

Comorbidity and Competing Risks for Mortality in Men With Prostate Cancer

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BACKGROUND: Accurate estimation of life expectancy is essential for men deciding between aggressive and conservative treatment of prostate cancer. The authors sought to assess the competing risks of nonprostate cancer and prostate cancer mortality among men with differing Charlson comorbidity index scores and tumor risks.

METHODS: The authors conducted a retrospective study of 1482 men with nonmetastatic prostate cancer diagnosed from 1997 to 2004 at the Greater Los Angeles and Long Beach Veterans Affairs Medical Centers. They performed Kaplan-Meier and competing risks regression analyses to assess survival outcomes. **RESULTS:** After a mean follow-up of 6.0 years, 370 (25%) men died from other causes, whereas 44 (3%) died of prostate cancer. At 10 years after diagnosis, men with Charlson scores 0, 1, 2, and 3+ had nonprostate cancer mortality rates of 17%, 34%, 52%, and 74%, respectively. In competing risks regression analysis, each point increase in Charlson score was associated with a 2-fold increase in hazard of nonprostate mortality. Men with Charlson 3+ had 8.5× the hazard of death from other causes, compared with men with the lowest scores (subhazard ratio, 8.5; 95% confidence interval, 6.2-11.7). After stratification by tumor risk, nonprostate mortality rates remained markedly elevated among men with higher Charlson scores, whereas prostate cancer mortality was rare, especially among low-risk and intermediate-risk groups (0.4%, 3%, and 8% for low, intermediate, and high risk, respectively). **CONCLUSIONS:** Men with the highest Charlson scores should consider conservative management of low-risk and intermediate-risk tumors, given their exceedingly high risk of death from other causes and low risk of prostate cancer mortality. *Cancer* 2011;117:4642-50. © 2011 American Cancer Society.

KEYWORDS: prostatic neoplasms, comorbidity, outcome assessment, prostate.

The first decision facing a man with a new diagnosis of clinically localized prostate cancer is whether to pursue aggressive treatment. Level I evidence shows that significant survival benefits do not develop until 8 to 10 years after treatment.¹ Because definitive local therapy risks morbidities that may significantly affect quality of life,²⁻⁵ it is widely accepted that most men whose comorbidity gives them a low probability of long-term survival should not be aggressively treated. As such, the American Urological Association and National Comprehensive Cancer Network treatment guidelines recommend using life expectancy to help triage patients with clinically localized disease between aggressive and nonaggressive management.^{6,7}

Despite the recognized role of life expectancy in medical decision making for men with prostate cancer, the determination of who is too ill to benefit from aggressive treatment remains ill-defined. This is largely because of the absence of a widely accepted method of assessing prognosis that incorporates an individual's health status. The American Urological Association suggests that clinicians use life tables to estimate prognosis, but because life tables are population-based, they fail to account for the individual's health; they overestimate 10-year life expectancy by as much as 22% in men undergoing prostatectomy.⁸ The National Comprehensive Cancer Network guidelines recommend adjusting life table estimates for the individual by adding or subtracting 50% of projected years based on whether the patient is in the highest or lowest quartile of health. Yet the National Comprehensive Cancer Network guidelines offer no method for categorizing patients as such.⁷

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See editorial on pages 4576-8, this issue.

DOI: 10.1002/cncr.26104, **Received:** August 19, 2010; **Revised:** November 26, 2010; **Accepted:** December 6, 2010, **Published online** April 8, 2011 in Wiley Online Library (wileyonlinelibrary.com)

Comorbidity indexes, such as that popularized by Charlson, offer an empirical method to incorporate an individual's health status into the estimation of prognosis. Her eponymous index estimates risk of mortality based on the presence of certain comorbidities.⁹ It is a strong predictor of overall and nonprostate cancer survival in men with prostate cancer¹⁰⁻¹² and has been incorporated into several nomograms for predicting overall survival.¹³⁻¹⁵ Unfortunately, all but 1 of these nomograms fail to isolate nonprostate cancer mortality as the outcome of interest. The remaining study was developed using only men who were aggressively treated, which may underestimate the true risks of comorbidity. For these reasons, the impact of comorbidity on nonprostate cancer mortality remains unclear.

In this study of 1482 men with newly diagnosed prostate cancer, we first sought to define the long-term risks of nonprostate cancer mortality among men with differing Charlson scores. To accomplish this, we calculated longitudinal mortality rates and created Kaplan-Meier survival curves for Charlson comorbidity groups. We then used competing risks regression analysis to further characterize the impact of comorbidity on nonprostate cancer mortality while accounting for prostate cancer mortality as a competing risk. Second, we sought to directly compare the risks of nonprostate cancer mortality with prostate cancer mortality among men with differing Charlson scores and low, intermediate, and high tumor risk. To this end, we created smoothed regression curves depicting long-term nonprostate and prostate cancer mortality, after stratification by Charlson score and tumor risk. We hoped to identify populations at considerable risk of short-term nonprostate cancer mortality but low risk of prostate cancer mortality; conservative management may better serve such men.

MATERIALS AND METHODS

Data Sources

We used the California Cancer Registry to identify men newly diagnosed with prostate cancer at the Greater Los Angeles and Long Beach Veterans Affairs (VA) Medical Centers from 1997 to 2004. We reviewed medical records to determine age, race, tumor characteristics, type of primary treatment, and comorbidities at diagnosis. We excluded men with no prostate cancer diagnosis ($n = 40$), histology other than adenocarcinoma ($n = 46$), incidental diagnosis at cystoprostatectomy ($n = 25$), insufficient data to determine comorbidities ($n = 206$), and meta-

static disease (clinical stage N1 or M1) ($n = 115$). Approval was granted by the institutional review boards at University of California, Los Angeles and the VA. The final analytic sample was 1482.

Outcome Assessment

Comorbidity

We assessed comorbidity using the age-unadjusted Charlson Comorbidity Index,⁹ the most extensively studied instrument for measuring comorbidity.¹⁶ The Charlson index estimates life expectancy based on the presence or absence of specific comorbidities; each comorbidity is weighted by its risk of mortality, and these weights are summed into a total score that is proportional to an individual's overall mortality risk. Comorbidities are weighted as follows: metastatic solid tumor (6), human immunodeficiency virus/acquired immunodeficiency syndrome (6), moderate-to-severe liver disease (3), hemiplegia (2), moderate-to-severe renal disease (2), diabetes with end-organ damage (2), any solid tumor (2), leukemia/lymphoma (2), myocardial infarction (1), congestive heart failure (1), peripheral vascular disease (1), cerebrovascular disease (1), dementia (1), chronic pulmonary disease (1), connective tissue disease (1), peptic ulcer disease (1), mild liver disease (1), and diabetes (1). We collected comorbidities at diagnosis by review of the interdisciplinary medical record. Comorbidities had to have been present at the time of treatment decision. For this study, we stratified men into 4 groups: Charlson scores 0, 1, 2, and 3+.

Tumor risk

Tumors were risk-stratified using the widely accepted D'Amico criteria, which use prostate-specific antigen (PSA), Gleason score, and clinical stage at diagnosis to predict risk of progression, overall mortality, and cancer-specific mortality. Tumors are classified as low, intermediate, or high risk.^{17,18}

Mortality

Survival was measured from date of diagnosis until date of death. We determined date of death using the medical record and the Social Security Death Index. Cause of death was determined using the medical record by the following algorithm. Men were considered to have died from prostate cancer based on: enrollment in hospice or palliative care for prostate cancer, advancing PSA despite secondary hormonal therapy or chemotherapy, or death as a sequela of metastatic disease (bony fracture or organ failure related to metastasis). Nonprostate cancer

mortality was defined as death from other causes as noted in the medical record. If cause of death could not be determined from the medical record, subjects were considered to have died from other causes if: PSA was stable 5 years after local treatment; PSA was stable 1 year before death after local treatment for D'Amico intermediate/high-risk disease or 2 years before death for low-risk disease; PSA was stable 6 months before death while on hormonal therapy for locally advanced or recurrent disease; or primary hormonal therapy, secondary hormonal therapy, or chemotherapy was not initiated within 6 months before death for locally advanced or recurrent disease.

Statistical Analysis

We first compared clinical and demographic characteristics of our population across Charlson groups using chi-square and Fisher exact tests. To define the unadjusted risks of nonprostate cancer mortality across Charlson groups over time, we created survival tables. We calculated nonprostate cancer mortality rates at each time point using life table analysis, after censoring those who were lost to follow-up or died of prostate cancer or unknown causes at each time point.

We then assessed the adjusted risks of nonprostate cancer mortality across Charlson groups using a competing risks regression model, correcting for age, race, tumor risk, and type of treatment. We used a maximum likelihood, competing-risks regression model as described by Fine and Gray.¹⁹ Our failure event was defined as nonprostate cancer mortality; the competing risk was prostate cancer mortality. Our predictor was Charlson group (0 = referent, 1, 2, and 3+). We adjusted for age, race, D'Amico risk strata, and treatment type. We chose model covariates a priori based on known correlation with comorbidity and survival outcomes. We elected to use a competing risks model rather than a Cox proportional hazards model, because the latter treats competing risks of the event of interest as censored observations, and its cause-specific hazard function does not have a direct interpretation in terms of survival probability.^{20,21} Results are reported as subhazard ratios (SHR) with 95% confidence intervals (CIs).

We then separately modeled nonprostate cancer, prostate cancer, and overall survival using Kaplan-Meier analysis, adjusting for age, race, tumor risk, and type of treatment. Additional covariates were included if they were unevenly distributed across Charlson groups. Because the addition of Gleason score did not affect the

significance of Charlson score in predicting survival outcomes, we omitted it from the final model.

For the 67 subjects who had an unknown cause of death, we conducted a sensitivity analysis to determine whether redistribution of these patients would significantly change our results. Whether unknowns were recoded as nonprostate deaths or prostate cancer deaths, or were excluded entirely, no Charlson group had a significant change in risk of prostate or nonprostate cancer mortality in Kaplan-Meier analysis. For this reason, we censored these men at the time of death in all survival analyses.

To characterize the risks of mortality across tumor risk and comorbidity, we stratified our cohort by D'Amico tumor risk and Charlson score. We then used competing risks regression analysis to determine the risks of prostate cancer and nonprostate cancer mortality over time for each group, while correcting for age, race, and type of treatment. A Lowess line smoother was applied to the Kaplan-Meier model to depict competing risks curves for each tumor risk/comorbidity-paired group. We used $P < .05$ to denote statistical significance, and all tests were 2-sided. Statistical analyses were performed in SAS 9.2 (SAS Institute Inc., Cary, NC) or Stata 11.0 (Stata Inc., College Station, Tex).

RESULTS

After reviewing all 1914 new cases, we identified 1482 men who satisfied the inclusion and exclusion criteria for the study. Of the 481 (32%) men who died during the observation period, 44 (3%) died of prostate cancer, and 370 (25%) died of other causes. Cause of death was unknown in 67 (5%) men. Mean follow-up for the entire cohort was 6.0 years (range, 0-13.3 years)—6.9 years (range, 0.1-13.3 years) among those living at the end of follow-up and 4.1 years (range, 0-11.9 years) among those deceased.

Table 1 summarizes the clinical and demographic features across Charlson groups. Older men and those who were given immediate androgen deprivation therapy were more likely to have higher Charlson scores. D'Amico tumor risk, clinical TNM classification, and PSA at diagnosis were not associated with comorbidity status, but there was a significant positive association between Gleason and Charlson scores.

Table 2 shows unadjusted nonprostate cancer mortality rates over time across Charlson groups. Nonprostate cancer mortality was significantly higher among men with

Table 1. Sample Characteristics (N=1482)

Characteristic	Total	Charlson Score 0	Charlson Score 1	Charlson Score 2	Charlson Score 3+	P
No. of patients	1482	641	424	237	180	<.0001
Age, No. (%)						
<56 years	148 (10.0)	80 (12.5)	47 (11.1)	13 (5.5)	8 (4.4)	
56-65 years	543 (36.6)	274 (42.7)	143 (33.7)	72 (30.4)	54 (30.0)	
66-75 years	533 (36.0)	206 (32.1)	156 (36.8)	101 (42.6)	70 (38.9)	
76-85 years	242 (16.3)	77 (12.0)	72 (17.0)	48 (20.3)	45 (25.0)	
>85 years	16 (1.1)	4 (0.6)	6 (1.4)	3 (1.3)	3 (1.7)	
Race/ethnicity, No. (%)						.3
White	661 (44.6)	287 (44.8)	179 (42.2)	121 (51.1)	74 (41.1)	
Black	543 (36.6)	230 (35.9)	158 (37.3)	81 (34.2)	74 (41.1)	
Hispanic	112 (7.6)	49 (7.6)	38 (9.0)	15 (6.3)	10 (5.6)	
Other	37 (2.5)	17 (2.7)	9 (2.1)	8 (3.4)	3 (1.7)	
Not disclosed	129 (8.7)	58 (9.0)	40 (9.4)	12 (5.1)	19 (10.6)	
PSA at diagnosis, No. (%)						.5
<10	902 (61.0)	404 (63.0)	247 (58.4)	149 (63.4)	102 (57.0)	
10-20	339 (22.9)	134 (20.9)	107 (25.3)	54 (23.0)	44 (24.6)	
>20	237 (16.0)	103 (16.1)	69 (16.3)	32 (13.6)	33 (18.4)	
Clinical T stage, No. (%)						.7
cT1	691 (46.6)	288 (44.9)	207 (48.8)	111 (46.8)	85 (47.2)	
cT2	642 (43.3)	286 (44.6)	178 (42.0)	106 (44.7)	72 (40.0)	
cT3, cT4	58 (3.9)	25 (3.9)	13 (3.1)	11 (4.6)	9 (5.0)	
cTx	91 (6.1)	42 (6.6)	26 (6.1)	9 (3.8)	14 (7.8)	
Gleason score at diagnosis, No. (%)						.008
≤6	860 (58.6)	404 (63.1)	247 (58.5)	122 (52.6)	87 (50.0)	
7	430 (29.3)	172 (26.9)	127 (30.1)	75 (32.3)	56 (32.2)	
≥8	178 (12.1)	64 (10.0)	48 (11.4)	35 (15.1)	31 (17.8)	
D'Amico tumor risk, No. (%)						.3
Low	516 (36.3)	234 (38.0)	140 (34.4)	85 (37.0)	57 (33.3)	
Intermediate	475 (33.4)	202 (32.8)	146 (35.9)	78 (33.9)	49 (28.7)	
High	432 (30.4)	179 (29.1)	121 (29.7)	67 (29.1)	65 (38.0)	
Treatment, No. (%)						<.0001
Aggressive	946 (65.0)	444 (70.4)	279 (67.1)	141 (59.7)	82 (47.4)	
Immediate ADT	188 (12.9)	66 (10.5)	56 (13.5)	35 (14.8)	31 (17.9)	
Delayed ADT/WW	322 (22.1)	121 (19.2)	81 (19.5)	60 (25.4)	60 (34.7)	

Abbreviations: ADT, androgen deprivation therapy; PSA, prostate-specific antigen; WW, watchful waiting.

Table 2. Subhazard Ratios and Longitudinal Mortality Rates for Nonprostate Cancer Mortality by Charlson Score

Charlson Score	Total No. of Patients	Nonprostate Cancer Deaths at End of Follow-up	SHR for NPCM (95% CI)	NPCM at 2 Years, %	4 Years, %	6 Years, %	8 Years, %	10 Years, %
0	636	69	1.0 (Ref)	2	5	7	13	17
1	424	100	2.2 (1.6-3.0)	5	12	18	27	34
2	237	92	3.9 (2.8-5.5)	9	21	34	46	52
3 +	180	108	8.5 (6.2-11.7)	23	41	54	66	74

Abbreviations: CI, confidence interval; NPCM, nonprostate cancer mortality; Ref, reference; SHR, subhazard ratio. Competing risks regression model adjusted for age, race, D'Amico tumor risk, and type of treatment.

higher Charlson scores. At 10 years after treatment, men with Charlson scores of 0, 1, 2, and 3+ had nonprostate cancer mortality rates of 17%, 34%, 52%, and 74%, respectively.

Competing risks regression analysis revealed an approximately 2-fold increased hazard of nonprostate cancer mortality for each point increase in Charlson score (Table 2). Men with Charlson scores of 3+ had an 8-fold increased risk of nonprostate cancer mortality, compared with men with Charlson scores of 0 (SHR, 8.5; 95% CI, 6.2-11.7). Intermediate (SHR, 1.4; 95% CI, 1.1-1.9) and high tumor risk (SHR, 1.6; 95% CI, 1.2-2.2) and age (SHR, 1.05; 95% CI, 1.04-1.07) were also significant predictors of nonprostate cancer mortality. These data suggest that a man would need to live 19 additional years to double his risk of nonprostate cancer mortality, which is roughly equivalent to an increase of 1 Charlson point. When age was reconsidered as a categorical variable grouped by decades of life beyond 55 years (56-65, 66-75, and >75), respective decades were associated with SHR of 1.6 (95% CI, 0.9-2.7), 2.1 (95% CI, 1.2-3.6), and 4.0 (95% CI, 2.2-7.1), whereas risks associated with Charlson scores remained the same.

Figure 1 depicts Kaplan-Meier curves showing long-term nonprostate cancer, prostate cancer, and overall survival by Charlson score. In Kaplan-Meier analysis, nonprostate and overall survival differed significantly across Charlson groups ($P < .0001$).

Table 3 lists survival outcomes after cohort stratification by Charlson score and D'Amico tumor risk. Prostate cancer mortality was extremely rare in the low-risk and intermediate-risk groups, regardless of whether men were treated aggressively or conservatively (Table 3). We identified 2 (<1%) prostate cancer deaths in the 252 men with low-risk tumors and only 9 (3%) among the 311 subjects with intermediate-risk tumors. Among 435 men with high-risk tumors, we identified 33 (8%) prostate cancer deaths.

Figure 2 presents smoothed regression curves showing competing risks of prostate cancer and nonprostate cancer mortality over time, among men with different Charlson scores and tumor risks. Regardless of tumor risk, higher Charlson scores were associated with significantly higher nonprostate cancer mortality rates. Prostate cancer mortality was a competitor for overall mortality only in the D'Amico high-risk group. Men with high-risk tumors and Charlson scores of 0 had nearly equal risk of prostate and nonprostate mortality at the end of follow-up (Fig. 2). However, in the Charlson 2 and 3+ groups, non-

prostate cancer mortality still dwarfed prostate cancer mortality over the period of follow-up.

DISCUSSION

This study attempts to simplify comorbidity's role in decision making by better defining the risks of nonprostate cancer mortality associated with different comorbidity states. In our cohort, men with Charlson scores 0, 1, 2, and 3+ had nonprostate cancer mortality rates of 17%, 34%, 52%, and 74%, respectively, at 10 years after treatment. Furthermore, in a competing risks regression model, men with Charlson scores 3+ had an 8.5× increased hazard of nonprostate mortality, compared with men having scores of 0. The prediction of long-term other-cause mortality is particularly relevant to men with prostate cancer, because randomized trials have shown that significant survival benefits of aggressive local treatment in men with low-risk and intermediate-risk tumors do not manifest until 8 to 10 years after treatment.¹ Men with higher Charlson scores may therefore wish to consider conservative management of such disease, because they are unlikely to live long enough to reap survival benefits of aggressive treatment.

To underscore our argument, we also compared the relative contributions of prostate cancer and nonprostate cancer mortality to overall mortality in the setting of differing comorbidity and tumor risk. Men with low and intermediate tumor risk and higher Charlson scores undoubtedly stand to benefit least from aggressive treatment, given high short-term risk of nonprostate cancer mortality and exceedingly low risk of death from prostate cancer. It is unlikely that our rates of prostate cancer mortality are low solely because the majority of our sample was aggressively treated. Large retrospective studies of conservatively managed populations^{22,23} have shown that low-risk and intermediate-risk tumors pose little threat to survival over the first 8 to 10 years after diagnosis, and randomized controlled trial evidence indicates that there is no significant survival difference between men who are aggressively or conservatively managed for such tumors in the short term.¹ Conversely, men with high-risk tumors have considerable short-term risk of prostate cancer mortality and therefore should consider aggressive treatment, even in the setting of a high Charlson score.

Other groups have created nomograms for predicting 10-year life expectancy incorporating Charlson score, but the impact of comorbidity on nonprostate cancer mortality in these studies may be obscured because of

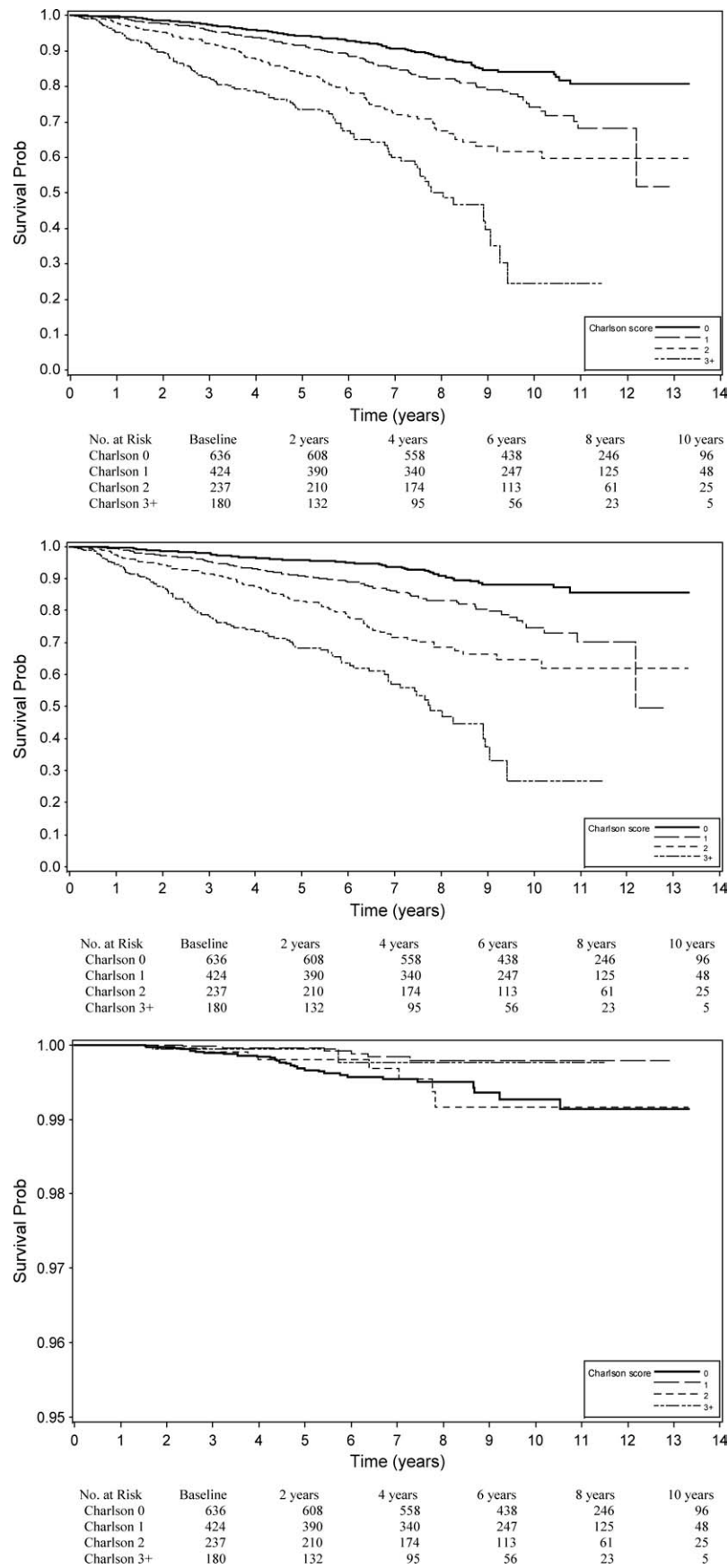


Figure 1. Kaplan-Meier curves for overall, nonprostate cancer-specific mortality, and prostate cancer-specific mortality by Charlson score are shown: (Top) overall mortality; (Middle) nonprostate mortality; (Bottom) prostate cancer mortality. Abbreviation: Prob, probability.

Table 3. Competing Risks for Survival by Comorbidity and Tumor Risk

Mortality	Charlson Score 0	Charlson Score 1	Charlson Score 2	Charlson Score 3+	Total
Low D'Amico tumor risk					
Total patients	234	140	85	57	516
Men alive at end of follow-up	212	105	56	32	405
Overall mortality	22	35	29	25	111
Prostate cancer mortality	2	0	0	0	2
Other cause mortality	17	34	26	24	101
Unknown cause mortality	3	1	3	1	8
Intermediate D'Amico tumor risk					
Total patients	202	146	78	49	475
Men alive at end of follow-up	168	109	44	13	334
Overall mortality	34	37	34	36	141
Prostate cancer mortality	5	0	4	0	9
Other cause mortality	22	29	27	35	113
Unknown cause mortality	7	8	3	1	19
High D'Amico tumor risk					
Total patients	179	121	69	66	435
Men alive at end of follow-up	125	75	22	12	234
Overall mortality	54	46	47	54	201
Prostate cancer mortality	21	6	4	2	33
Other cause mortality	27	28	36	44	135
Unknown cause mortality	6	12	7	8	33
Unknown D'Amico tumor risk					
Total patients	26	17	5	8	56
Men alive at end of follow-up	20	4	2	2	28
Overall mortality	6	13	3	6	28
Prostate cancer mortality	0	0	0	0	0
Other cause mortality	4	9	3	5	21
Unknown cause mortality	2	4	0	1	7

limitations associated with patient and outcome selection. Tewari et al analyzed 1611 men with clinical T1-2 prostate cancer to create life tables predicting overall survival, based on age, race, Gleason score, PSA, treatment type, and Charlson score.¹⁴ However, because comorbidity was stratified dichotomously—Charlson score ≤ 1 versus >1 —their data lack sufficient granularity to allow for broader comparisons of survival among men with various degrees of comorbidity. Walz et al analyzed 9131 men treated with radical prostatectomy or radiation therapy without secondary therapy and created a nomogram predicting 10-year survival, based on age, Charlson score, and type of treatment.¹⁵ Although their nomogram was internally accurate, it may have underestimated the impact of comorbidity, because it was developed using only men who were aggressively treated. Because these men were deemed well enough to receive aggressive treatment, they were likely to have been healthier in both measured and unmeasured factors. Our inclusion of men on watchful waiting and androgen deprivation therapy

may be 1 reason that the impact of comorbidity on nonprostate cancer mortality appears more pronounced. To test this hypothesis, we excluded men treated with watchful waiting or immediate hormonal therapy from our competing risks regression analysis; as expected, we found that the SHR for nonprostate cancer mortality associated with a Charlson score 3+ decreased to 7.1 (95% CI, 4.5-11.3). Other unmeasured factors specific to our VA population (eg, alcoholism, smoking status, homelessness) may also amplify the risks of comorbidity on nonprostate cancer survival in our cohort.

The measurement of comorbidity has room for improvement. Unlike other measures, the Charlson index primarily focuses on disease presence and not severity.²⁴ Therefore, it is unable to capture the spectrum of severity within a given comorbid condition. This is particularly relevant for men with comorbidities that are either few in number but life threatening in severity or many in number but mild in severity. Furthermore, the Charlson index's applicability to prostate cancer may not be

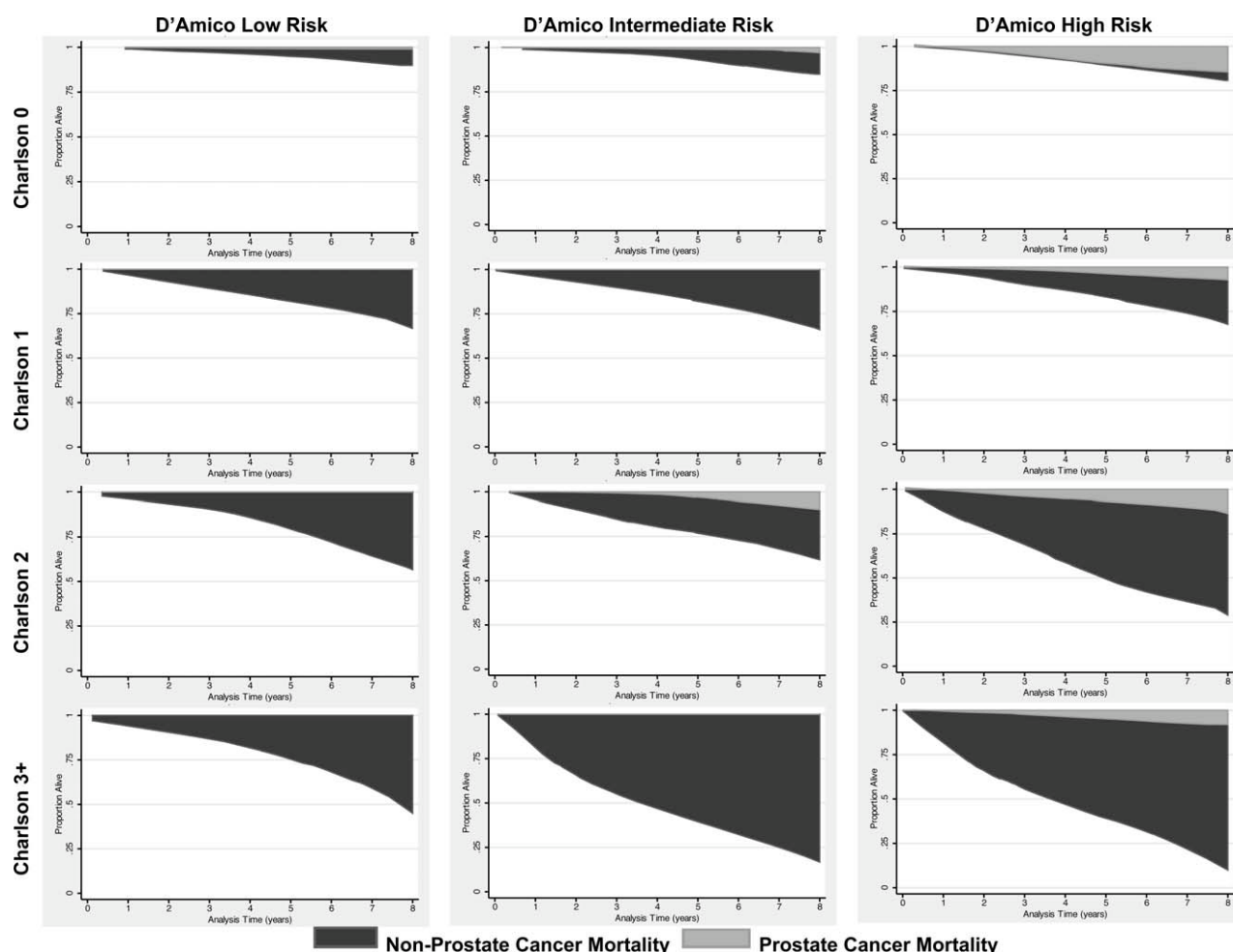


Figure 2. Competing risks for mortality are shown by Charlson score and D'Amico tumor risk.

optimized, because its weighting is based on an endpoint of 1-year rather than 10-year mortality, a population of medical inpatients rather than outpatients with prostate cancer, and outdated data from the 1980s.

Our study is limited by several factors. First, because our population was drawn from the VA, both measured (eg, race) and unmeasured (eg, alcoholism, homelessness) risk factors may not be representative of the US population and may thus limit the generalizability of our findings. Second, because patients with severe comorbidity may have more frequent office/hospital visits and more thorough documentation of comorbidities compared with men with mild comorbidity, this may exaggerate the difference in comorbidity scores between these groups. Third, because the majority of our population was treated, rates of prostate cancer mortality may be lower than those in a watchful waiting population. However, contempo-

rary data suggest that these differences would be slight for low-risk and intermediate-risk groups observed >10 years.^{22,23} Lastly, because some men were lost to follow-up before death, we needed to create ad hoc definitions for cancer-specific and other-cause mortality for these men. We therefore defined both prostate and nonprostate cancer mortality conservatively, based on historical survival estimates of untreated,²³ recurrent,^{25,26} and castrate-resistant disease.^{27,28}

For men with newly diagnosed prostate cancer, the decision of whether to pursue aggressive treatment hinges on comorbidity. This study provides a foundation for clinical decision making based on comorbidity by standardizing the risks of nonprostate cancer mortality associated with Charlson scores in a modern prostate cancer population. We contend that men with higher Charlson scores should strongly consider conservative management

of low-risk and intermediate-risk tumors, given the high likelihood of death from other causes before survival benefits of aggressive treatment can be realized.

FUNDING SOURCES

No specific funding was disclosed.

CONFLICT OF INTEREST DISCLOSURES

The authors made no disclosures.

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