Impact of Comorbidity on Survival Among Men With Localized Prostate Cancer

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ABSTRACT

Purpose

To provide patients and clinicians more accurate estimates of comorbidity-specific survival stratified by patient age, tumor stage, and tumor grade.

Patients and Methods

We conducted a 10-year competing risk analysis of 19,639 men 66 years of age and older identified by the Surveillance, Epidemiology, and End Results (SEER) program linked to Medicare program files. All men were diagnosed with localized prostate cancer and received no surgery or radiation within 180 days of diagnosis. The analysis was stratified by tumor grade and stage and by age and comorbidity at diagnosis classified using the Charlson comorbidity index. Underlying causes of death were obtained from SEER.

Results

During the first 10 years after diagnosis, men with moderately and poorly differentiated prostate cancer were more likely to die from causes other than their disease. Depending on patient age, Gleason score, and number of comorbidities present at diagnosis, 5-year overall mortality rates for men with stage T1c disease ranged from 11.7% (95% CI, 10.2% to 13.1%) to 65.7% (95% CI, 55.9% to 70.1%), and prostate cancer–specific mortality rates ranged from 1.1% (95% CI, 0.0% to 2.7%) to 16.3% (95% CI, 13.8% to 19.4%). Ten-year overall mortality rates ranged from 28.8% (95% CI, 25.3% to 32.6%) to 94.3% (95% CI, 87.4% to 100%), and prostate cancer–specific mortality rates ranged from 2.0% (95% CI, 0.0% to 5.3%) to 27.5% (95% CI, 21.5% to 36.5%).

Conclusion

Patients and clinicians should consider using comorbidity-specific data to estimate the threat posed by newly diagnosed localized prostate cancer and the threat posed by competing medical hazards.

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INTRODUCTION

Because prostate cancer frequently has a long natural history, many professional organizations recommend that screening and treatment should be limited to men with a life expectancy greater than 10 years.¹ The National Comprehensive Cancer Network prostate cancer practice guidelines suggest that radical surgery and/or radiation therapy should only be offered to men who are likely to survive more than 10 years, whereas the United States Preventive Services task force recently reaffirmed that men 75 years of age and older are unlikely to benefit from prostate cancer screening because relatively few of these men are likely to survive more than a decade.^{2,3}

These recommendations have been validated by two widely publicized randomized trials evaluating the benefit of prostate-specific antigen (PSA) testing for prostate cancer. The Prostate, Lung,

Colorectal, and Ovarian trial sponsored by the National Cancer Institute concluded that after 7 to 10 years of follow-up, prostate cancer mortality was very infrequent and did not differ significantly among men who were screened compared with the controls.⁴ The European Randomized Study of Screening for Prostate Cancer trial concluded that after 8 years of follow-up, PSA-based screening could reduce the death rate from prostate cancer by 20%, but at the risk of identifying many men who would not benefit from diagnosis and treatment.⁵

In contemporary clinical practice, treatment decisions are predominantly influenced by patients' life expectancy and tumor histology. Unfortunately, physicians often have difficulty providing accurate estimates of patients' life expectancy after initial cancer diagnosis.⁶ Patients have an even more distorted perception of the risks posed by their disease and the benefits of intervention. In a recently administered

Table 1. Charlson Comorbidity Index

Condition	Assigned Weight
Myocardial infarction	1
Congestive heart failure	1
Peripheral vascular disease	1
Cerebrovascular disease	1
Dementia	1
Chronic pulmonary disease	1
Connective tissue disease	1
Ulcer disease	1
Liver disease, mild	1
Diabetes	1
Hemiplegia	2
Renal disease, moderate or severe	2
Diabetes with end organ damage	2
Any malignancy	2
Leukemia	2
Malignant lymphoma	2
Liver disease, moderate or severe	3
Metastatic solid malignancy	6

mail survey, Mohan et al⁷ demonstrated that patients with localized prostate cancer grossly underestimate their life expectancy without treatment and grossly overestimate the survival benefit associated with treatment.

We have previously published 10-year outcomes after conservative management of localized prostate cancer.⁸ These estimates did not highlight the impact of patient comorbidities. To provide patients and clinicians more accurate estimates of comorbidity-specific survival stratified by patient age, tumor stage, and tumor grade, we assembled a large population-based cohort of 19,639 men with localized stage T1c or T2 prostate cancer who were managed conservatively after diagnosis. The resulting competing risk analyses should assist patients and their physicians to evaluate the risks posed by localized prostate cancer and their existing medical conditions.

PATIENTS AND METHODS

Data Sources

Data were obtained from Medicare insurance program files linked to the population-based Surveillance, Epidemiology, and End Results (SEER) cancer registries. The SEER regions sampled approximately 14% of the US population before 2000 and 25% thereafter. The Medicare database includes information on approximately 97% of men age 65 years and older; 93% of patients are linked to the SEER database.

Cancer stage and grade for each case were abstracted from SEER data files. The SEER grading convention before 2003 characterized Gleason 2 to 4 tumors as well differentiated, Gleason 5 to 7 tumors as moderately differentiated, and Gleason 8 to 10 as poorly differentiated. Treatment information was obtained from both SEER and Medicare files. A Charlson comorbidity score was derived from Medicare claims during the year before prostate cancer diagnosis using a validated algorithm.⁹

Table 2. Characteristics of Men Receiving Active Surveillance/Conservative Management for Clinically Localized Prostate Cancer by Comorbidity (T1c/T2)

Characteristic	Comorbidity = 0 (n = 14,130)		Comorbidity = 1 (n = 3,535)		Comorbidity = 2+ (n = 1,974)	
	No.	%	No.	%	No.	%
Age at diagnosis, years						
Median	77		78		78	
IQR	72-82		74-82		74-82	
Black race	1,752	12.4	519	14.7	380	19.3
Married at diagnosis	8,746	61.9	2,074	58.7	1,100	55.7
Urban residence	11,579	81.9	2,946	83.3	1,641	83.1
Zip code-level income, US\$						
Median	44,025		43,003		41,573	
IQR	33,757-59,397		32,580-57,554		31,396-56,041	
SEER regions						
Northeast	2,632	18.6	745	21.1	406	20.6
North-central	2,715	19.2	657	18.6	427	21.6
West	6,633	46.9	1,554	43.9	785	39.8
South	2,150	15.2	579	16.4	356	18.0
Cancer grade, Gleason score						
Moderately differentiated, 5-7	9,499	67.2	2,309	65.3	1,199	60.7
Poorly differentiated, 8-10	4,631	32.8	1,226	34.7	775	39.3
Clinical stage						
T1c	6,389	45.2	1,629	46.1	900	45.6
T2	7,741	54.8	1,906	53.9	1,074	54.4
Year of diagnosis						
1992-1996	2,757	19.5	540	15.3	296	14.9
1997-2003	11,373	80.5	2,995	84.7	1,678	85.0
Use of PADT	6,280	44.4	1,893	53.6	1,093	55.4
Vital status at last follow-up: alive as of December 31, 2007	8,512	60.2	1,808	51.2	805	40.8

Abbreviations: IQR, interquartile range; SEER, Surveillance, Epidemiology, and End Results; PADT, primary androgen deprivation therapy.

Table 3. Sample Sizes by Age, Comorbidity, and Vital Status As of December 31, 2005

Characteristic	Age at Diagnosis			
	66-74 Years		75+ Years	
	No.	%	No.	%
Moderately differentiated cancer				
Gleason 5-7, T1c, comorbidity = 0				
Overall sample size	1,949	100	2,689	100
Died of prostate cancer	33	2	126	5
Died of other causes	203	10	603	22
Alive	1,713	88	1,960	73
Gleason 5-7, T1c, comorbidity = 1				
Overall sample size	NA		771	100
Died of prostate cancer	NA		32	4
Died of other causes	72	19	245	32
Alive	295	80	494	64
Gleason 5-7, T1c, comorbidity ≥ 2				
Overall sample size	NA		394	100
Died of prostate cancer	NA		12	3
Died of other causes	60	30	150	38
Alive	131	66	232	59
Gleason 5-7, T2, comorbidity = 0				
Overall sample size	1,811	100	3,050	100
Died of prostate cancer	98	5	231	8
Died of other causes	289	16	922	30
Alive	1,424	79	1,897	62
Gleason 5-7, T2, comorbidity = 1				
Overall sample size	355	100	813	100
Died of prostate cancer	20	6	47	6
Died of other causes	89	25	327	40
Alive	246	69	439	54
Gleason 5-7, T2, comorbidity ≥ 2				
Overall sample size	NA		433	100
Died of prostate cancer	NA		26	6
Died of Other Causes	80	46	217	50
Alive	92	53	190	44
Poorly differentiated				
Gleason 8-10, T1c, comorbidity = 0				
Overall sample size	481	100	1,270	100
Died of prostate cancer	42	9	138	11
Died of other causes	37	8	214	17
Alive	402	84	918	72
Gleason 8-10, T1c, comorbidity = 1				
Overall sample size	NA		363	100
Died of prostate cancer	NA		26	7
Died of other causes	17	14	89	25
Alive	102	82	248	68
Gleason 8-10, T1c, comorbidity ≥ 2				
Overall sample size	NA		222	100
Died of prostate cancer	NA		17	8
Died of other causes	29	34	61	27
Alive	51	60	144	65
Gleason 8-10, T2, comorbidity = 0				
Overall sample size	813	100	2,067	100
Died of prostate cancer	111	14	288	14
Died of other causes	114	14	536	26
Alive	588	72	1,243	60
Gleason 8-10, T2, comorbidity = 1				
Overall sample size	NA		563	100
Died of prostate cancer	NA		54	10
Died of other causes	44	25	165	29
Alive	125	71	344	61

(continued in next column)

Table 3. Sample Sizes by Age, Comorbidity, and Vital Status As of December 31, 2005 (continued)

Characteristic	Age at Diagnosis			
	66-74 Years		75+ Years	
	No.	%	No.	%
Gleason 8-10, T2, comorbidity ≥ 2				
Overall sample size	NA		365	100
Died of prostate cancer	NA		27	7
Died of other causes	29	28	117	32
Alive	66	64	221	61

Abbreviation: NA, not available because Surveillance, Epidemiology, and End Results–Medicare privacy rules prohibit disclosure of numbers of less than 11 in any specific cell.

Study Participants

The study cohort consisted of men 66 years of age and older who were diagnosed with localized prostate cancers between January 1, 1992, and December 31, 2005 ($N = 157,381$). The following men were excluded from the analysis: 95,256 men who received attempted curative therapy such as prostatectomy or radiation within 180 days of diagnosis, 6,603 men who died as a result of any cause within 180 days of diagnosis, 10,277 men who had other cancer diagnoses, 5,913 men with stage T1a or T1b disease, 258 men with well-differentiated disease, and 173 men who received androgen deprivation therapy before diagnosis. In addition, we excluded 16,333 men who did not have both Medicare Part A and Part B as their primary health insurance coverage during the study period, 2,537 men with missing data, and 392 men with an unknown cancer grade. The final population consisted of 14,130 men with Charlson score of 0, 3,535 men with Charlson score of 1, and 1,974 men with Charlson score ≥ 2 . A summary of the Charlson scoring system is provided in Table 1. Cancers detected by PSA testing were classified as T1c, whereas the remaining cancers were classified as T1a, T1b, or T2. In the SEER-Medicare database, the vital status of patients is derived from Medicare Enrollment Database, which is updated every night from the Social Security Administration. Overall mortality rates were derived from survival data available through December 31, 2007. Underlying causes of death were obtained from the SEER program, which derives this information from state death certificates. Usually this information becomes available within 2 years of the date of death. As a consequence, prostate cancer–specific mortality rates were derived from data available through December 31, 2005. Previous studies have confirmed that prostate cancer deaths can be identified reliably from death certificates if results are classified simply as death as a result of prostate cancer or death resulting from another cause.^{10,11}

Statistical Analyses

The primary study end points were time to death resulting from prostate cancer and time to death resulting from other causes, stratified by patient age, cancer grade, cancer stage, and Charlson comorbidity score at the time of diagnosis. Estimates of competing risks were computed using cumulative incidence functions with competing risk adjustments for death resulting from prostate cancer and from other causes as described in Putter, Fiocco, and Geskus.^{12,13} To provide more stable estimates of the survival curves, we used a nearest-neighbor hazard smoother with an Epanechnikov Kernel as implemented in the R statistical system (R Foundation for Statistical Computing, Vienna, Austria).¹⁴ Covariate adjustment for competing risks was conducted as described in Putter et al.¹³ Bootstrap confidence intervals for the 10-year survival rates were obtained using 1,000 bootstrap replications.¹⁵ Median follow-up time was computed following the method described in Clark et al¹⁶ and Schemper and Smith.¹⁷

RESULTS

Most patients (72%) in our study cohort had no significant comorbidities (Charlson score = 0), 18% had one significant comorbidity, and 10% had two or more comorbidities. About two thirds (66%) of the patients were classified as having moderately differentiated disease (Gleason score 5 to 7), and about one third (34%) had poorly differentiated disease (Gleason score 8 to 10). Approximately 45% of the patients had screen-detected disease (T1c), whereas 55% had palpable disease (T2). The median age at diagnosis was 77 years, and the median follow-up for the study population was 6 years.

At the end of the study period, 60%, 51%, and 41% of men with zero, one, or two or more comorbidities were still alive, respectively. Only 5% and 11% of men with moderately or poorly differentiated disease, respectively, died as a result of prostate cancer. Baseline characteristics and long-term outcomes of the study population classified by comorbidity are summarized in Table 2. Sample sizes by age, comorbidity, and vital status as of December 31, 2005, are summarized in Table 3.

Appendix Figures A1 and A2 (online only) illustrate the competing risk of death according to age at diagnosis, cancer stage, cancer grade, and comorbidity score. Our results demonstrate that comorbidities negatively impact overall survival in men with localized prostate cancer. Men with stage T1c Gleason score 5 to 7 prostate cancer and no comorbidities have a 2% to 4% chance of dying as a result of prostate cancer within 5 years of diagnosis and a 5% to 14% chance within 10 years. During this same period they have a 12% to 48% chance of dying as a result of any cause within 5 years of diagnosis and a 29% to 83% chance within 10 years, depending on their age at diagnosis and comorbidity. Men with two or more comorbidities have

a 43% to 48% chance of dying as a result of any cause within 5 years and a 74% to 83% chance within 10 years, depending on their age at diagnosis. Prostate cancer mortality rates for men with stage T2 Gleason score 5 to 7 prostate cancer are only slightly higher than the rates for men with stage T1c disease.

Men with stage T1c Gleason score 8 to 10 localized prostate cancer also have a substantial risk of dying as a result of competing hazards. Men with no comorbidities have an equal chance of dying as a result of prostate cancer or a competing hazard as compared with men with two or more comorbidities, who have a substantially higher risk of dying as a result of a competing medical hazard. Men with stage T2 Gleason score 8 to 10 prostate cancer have a similar risk of dying as a result of prostate cancer or a competing hazard.

Table 4 summarizes the 5- and 10-year prostate cancer-specific and overall mortality rates for men with screen-detected (stage T1c) moderately and poorly differentiated disease. For men age 66 to 74 years, the overall 5-year mortality rate for men with Gleason score 5 to 7 disease rises from 11.7 (95% CI, 10.2 to 13.1) to 42.5 (95% CI, 36.1 to 48.5), and the overall 10-year mortality rate rises from 28.8 (95% CI, 25.3 to 32.6) to 83.1 (95% CI, 67.4 to 97.2) per 100 as the number of comorbidities present at diagnosis increases from zero to two or more. In contrast, these men face 5- and 10-year prostate cancer-specific mortality rates of 1.6 (95% CI, 1.1 to 2.4) to 4.3 (95% CI, 1.6 to 8.3) and 4.8 (95% CI, 2.8 to 8.4) to 5.3 (95% CI, 2.5 to 10.0) per 100, respectively. For men with Gleason score 8 to 10 disease, the overall 5- and 10-year mortality rates ranged from 26.4 (95% CI, 22.2 to 30.8) to 52.0 (95% CI, 42.1 to 64.5) and 55.0 (95% CI, 43.9 to 65.9) to 64.3 (95% CI, 52.0 to 84.9) per 100, respectively. As expected, the 5- and 10-year prostate cancer-specific mortality rates were somewhat higher in this high-risk group, ranging from 13.6 (95% CI, 9.6 to 17.8)

Table 4. Overall and Prostate Cancer-Specific Mortality Rates for Men by Years With Localized Prostate Cancer (T1c)

Characteristic	Age at Diagnosis							
	66-74 Years				75+ Years			
	5-Year Mortality		10-Year Mortality		5-Year Mortality		10-Year Mortality	
	Rate per 100*	95% CI†	Rate per 100*	95% CI†	Rate per 100*	95% CI†	Rate per 100*	95% CI†
T1c, Gleason 5-7, comorbidity = 0								
Overall mortality	11.7	10.2 to 13.1	28.8	25.3 to 32.6	26.3	24.8 to 28.0	67.1	63.3 to 72.4
Prostate cancer specific mortality	1.6	1.1 to 2.4	4.8	2.8 to 8.4	4.4	3.4 to 5.1	14.0	10.6 to 20.9
T1c, Gleason 5-7, comorbidity = 1								
Overall mortality	25.3	20.7 to 29.5	50.5	41.5 to 59.2	39.4	35.9 to 42.5	76.8	70.5 to 82.9
Prostate cancer-specific mortality	1.1	0.0 to 2.7	2.0	0.0 to 5.3	5.1	3.3 to 7.2	9.1	5.5 to 14.4
T1c, Gleason 5-7, comorbidity ≥ 2								
Overall mortality	42.5	36.1 to 48.5	83.1	67.4 to 97.2	48.1	42.7 to 52.7	74.4	63.7 to 84.7
Prostate cancer-specific mortality	4.3	1.6 to 8.3	5.3	2.5 to 10.0	4.0	1.7 to 6.5	5.0	2.5 to 8.7
T1c, Gleason 8-10, comorbidity = 0								
Overall mortality	26.4	22.2 to 30.8	55.0	43.9 to 65.9	41.4	38.3 to 44.0	77.0	71.5 to 82.5
Prostate cancer specific mortality	13.6	9.6 to 17.8	25.7	15.9 to 40.6	16.3	13.8 to 19.4	27.5	21.5 to 36.5
T1c, Gleason 8-10, comorbidity = 1								
Overall mortality	30.7	23.7 to 41.0	52.0	38.0 to 77.0	47.2	41.8 to 52.5	92.4	79.3 to 99.7
Prostate cancer-specific mortality	11.6	3.0 to 23.4	20.2	4.1 to 46.6	11.2	7.3 to 16.1	23.7	9.5 to 44.7
T1c, Gleason 8-10, comorbidity ≥ 2								
Overall mortality	52.0	42.1 to 64.5	64.3	52.0 to 84.9	65.7	55.9 to 70.1	94.3	87.4 to 100.0
Prostate cancer-specific mortality	9.6	2.4 to 19.3	13.7	2.7 to 33.4	12.8	7.3 to 18.9	18.8	9.3 to 36.8

*The mortality rates were derived by using smoothed cumulative incidence curves as described in the text.

†CIs were estimated using a bootstrap with 1,000 replications.

to 9.6 (95% CI, 2.4 to 19.3) and 25.7 (95% CI, 15.9 to 40.6) to 13.7 (95% CI, 2.7 to 33.4) per 100 for men with no comorbidities to two or more comorbidities, respectively.

For men age 75 years and older at diagnosis, 5- and 10-year overall mortality rates ranged from 26.3 (95% CI, 24.8 to 28.0) to 39.4 (95% CI, 35.9 to 42.5) and 67.1 (95% CI, 63.3 to 72.4) to 76.8 (95% CI, 70.5 to 82.9) per 100 for those men with Gleason score 5 to 7 disease, respectively. These rates are somewhat higher than those noted for younger men. Five- and 10-year prostate cancer-specific rates were also somewhat higher, ranging from 4.4 (95% CI, 3.4 to 5.1) to 4.0 (95% CI, 1.7 to 6.5) and 14.0 (95% CI, 10.6 to 20.9) to 5.0 (95% CI, 2.5 to 8.7) per 100 for men with no comorbidities to two or more comorbidities, respectively. For men age 75 years and older at diagnosis with Gleason score 8 to 10 disease, the 5- and 10-year overall mortality rates ranged from 41.4 (95% CI, 38.3 to 44.0) to 65.7 (95% CI, 55.9 to 70.1) and 77.0 (95% CI, 71.5 to 82.5) to 94.3 (95% CI, 87.4 to 100) per 100, respectively. The 5- and 10-year prostate cancer-specific mortality rates were comparable to those of the younger men, ranging from 16.3 (95% CI, 13.8 to 19.4) to 12.8 (95% CI, 7.3 to 18.9) and 27.5 (95% CI, 21.5 to 36.5) to 18.8 (95% CI, 9.3 to 36.8), respectively, per 100.

Table 5 summarizes the 5- and 10-year prostate cancer-specific and overall mortality rates for men with stage T2 moderately and poorly differentiated disease. Overall, the 5- and 10-year rates and trends were comparable to those of the men presenting with T1c disease. Both the overall mortality rate and the prostate cancer-specific mortality rates for men with stage T2 disease were slightly higher when compared with those of men with stage T1c disease. The 5- and 10-year prostate cancer-specific mortality rates were also somewhat higher among men with Gleason score 8 to 10 disease when

compared with men with Gleason score 5 to 7 disease for men with no comorbidities to two or more comorbidities.

For men age 75 years and older at diagnosis, the 5- and 10-year overall mortality rates for men with Gleason score 5 to 7 disease were somewhat higher than those of younger men. Five- and 10-year prostate cancer-specific rates were also somewhat higher. For men age 75 years and older diagnosed with Gleason score 8 to 10 disease, the 5- and 10-year overall mortality rates were comparable to those of the younger men.

DISCUSSION

An accurate estimate of overall and disease-specific survival is critical for an informed discussion of treatment options among men with newly diagnosed prostate cancer. Long-term survival depends, in part, on risks posed by the tumor and risks posed by existing comorbidity. Our study, the largest population-based study in the United States, shows that a higher comorbidity score is, in general, associated with higher overall mortality and lower prostate cancer-specific mortality.

Over a decade ago, we explored these issues using data from a population-based cohort of men diagnosed with localized prostate cancer in Connecticut who did not receive either surgery or radiation therapy.¹⁸ We demonstrated that an assessment of patient comorbidities using standardized instruments could be used to stratify patients according to their risk of dying from competing medical hazards. This concept has been validated by several authors who have demonstrated that the measurement of patient comorbidities combined with patient age and tumor grade can provide estimates of long-term survival with

Table 5. Overall and Prostate Cancer-Specific Mortality Rates for Men by Years With Localized Prostate Cancer (T2)

Characteristic	Age at Diagnosis							
	66-74 Years				75+ Years			
	5-Year Mortality		10-Year Mortality		5-Year Mortality		10-Year Mortality	
	Rate per 100*	95% CI†	Rate per 100*	95% CI†	Rate per 100*	95% CI†	Rate per 100*	95% CI†
T2, Gleason 5-7, comorbidity = 0								
Overall mortality	14.0	12.7 to 15.5	35.5	32.3 to 39.0	31.2	29.9 to 32.9	67.4	64.9 to 75.3
Prostate cancer-specific mortality	3.7	2.9 to 4.6	9.5	7.5 to 11.7	6.6	5.5 to 7.4	14.2	12.0 to 16.8
T2, Gleason 5-7, comorbidity = 1								
Overall mortality	26.4	22.0 to 31.0	65.5	56.4 to 79.2	43.3	39.7 to 46.4	77.3	72.5 to 82.8
Prostate cancer-specific mortality	5.7	3.4 to 8.5	11.9	6.9 to 23.9	5.5	4.1 to 7.2	13.3	7.9 to 21.3
T2, Gleason 5-7, comorbidity ≥ 2								
Overall mortality	40.4	33.9 to 48.2	74.6	64.2 to 85.1	57.8	53.6 to 62.1	88.9	84.0 to 94.4
Prostate cancer specific mortality	0.6	0.0 to 2.0	1.0	0.0 to 3.7	6.0	3.8 to 8.7	9.9	5.9 to 18.2
T2, Gleason 8-10, comorbidity = 0								
Overall mortality	31.5	28.0 to 34.3	61.5	55.0 to 67.1	50.0	47.7 to 52.4	83.4	80.2 to 86.7
Prostate cancer-specific mortality	18.2	14.6 to 21.5	23.9	23.9 to 35.6	18.9	16.5 to 20.9	27.9	24.3 to 31.7
T2, Gleason 8-10, comorbidity = 1								
Overall mortality	42.7	35.6 to 51.1	77.2	63.7 to 93.6	56.5	51.6 to 60.5	87.6	81.4 to 93.8
Prostate cancer-specific mortality	5.5	1.7 to 10.2	8.7	2.1 to 18.9	14.8	10.8 to 19.1	19.6	14.0 to 25.8
T2, Gleason 8-10, comorbidity ≥ 2								
Overall mortality	51.2	40.8 to 60.1	93.8	80.1 to 99.9	63.7	58.8 to 69.2	88.8	80.0 to 99.5
Prostate cancer-specific mortality	13.0	5.4 to 23.1	18.4	7.6 to 37.6	13.8	8.3 to 18.3	15.7	9.6 to 22.6

*The mortality rates were derived by using smoothed cumulative incidence curves as described in the text.

†CIs were estimated using a bootstrap with 1,000 replications.

moderate accuracy.¹⁹⁻²¹ The prediction rules developed have c-statistics in the range of 0.70 to 0.84, suggesting that survival estimates will be correct approximately three of every four times. Unfortunately, the estimates provided in our 1996 publication were based on a cohort of patients diagnosed before the advent of PSA testing. They do not incorporate the impact of the lead time associated with screening for PSA, and as a consequence, they underestimate long-term survival outcomes.

The tables presented in this article as well as the figures available in the Appendix (online only) use the Charlson comorbidity instrument to assess patient comorbidities. This instrument was originally developed to predict 1-year mortality in patients suffering from breast cancer, but has since been validated for use in estimating long-term survival among patients with multiple different cancers.^{22,23} It has the added advantage of being validated in a clinical setting, as well as in the analysis of large administrative data sets.²⁴

The impact of PSA testing most likely explains the substantial improvement in survival that we observed in this report when compared with our earlier analysis conducted more than a decade ago. PSA testing advances the date of diagnosis by as much as 13 years, resulting in longer patient survival after diagnosis.²⁵ Furthermore, systematic upgrading of Gleason scores has resulted in an apparent survival improvement for men classified by tumor grade.²⁶

Our results have several limitations. Our analysis only involves men age 66 years and older. Men younger than age 66 are much less likely to succumb to a competing medical hazard, and therefore our results cannot be applied to younger patients. Our results could not be stratified by individual tumor grade. Before 2003, the SEER system grouped Gleason scores 5 to 7 together as moderately differentiated disease and Gleason scores 8 to 10 together as poorly differentiated disease. Our report most likely overestimates prostate cancer–specific survival for men with Gleason 7 disease and underestimates prostate cancer–specific survival for men with Gleason 5 disease. This is balanced by the fact that many of these men received antiandrogen therapy, which may negatively impact overall survival, thereby underestimating prostate cancer–specific survival and overestimating overall survival.

Our follow-up was limited to 10 years. Most men with Charlson score ≥ 2 succumbed to a competing medical hazard during that time period. Men with no or one comorbidity often survived for at least 10 years. Longer follow-up will be needed to determine the relative impact of prostate cancer and competing medical hazards on long-term survival. Finally, we do not have data concerning why the men identified in this study chose active surveillance or watchful waiting as their primary treatment option. There may be unmeasured patient or disease factors that impact prostate specific–survival or all-cause survival. Accordingly, our results may or may not be applicable to men who undergo surgery or radiation therapy.

Our analysis has several strengths. The study was population-based, encompassed a wide geographic area, and had a large sample

size, giving us sufficient statistical power to provide stable survival estimates. Our results also report outcomes specific for older men. Most case series reports do not include information concerning outcomes among men older than 70 years. Our analysis has information on outcomes of approximately 20,000 men who were managed conservatively after a diagnosis of localized prostate cancer.

In summary, our findings suggest that relatively few men diagnosed with localized prostate cancer older than 65 years will die as a result of prostate cancer within 10 years of diagnosis. Most men with either no or one comorbidity will survive at least 10 years, whereas men with two or more comorbidities have a substantial risk of dying as a result of a competing medical hazard within this time frame. Men with poorly differentiated disease face a more substantial risk of dying as a result of prostate cancer when compared with men with moderately differentiated disease and an equivalent risk of dying as a result of competing medical hazards. Patients and clinicians should use the tables presented in this article (and the figures presented in the Appendix) to understand the risks posed by prostate cancer and by competing medical hazards before selecting the therapeutic approach that is most appropriate for them.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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