancer registry								
West	232 085	49.4	62 867	51.4	112 253	48.8	56 965	50.7
Central	98 571	21.0	23 037	18.8	50 555	22.0	24 979	22.3
East	133 997	28.5	36 494	29.8	67 188	29.2	30 315	27.0
Year of prostate cancer diagnosis								
2004–2005	76 307	16.3	22 956	18.8	35 653	15.5	17 698	15.8
2006–2007	89 093	19.0	25 537	20.9	43 543	18.9	20 013	17.8
2008–2009	81 993	17.5	20 784	17.0	41 927	18.2	19 282	17.2
2010–2011	86 467	18.4	22 323	18.2	43 965	19.1	20 179	18.0
2012–2013	70 074	14.9	17 419	14.2	35 059	15.2	17 596	15.7
2014–2015	60 719	12.9	13 379	10.9	29 849	13.0	17 491	15.6
PSA level (ng/ml)								
<10	331 436	70.6	122 398	100.0	158 898	76.3	50 140	48.5
10–20	68 437	14.6	0	0.0	49 492	23.8	18 945	18.3
>20	34 205	7.3	0	0.0	0	0.0	34 205	33.1
Gleason score								
<6	190 683	40.6	122 398	100.0	58 983	26.2	9302	8.5
7	203 760	43.4	0	0.0	166 241	73.8	37 519	34.3
8–10	62 701	13.4	0	0.0	0	0.0	62 701	57.3
AJCC T stage								
T1 to T2a	215 897	46.0	94 926	77.6	85 193	37.0	35 778	31.9
T2b, T2c	120 556	25.7	0	0.0	105 928	46.1	14 628	13.0
T2NOS	85 432	18.2	27 472	22.4	38 875	16.9	19 085	17.0
T3	42 768	9.1	0	0.0	0	0.0	42 768	38.1

AJCC: American Joint Committee on Cancer; PSA: prostate-specific antigen; SEER: Surveillance, Epidemiology, and End Results.

Table 1 (cont'd). Patient characteristics

Characteristic	Overall (N=464 653)		Low-risk (n=122 398, 26.3%)		Intermediate-risk (n=229 996, 49.5%)		High-risk (n=112 259, 24.2%)	
	n	%	n	%	n	%	n	%
Initial therapy for prostate cancer								
None	102 663	21.9	45 696	37.3	35 312	15.4	21 655	19.3
Radiation	160 820	34.2	53 054	43.4	70 895	30.8	36 871	32.8
Prostatectomy	179 949	38.3	16 767	13.7	115 359	50.2	47 823	42.6
Other initial therapy	21 221	4.5	6881	5.6	8430	3.7	5910	5.3

AJCC: American Joint Committee on Cancer; PSA: prostate-specific antigen; SEER: Surveillance, Epidemiology, and End Results.

2 shows the distribution of cause of death. CVM and other causes were the most common causes of death (22.9% and 39.1% of all deaths, respectively). Prostate cancer was the most common cause of death from cancer (16.9% of all deaths, 44.6% of cancer deaths). Miscellaneous malignant cancer (10.3% of all deaths, 27.2% of cancer deaths), lung cancer (6.5% of all deaths, 17.2% of cancer deaths), and pancreatic cancer (2.0% of all deaths, 5.3% of cancer deaths) comprised the majority of cancer-related deaths from non-prostate cancers.

Table 3 presents hazard ratios (HR) for overall and cause-specific mortality by prostate cancer risk group, adjusted for age, race, marital status, poverty indicator, geographic region, year of diagnosis, and initial therapy. Men with prostate cancer classified as high-risk (HR= 2.38, 95% CI 2.33, 2.43) or intermediate-risk (HR 1.47, 95% CI 1.44, 1.50) were more likely to die from any cause during the study period compared to those with low-risk cancer. The impact of risk group on cause-specific mortality was examined for PCM, non-PCM, CVM, and all other causes. As expected, men in the high-risk group had markedly increased risk of PCM compared to low-risk patients (HR 13.70, 95% CI 12.69, 14.79); the risk of PCM was significantly increased for intermediate-risk patients as well (HR 3.03, 95% CI 2.79, 3.28). High-risk patients also had the highest risks of death for non-PCM, CVM, and other causes; they had significantly greater risks for each specific cause of death that comprised OCM, with the exception of Alzheimer's disease (data not shown).

Several patient characteristics examined in addition to prostate cancer risk group were associated with increased mortality (Table 3). While Black patients did not have higher risk for PCM compared to White patients, modest but statistically significant higher risks were seen for all other causes of death. Men of other races had significantly lower risk of dying compared to White patiens for all causes of death. Unmarried men and those living in areas with greater poverty were more likely to die during the study followup period.

Fig. 1 examines the impact over time that initial prostate cancer therapy and risk group had on overall mortality and on PCM and OCM. Men who underwent a prostatectomy had lower cumulative mortality rates compared to those with radiation as their initial therapy, irrespective of prostate cancer risk group. Within each therapy group, high-risk patients had higher cumulative mortality rates than intermediate- or low-risk patients. This data should be interpreted with caution, as use of concurrent or subsequent ADT is unknown.

Discussion

Treatment decisions for patients with localized prostate cancer must consider the long natural history of the disease, risks of treatment, and the competing risks of mortality between prostate cancer and other causes. Two large, randomized trials conducted in the PSA era demonstrated the protracted course of localized prostate cancer and the minimal impact of radical treatment (surgery or radiation) on overall survival.[8,9] While these studies added further support for active surveillance in low-risk patients, the risk of PCM is more significant in patients with high-grade disease (Gleason score 8–10), who have a 15-year PCM of 22–27%.[10]

Table 2. Leading causes of death from cancer and other conditions in men with localized prostate cancer, SEER 2004–2015

Cause of death	Number of deaths	% of deaths
All causes	64 794	
Cancers	24 582	37.9
Prostate cancer	10 967	16.9
Miscellaneous malignant cancer	6680	10.3
Lung or bronchus cancer	4236	6.5
Pancreas cancer	1309	2.0
Colon (excluding rectum)	882	1.4
Urinary bladder	508	0.8
Non-cancer causes	40 212	62.1
Cardiovascular disease	14 852	22.9
Any other non-cancer	13 213	20.4
COPD and allied conditions	3303	5.1
Cerebrovascular diseases	2779	4.3
Diabetes mellitus	1679	2.6
Accidents and adverse effects	1664	2.6
Alzheimer's disease	1562	2.4
Pneumonia and influenza	1160	1.8

SEER: Surveillance, Epidemiology, and End Results.

Table 3. Multivariable models of overall and cause-specific mortality in men with localized prostate cancer, SEER 2004–2015

Category	Overall mortality	PCM	OCM		
			Non-PCM	CVM	Other causes
Prostate cancer risk group (ref = low-risk)					
High-risk	2.38 (2.33, 2.43)	13.71 (12.70, 14.80)	1.39 (1.32, 1.46)	1.53 (1.46, 1.60)	1.48 (1.43, 1.53)
Intermediate-risk	1.47 (1.44, 1.50)	3.03 (2.80, 3.29)	1.25 (1.20, 1.31)	1.35 (1.29, 1.41)	1.30 (1.26, 1.34)
Age group (ref =<55 years)					
55–64 years	1.61 (1.53, 1.69)	1.03 (0.94, 1.13)	2.11 (1.91, 2.33)	1.78 (1.60, 1.99)	1.56 (1.44, 1.69)
65–74 years	2.85 (2.72, 2.99)	1.14 (1.04, 1.26)	3.63 (3.28, 4.01)	3.22 (2.90, 3.58)	3.17 (2.93, 3.43)
75–84 years	5.34 (5.09, 5.60)	1.50 (1.36, 1.65)	4.70 (4.23, 5.22)	6.24 (5.60, 6.95)	6.46 (5.96, 7.00)
≥85 years	11.02 (10.44, 11.63)	2.12 (1.89, 2.36)	4.26 (3.72, 4.89)	12.24 (10.87, 13.78)	10.90 (9.96, 11.93)
Race (ref = White)					
Black	1.16 (1.14, 1.19)	1.02 (0.97, 1.07)	1.13 (1.08, 1.19)	1.26 (1.21, 1.32)	1.16 (1.12, 1.20)
American Indian/AK Native, Asian/ Pacific Islander, and unknown	0.62 (0.60, 0.64)	0.59 (0.54, 0.65)	0.74 (0.68, 0.80)	0.61 (0.56, 0.66)	0.69 (0.65, 0.73)
Marital status (ref = Married)					
Unmarried	1.37 (1.35, 1.40)	1.18 (1.12, 1.23)	1.17 (1.12, 1.22)	1.44 (1.39, 1.50)	1.37 (1.33, 1.41)
Unknown	1.09 (1.06, 1.12)	1.10 (1.03, 1.16)	0.95 (0.89, 1.00)	1.12 (1.06, 1.18)	1.12 (1.08, 1.16)
Poverty (ref = Q1)					
Q2	1.09 (1.06, 1.11)	1.14 (1.08, 1.21)	1.07 (1.02, 1.12)	1.06 (1.01, 1.11)	1.06 (1.03, 1.1)
Q3	1.14 (1.11, 1.16)	1.21 (1.14, 1.28)	1.08 (1.03, 1.13)	1.15 (1.10, 1.21)	1.08 (1.04, 1.12)
Q4	1.28 (1.25, 1.31)	1.25 (1.18, 1.32)	1.14 (1.09, 1.20)	1.29 (1.23, 1.35)	1.26 (1.22, 1.31)
Region (ref = West)					
Central	1.18 (1.16, 1.21)	0.95 (0.91, 1.00)	1.19 (1.14, 1.25)	1.15 (1.11, 1.20)	1.22 (1.18, 1.26)
East	1.05 (1.03, 1.07)	0.95 (0.90, 0.99)	1.02 (0.98, 1.06)	1.03 (0.99, 1.07)	1.10 (1.07, 1.13)

Numbers represented as hazard ratio with 95% confidence intervals adjusted for age, race (white, black, other), year of prostate cancer diagnosis, poverty level, marital status, and geographic region of SEER registry; stratified by initial therapy for prostate cancer. Cause of death categories: CVM: cardiovascular mortality; OCM: other-cause mortality; PCM: prostate cancer mortality; SEER: Surveillance, Epidemiology, and End Results.

To help clinicians and patients, prior authors have developed nomograms that incorporate age, comorbidity, and primary treatment to predict PCM and OCM.[11,12] Other authors have focused on developing models that predict OCM using comorbidity.[4,5] For example, in the Prostate Cancer Outcomes Study, among 3183 men diagnosed with non-metastatic prostate cancer in 1994–1995, cumulative incidence curves for other-cause mortality demonstrate a direct relationship between higher OCM and risk group.[4] In a SEER-Medicare study of patients undergoing surgery or observation for localized prostate cancer, higher stage was significantly associated with OCM on multivariate analysis.[11] Similarly, in a multicenter study of patients undergoing surgery or radiation, multivariable analysis showed overall survival was associated with PSA, biopsy Gleason score, and clinical stage.[13]

In the current study, in addition to the expected significant increase in PCM, men classified as high-risk were also more likely to die from other causes, including a 39% increase in other cancers, 53% increase in diseases of the heart, and 48% increase in other conditions. These increases are adjusted for known sociodemographic risk factors associated with CVM and OCM that were included in the models, but other alternative explanations — behaviors such as smoking, and clinical factors, including comorbidities and treatment effects — could not be ruled out due to limitations in the SEER dataset.

One possible explanation for our findings is that patients with more comorbidities are diagnosed with more advanced

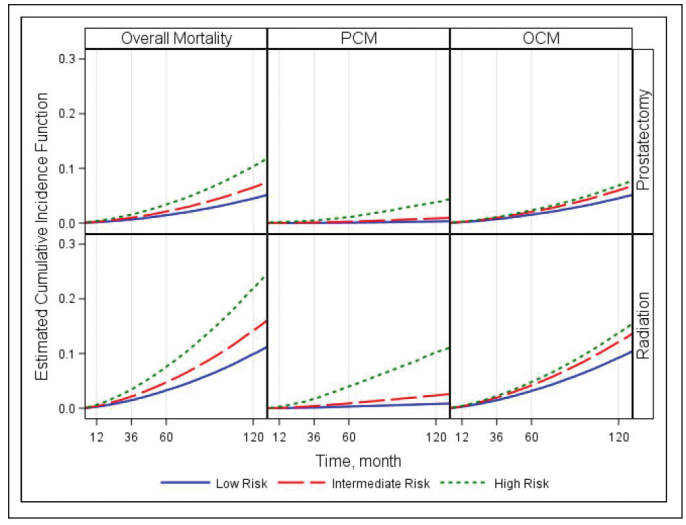

Fig. 1. Adjusted estimations of cumulative incidence functions for overall mortality, prostate cancer mortality (PCM), and other-cause mortality (OCM) in men with localized prostate cancer, by risk group and initial therapy for prostate cancer, Surveillance, Epidemiology, and End Results (SEER) 2004–2015.

disease due to less frequent or later screening. We would then expect comorbidity to be associated with PCM. However, two prior studies found no relationship between number of comorbidities and PCM in men with localized prostate cancer.[4,12]

Another explanation is that the type or burden of treatment may be correlated with more advanced disease and higher risk of OCM. In patients with localized prostate cancer, several studies have demonstrated an association with radiation therapy and ADT with increased OCM compared to surgery.[12-15] While these studies tried to control for age and comorbidities, it is likely that this association is at least in part due to confounding factors aside from treatment. In a large, population-based cohort, there was no association between ADT and other-cause mortality.[16] In the current study, the relationship between risk group and OCM was similar between patients initially treated with surgery and those treated with radiation. Unfortunately, due to limitations of this data, the use and impact of ADT is unknown. Further analysis using a more granular dataset, such as SEER-linked to Medicare, could elucidate the impact of ADT but would be limited to men 65 years of age and older.

Other limitations of using SEER data, particularly for urologic oncology, are well-described.[7] Misclassification of cause of death could impact our primary outcome of OCM, but SEER definitions for cause of death have previously been demonstrated to be accurate.[17] In this study, diagnosis date for prostate cancer ranged from 2004–2015; patients had unequal followup time during the study period and the median followup for this study was about five years. Therefore, fewer men were available in the analysis for later survival times due to their later year of diagnosis. We accounted for this by including year of diagnosis in the models; furthermore, analyses restricted to men diagnosed in 2004 who had the longest potential followup time (up to 11 years) showed very similar patterns for causes of death. In addition, important known risk factors for overall and cause-specific mortality are not recorded in the SEER data. Important lifestyle and clinical factors, such as smoking, alcohol intake, diet, family history, comorbidities, and unmeasured treatment measures (including hormonal therapy) cannot be ruled out as explanatory variables for the observed associations with prostate cancer risk group.

Conclusions

We found a direct association between higher prostate cancer risk group and other-cause mortality. Validation of our findings in a cohort of patients with known comorbidities and more granular treatment data should be explored. Prostate cancer risk group should be considered in development of models predicting OCM and overall mortality. The impact of treatment burden and OCM should be further evaluated. These findings may help clinicians and patients decide on observation vs. treatment for localized prostate cancer.

Competing interests: The authors report no competing personal or financial interests related to this work.

This paper has been peer-reviewed

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. *CA Cancer J Clin* 2019;69:7-34. https://doi.org/10.3322/caac.21551
2. D'Amico AV, Whittington R, Malkowicz SB, et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. *JAMA* 1998;280:969-74. https://doi.org/10.1001/jama.280.11.969
3. NCCN Clinical Practice Guidelines: Prostate cancer 2019. Available at www.nccn.org. Accessed Feb. 19, 2019
4. Daskivich TJ, Fan KH, Koyama T, et al. Prediction of long-term other-cause mortality in men with early-stage prostate cancer: Results from the Prostate Cancer Outcomes Study. *Urology* 2015;85:92-100. https://doi.org/10.1016/j.urology.2014.07.003
5. Kent M, Penson DF, Albertsen PC, et al. Successful external validation of a model to predict other cause mortality in localized prostate cancer. *BMC Med* 2016;14:25. https://doi.org/10.1186/s12916-016-0572-z
6. Cooperberg MR, Broering JM, Carroll PR. Risk assessment for prostate cancer metastasis and mortality at the time of diagnosis. *J Natl Cancer Inst* 2009;101:878-87. https://doi.org/10.1093/jnci/djp122
7. Scosyrev E, Messing J, Noyes K, et al. Surveillance Epidemiology and End Results (SEER) program and population-based research in urologic oncology: An overview. *Urol Oncol* 2012;30:126-32. https://doi.org/10.1016/j.urolonc.2009.11.005
8. Hamdy FC, Donovan JL, Lane JA, et al. 10-year outcomes after monitoring, surgery, or radiotherapy for localized prostate cancer. *N Engl J Med* 2016;375:1415-24. https://doi.org/10.1056/NEJMoa1606220
9. Wilt TJ, Jones KM, Barry MJ, et al. Followup of prostatectomy vs. observation for early prostate cancer. *N Engl J Med* 2017;377:132-42. https://doi.org/10.1056/NEJMoa1615869
10. Lu-Yao GL, Albertsen PC, Moore DF, et al. Fifteen-year outcomes following conservative management among men aged 65 years or older with localized prostate cancer. *Eur Urol* 2015;68:805-11. https://doi.org/10.1016/j.eururo.2015.03.021
11. Abdollah F, Sun M, Schmitges J, et al. Cancer-specific and other-cause mortality after radical prostatectomy vs. observation in patients with prostate cancer: Competing-risks analysis of a large North American population-based cohort. *Eur Urol* 2011;60:920-30. https://doi.org/10.1016/j.eururo.2011.06.039
12. Kutikov A, Cooperberg MR, Paciorek AT, et al. Evaluating prostate cancer mortality and competing risks of death in patients with localized prostate cancer using a comprehensive nomogram. *Prostate Cancer Prostatic Dis* 2012;15:374-9. https://doi.org/10.1038/pcan.2012.21
13. Kibel AS, Ciezki JP, Klein EA, et al. Survival among men with clinically localized prostate cancer treated with radical prostatectomy or radiation therapy in the prostate specific antigen era. *J Urol* 2012;187:1259-65. https://doi.org/10.1016/j.juro.2011.11.084
14. Cooperberg MR, Vickers AJ, Broering JM, et al. Comparative risk-adjusted mortality outcomes after primary surgery, radiotherapy, or androgen deprivation therapy for localized prostate cancer. *Cancer* 2010;116:5226-34. https://doi.org/10.1002/cncr.25456
15. Wallis CJD, Satkunasivam R, Herschorn S, et al. Association between primary local treatment and non-prostate cancer mortality in men with non-metastatic prostate cancer. *Urology* 2018;114:147-54. https://doi.org/10.1016/j.urology.2017.12.013
16. Wallis CJD, Satkunasivam R, Herschorn S, et al. Null association between androgen deprivation therapy and non-prostate cancer mortality among older men with nonmetastatic prostate cancer. *Urol Oncol* 2018;36:241e1-6. https://doi.org/10.1016/j.urolonc.2018.02.001
17. Penson DF, Albertsen PC, Nelson PS, et al. Determining cause of death in prostate cancer: Are death certificates valid? *J Natl Cancer Inst* 2001;93:1822-3. https://doi.org/10.1093/jnci/93.23.1822

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Supplementary Table. 1. ICD-9 and ICD-10 codes for causes of death from cancer and other conditions in men with localized prostate cancer, SEER 2004–2015

Cause of death	ICD-9 codes	ICD-10 codes	SEER cause of death Re-code
Cancers			
Prostate cancer	185	C61	54, 57, 61
Lung or bronchus cancer	162.2–162.5, 162.8–162.9	C34	39
Pancreas cancer	157	C25	33
Colon (excluding rectum)	153, 159.0	C18, C26.0	14
Urinary bladder	188	C67	58
Miscellaneous malignant cancer		Any other cancer code	
Other causes			
Heart disease	309–398, 402, 404, 410–429	309-398, 402, 404, 410–429	154
COPD & allied conditions	490–493, 519.3	490–496	175
Cerebrovascular diseases	430–438	430–438	160
Diabetes mellitus	250	250	148
Accidents & adverse effects	800–849	800–849	199
Alzheimer's disease	N/A	331.0	151
Pneumonia and influenza	470–474, 480–486	480–487	172
Any other non-cancer		Any other non-cancer code	

SEER: Surveillance, Epidemiology, and End Results.