Project Report

Projecting individualized cancer-specific death risks and other competing cause death risks among elderly men diagnosed with prostate cancer

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Yan Yan, MD, Ph.D and Jay Piccirillo, MD, FACS

Summary and description in lay language

Prostate cancer is the most common cancer among men in the US and the second leading cause of cancer death. As in other cancers, the majority of men diagnosed with prostate cancer are elderly. While some prostate cancer patients die from this disease, most of them die from other causes because prostate tumors usually grow slowly and prostate cancer patients are usually old with many other health conditions.

Death from prostate cancer and from other causes is usually associated with different risk factors and has different implications for health care needs. Thus, it is very important to categorize prostate cancer patients into subgroups at the different risks of dying from prostate cancer or dying from other causes. The purposes of the current project are to identify the risk factors related to different causes of death, and then to predict individualized probabilities of death from prostate cancer and from other causes using the risk factor information.

We used all prostate cancer patients diagnosed between 1991-1999 in the SEER program and enrolled in the Medicare program, and the newly merged SEER-Medicare datasets to obtain all information including demographics, tumor grade and stage, primary treatment options, comorbidity, and vital status, etc. With the statistical tool we have previously developed, we estimated several types of individualized probabilities based on patient characteristics: the absolute cause-specific death probability, the conditional cause-specific death probability, the relative risk of death from prostate cancer versus from other causes. The absolute cause-specific death probability tells us how likely a prostate cancer patient with certain characteristics (age, race, tumor stage and grade, treatment options, and comorbidity etc.) in the future will die from prostate cancer or from other causes. The conditional cause-specific death probability tells us how likely the prostate cancer patient will die from prostate cancer or from other causes in the near future given his updated information. The relative risk tells us the importance that the patient will die from prostate cancer versus from other causes.

These probabilities will have many applications in clinical and public health practice. Clinicians can use the absolute cause-specific death probability to consult individual patients about optimal treatment options before treatment, and can use the conditional cause-specific death probability with the relative risk estimates to formulate more effective prevention and treatment strategies for reducing death risks from prostate cancer and from other causes. Health care policy makers can use the absolute cause-specific death probability to make the long-term plan about future health care needs, and can use the conditional cause-specific death probability with the relative risk estimates to adjust their long-term plan for possible changes. In addition, these probabilities enable prostate cancer patients to better understand their prognoses, therefore, to more actively participate in the joint-decision making.

Introduction

Prostate cancer is the most common malignancy and the second leading cause of death in men in the US, with approximately 230,110 new cases and 29,900 deaths anticipated in 2004; over 98% of these deaths will occur in the elderly patient population.[1] As in other cancers, the overall mortality of prostate cancer has been extensively studied, the cause-specific mortality in these patients is much less reported.

Studying the causes of death in elderly prostate cancer patients has several importances. First, the majority of prostate cancer patients die from other competing causes, due to both a slow progression of the cancer and a high prevalence of comorbid conditions. [2-4] Second, the risk factors for death from prostate cancer are usually different from those for death from other causes. [5-9] Third, the death from prostate cancer often has different implications than the death from other causes.

The common approach to estimating the risk of death from prostate cancer uses "cancer specific survival function", obtained by the Kaplan-Meier method with censoring those who die from other causes. Likewise, for estimating the risk of death from other causes, this approach censors those who die from prostate cancer. This approach cannot predict individualized death probabilities since it cannot effectively use patient characteristic information. More importantly, this approach violates the crucial statistical assumption underlying the Kaplan-Meier method and overestimates the death probabilities, as we demonstrated in AIDS study settings.[10]

Two studies estimated the probabilities of death from prostate cancer and from other causes: one by Albertsen [7]and another by Sweat [8]. Their estimates came from pre-PSA era patients. Application of these probability estimates to patients diagnosed after 1991 may be difficult, since PSA testing has detected prostate tumors at earlier stages and a substantial proportion of the tumors detected are less aggressive. Besides, although many studies have shown that African American patients are more likely to have aggressive tumors and tend to have different treatment outcomes than the patients of other ethnic origins, however, race information was not included in those estimations.

The objectives of the current study are to identify the risk factors for different causes of death, then to estimate the probabilities of death from prostate cancer or from other causes using the risk factor information in the elderly prostate cancer patients.

Methods

Study population and data

The study population consists of all prostate cancer patients in SEER-Medicare databases who were 66 years or older at the diagnosis between Jan 1, 1992 and Dec 31, 1995. The study period started 12 months prior to the date of diagnosis and ended with death for those who died before Dec 31,2000 or on Dec 31,2000 for those who were alive beyond that date. We excluded the following cases - those with diagnoses based only on autopsy or death certificates, those without the information on the month of diagnoses, those younger than 66 years at diagnosis, and those without complete Part A and Part B coverage or ever enrolled into HMO during the study period.

Assessment of demographic, comorbidity and tumor characteristics and treatment

Two demographic variables- race and age at diagnosis come from Patient Enrollment and Diagnosis Summary File (PEDSF). Severity of comorbid conditions was quantified by the Charlson index using data from the hospital inpatient, hospital outpatient, and physician/supplier files. Two SAS Macros supplied by NCI were used to code the comorbidity conditions. For stage, we followed the SEER coding guide, and group patients into T1, T2, T3, or T4N1M1. For grade, we categorized patients as well differentiated, moderately differentiated, poorly differentiated, and undifferentiated. Treatment was characterized as surgery, radiation therapy and watchful waiting.

Statistical methods:

In this project, we estimated three types of probabilities: the absolute cause-specific death probabilities, the conditional cause-specific death probabilities, and the relative risks of death from prostate cancer versus death from other causes.The estimation of these probabilities was made for each of the three treatment options- surgery, radiation therapy, and watchful waiting. The details of statistical methods were published in our previous work [10-12], Briefly, we first use Cox proportional hazard model to select important prognostic factors associated with risk of death from prostate cancer and death from other competing causes. Then, we used Breslow's method to obtain cause-specific baseline hazard functions and cause specific hazard functions with the selected important prognostic factors. With cause specific hazard functions with the covariates, we used Aalan type of estimators to obtain the absolute cause-specific death probabilities, and therefore conditional cause-specific death probabilities and the relative risks of death from prostate cancer versus from other competing causes.

Results

With each treatment group – surgery, radiation therapy and watchful waiting, the absolute probabilities of death from prostate cancer or other causes vary with patient and tumor characteristics. Table 1 and Table 2 present death risk profiles for selected 6 patients, 2 in each treatment group.

Table 1. Absolute Probabilities of Death From Prostate Cancer And Other Competing Causes For Six Patients At Selected Times During Follow-up

	Patient A		Patient B	
month	(1)	(2)	(1)	(2)
12	0.009	0.023	0.001	0.062
24	0.013	0.044	0.001	0.117
36	0.021	0.066	0.002	0.172
48	0.038	0.090	0.003	0.231
60	0.049	0.114	0.003	0.290
72	0.066	0.139	0.004	0.347
84	0.078	0.168	0.005	0.409
96	0.091	0.197	0.006	0.470

	Patient C		Patient D	
month	(1)	(2)	(1)	(2)
12	0.059	0.026	0.014	0.057
24	0.142	0.059	0.033	0.133
36	0.207	0.095	0.048	0.216
48	0.278	0.131	0.065	0.300
60	0.347	0.164	0.082	0.380
72	0.400	0.196	0.095	0.456
84	0.445	0.225	0.106	0.528
96	0.476	0.254	0.114	0.596

	Patient E		Patient F	
month	(1)	(2)	(1)	(2)
12	0.164	0.055	0.004	0.121
24	0.343	0.097	0.010	0.228
36	0.474	0.130	0.015	0.331
48	0.558	0.154	0.018	0.423
60	0.611	0.174	0.021	0.509
72	0.658	0.191	0.024	0.588
84	0.691	0.203	0.026	0.654
96	0.708	0.214	0.027	0.724

Notes

1. Characteristics of selected patients:
Patient A: surgical patients aged 66-70 with stage T3/T4/N1/M1, poorly differentiated tumors, and Charlson score of 1.

Patient B: surgical patients aged 66-70 with stage T1/T2, well differentiated tumor, and Charlson score of 2+.
Patient C: Black radiation patients aged 71-75 with stage T3/T4/N1/M1, poorly differentiated tumors, and Charlson score of 0.
Patient D: Black radiation patients aged 71-75 with stage T3/T4/N1/M1, well differentiated tumors, and Charlson score of 2+.
Patient E: Black conservatively managed patients aged 71-75 with stage T4/N1/M1, poorly differentiated tumors, and Charlson score of 0.
Patient F: Black conservatively managed patients aged 71-75 with stage T1, well differentiated tumors, and Charlson score of 2+.

2.Column (1)- death from prostate cancer and Column (2)- death from other competing causes.

Table 2. Conditional Probabilities And Relative Risks Of Death From Prostate Cancer And Other Competing Causes Within Next 6 Months At Selected Times

	Patient A			Patient B		
Month	(1)	(2)	(3)	(1)	(2)	(3)
0	0.007	0.012	1.772	0.001	0.032	63.572
12	0.003	0.011	3.146	0.000	0.029	112.989
24	0.004	0.013	3.072	0.000	0.035	110.824
36	0.009	0.012	1.273	0.001	0.032	45.785
48	0.007	0.013	1.738	0.001	0.035	62.476
60	0.009	0.014	1.544	0.001	0.039	55.470
72	0.009	0.020	2.323	0.001	0.055	84.203
84	0.005	0.020	4.052	0.000	0.055	145.208
96	0.023	0.018	0.772	0.002	0.048	27.835
	Patient C			Patient D		
Month	(1)	(2)	(3)	(1)	(2)	(3)
0	0.026	0.009	0.360	0.006	0.021	3.513
12	0.043	0.017	0.398	0.010	0.038	3.880
24	0.044	0.023	0.524	0.010	0.051	5.113
36	0.062	0.024	0.387	0.014	0.053	3.773
48	0.059	0.028	0.477	0.013	0.063	4.650
60	0.047	0.029	0.619	0.011	0.064	6.030
72	0.061	0.038	0.614	0.014	0.083	5.983
84	0.051	0.040	0.801	0.011	0.088	7.804
96	0.056	0.064	1.141	0.012	0.139	11.152
	Patient E			Patient F		
Month	(1)	(2)	(3)	(1)	(2)	(3)
0	0.084	0.032	0.376	0.002	0.068	31.508
12	0.118	0.027	0.231	0.003	0.059	19.366
24	0.128	0.031	0.246	0.003	0.069	20.632
36	0.125	0.031	0.250	0.003	0.068	21.016
48	0.108	0.039	0.362	0.003	0.084	30.376
60	0.122	0.041	0.333	0.003	0.087	27.819
72	0.106	0.040	0.380	0.003	0.085	31.843
84	0.078	0.052	0.658	0.002	0.106	55.355
96	0.111	0.063	0.565	0.003	0.128	47.583

Notes:
Column (1)-death from prostate cancer, Column (2)- death from other competing causes, and Column (3)- relative risk of death from other causes versus from prostate cancer.

See notes in table 4 for patient characteristics.

Discussion

This study used patient and tumor characteristics to predict probabilities of death from prostate cancer and other competing causes. Majority of prostate cancer patients die from other causes. Comorbidity is strongly associated with the hazard of dying from other competing causes. We are drafting manuscripts from this project, and this project will be extended to study effect of comorbidity on death from prostate cancer and from other competing risks.

Reference

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