

Incidence of Cardiovascular and Cerebrovascular Events Among Men With Prostate Cancer

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BACKGROUND

- In 2008, an estimated 186,320 new cases of prostate cancer will be diagnosed in the United States (US).¹
- More than 90% of all prostate cancers diagnosed have a 5-year relative survival rate approaching 100%.¹
- Men diagnosed with prostate cancer have increased noncancer mortality rates compared with men in the general population, which may be attributable to treatment choices.²

METHODS

Design

- This is a retrospective cohort study of men diagnosed with prostate cancer.

Data Source

- This study was conducted with data from the Surveillance, Epidemiology and End Results (SEER)-Medicare linked database, which contains clinical and administrative information on individuals aged 65 years and older with incident cancers from population-based cancer registries within the US, linked with comprehensive longitudinal health care utilization data from Medicare and vital records data.^{3,4} This database includes approximately 2.4 million cancer patients.⁴

- The following SEER-Medicare data files were used in this analysis:

- The Patient Entitlement and Diagnosis Summary File (PEDSF) includes information on each person's month and year of birth, date of death (if any), underlying cause of death, sex, race, and state of residence.
- The Medicare Provider Analysis and Review (MEDPAR) file includes all Part A short-stay hospital, long-stay hospital, and skilled nursing facility bills.
- Carrier claims (NCH) records include all Part B bills, the majority of which are from physicians but which also include claims from other noninstitutional providers such as independent clinical laboratories, ambulance providers, and stand-alone ambulatory surgical centers.
- The outpatient claims file contains Part B claims from institutional outpatient providers such as hospital outpatient departments, outpatient rehabilitative facilities, and rural health clinics.

OBJECTIVES

This study was designed to estimate the incidence of the following outcomes in patients diagnosed with prostate cancer:

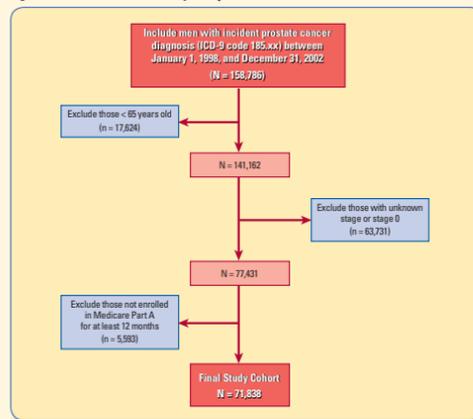
- Acute myocardial infarction (AMI)
- Coronary artery disease (CAD)
- Congestive heart failure (CHF)
- Stroke
- Sudden cardiac death (SCD)
- Cardiovascular death
- Cerebrovascular death



Study Population

- The study included all men aged 65 years and older with a first diagnosis of prostate cancer (ICD-9 code 185.xx) between January 1, 1998, and December 31, 2002.
- Men had to be enrolled in Medicare Part A at least 12 months prior to the prostate cancer diagnosis.
- Figure 1 shows the identification of the study cohort.

Figure 1. Identification of Study Sample



Study Outcomes

The following outcomes were identified at any time following the diagnosis of prostate cancer. Event definitions were based on algorithms from published studies.⁵⁻⁸ The positive predictive values reported in these studies ranged from 94% to 96%.^{5,7,8}

Study Outcomes continued

Myocardial Infarction

- Hospitalization lasting at least 3 days (less if subject died during hospitalization) and no more than 180 days with principal or secondary ICD-9 discharge diagnosis codes 410.x1.
- Includes patients who died from AMI without prior hospitalization.
- Excludes readmissions for AMI (410.x2) to identify only first hospitalizations.⁵

Coronary Artery Disease

- Hospitalization episode with diagnosis of CAD as the principal diagnosis or two or more outpatient visits with a primary or secondary diagnosis code for CAD.
- ICD-9 codes for CAD include the codes indicative of AMI (410.x1), other acute forms of ischemic heart disease (411.1, 411.8x), and angina pectoris (413.x), as well as procedure codes for coronary revascularization (ICD-9 procedure code 36.0-36.03, 36.05, 36.09-36.19; CPT codes 33510-23, 33530, 92980-82, 92984, 92995-6).⁶
- Includes patients who died from heart disease without prior hospitalization.

Congestive Heart Failure

- Hospitalization episode with ICD-9 diagnosis code of 428.xx as the principal diagnosis.⁷
- Includes patients who died from CHF without prior hospitalization.

Stroke

- Hospitalization episode with ICD-9 diagnosis code in any position in a hospital claim: hemorrhagic: 430, 431; ischemic: 433.x1, 434.x1, and 436.⁸
- Includes patients who died of stroke without prior hospitalization.

Sudden Cardiac Death⁵

- An outcome of SCD must meet at least one of the following criteria:
- Sudden death, cause unknown (ICD-9 code 798.2; ICD-9 code 798), instantaneous death (ICD-9 code 798.1; ICD-10 code R96.0), death less than 24 hours after symptoms (ICD-9 codes 798.2; ICD-10 code R96.1), or unattended death (ICD-9 code 798.2; ICD-9 code 798.7; ICD-10 code R98).
- Hospitalization episode with primary or secondary ICD-9 diagnosis of ventricular fibrillation and flutter (ICD-9 code 427.4x; ICD-10 code I49.0), or cardiac arrest (ICD-9 code 427.2; ICD-9 code 427.5; ICD-10 code I46.0-146.9), or paroxysmal ventricular tachycardia (ICD-9 code 427.1; ICD-10 code I47.2) resulting in cardiac death.

Cardiovascular Death

- Listed with cause from acute or chronic rheumatic fever, hypertensive disease, ischemic heart disease, diseases of pulmonary circulation, other forms of heart disease, diseases of arterioles and capillaries, and SCDs.

Cerebrovascular Death

- Listed with cause from subarachnoid hemorrhage, intracerebral hemorrhage, other and unspecified intracranial hemorrhage, occlusion and stenosis of precerebral arteries, occlusion of cerebral arteries, acute but ill-defined cerebrovascular disease, other and ill-defined cerebrovascular disease, or late effects of cerebrovascular disease.

Analysis

- Incidence rates were estimated by dividing the number of patients with an event by the amount of person-years contributed by cohort members. Incidence rates are expressed by number of events per 1,000 person-years.
- The 95% confidence intervals (CIs) for incidence rates were calculated using the exact method based on the Poisson distribution.
- Person time was calculated from time of diagnosis of prostate cancer to the earliest time of first cardiovascular event, date of death, or December 31, 2004, with person-year as the unit.

RESULTS

Characteristics of Patients With Prostate Cancer in the SEER-Medicare Database

Table 1 outlines the characteristics of the cohort of 71,838 men who had prostate cancer:

- 63% were in Stage 1 at the time of prostate cancer diagnosis.
- 43% were 75 years of age or older.
- 52% had pre-existing cardiovascular disease.
- 9% had pre-existing cerebrovascular disease.

- The most common treatment during the first 6 months following prostate cancer diagnosis was GnRH therapy (32%).

Table 1. Characteristics of Patients With Prostate Cancer in SEER-Medicare Database, 1/1/98-12/31/02 (N = 71,838)

Characteristic	n	% of Total
Age (years)		
65-69	18,291	25%
70-74	22,704	32%
75+	30,843	43%
Stage		
1	44,944	63%
2	11,926	17%
3	6,059	8%
4	8,909	12%
Race		
White	60,052	84%
Black	7,049	10%
Other	3,478	5%
Unknown	1,259	2%
Pre-existing cardiovascular disease		
Yes	37,065	52%
No	34,773	48%
Pre-existing cerebrovascular disease		
Yes	6,106	9%
No	65,732	92%

GnRH = gonadotropin-releasing hormone therapies (i.e., leuprolide, goserelin, and abarelix).

Table 1. Continued

Characteristic	n	% of Total
First course of treatment*		
Surgery only	14,260	20%
Radiation only	18,597	26%
Surgery and radiation only	3,307	5%
GnRH only	22,705	32%
Orchiectomy only	848	1%
No treatment	11,782	16%

*First course of treatment was identified by reviewing SEER data, which include treatments received within 4 months of cancer diagnosis, as well as Medicare claims during the first 6 months after diagnosis. Excludes patients who received both orchiectomy and GnRH.

Incidence of Cardiovascular and Cerebrovascular Events in Patients With Prostate Cancer

- Table 2 provides the overall number of events and crude estimated incidence rates (95% CIs) for each study event. Figures 2-4 show incidence rates by age, pre-existing cardiovascular disease and cerebrovascular disease, and cancer stage, respectively.

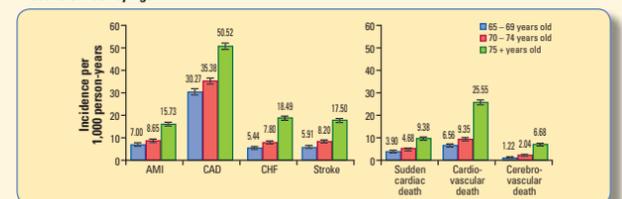
- Event rates increased with age, were higher in patients enrolled with advanced (Stage 4) prostate cancer than in those with Stages 1-3, and were substantially higher in patients with pre-existing cardiovascular or cerebrovascular disease.

Table 2. Incidence of Cardiovascular and Cerebrovascular Events in Patients With Prostate Cancer

Type of Event	Number of Events	Incidence Per 1,000 Person-Years	95% CI
AMI	2,763	10.99	(10.58, 11.41)
CAD	9,527	39.93	(39.14, 40.74)
CHF	2,845	11.34	(10.93, 11.76)
Stroke	2,818	11.23	(10.81, 11.65)
Sudden cardiac death	1,608	6.32	(6.02, 6.64)
Cardiovascular death	3,811	14.98	(14.51, 15.47)
Cerebrovascular death	928	3.65	(3.42, 3.89)

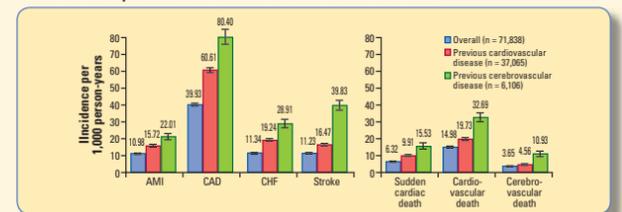
CAD = coronary artery disease; CHF = congestive heart failure; AMI = acute myocardial infarction.

Figure 2. Incidence of Cardiovascular and Cerebrovascular Events in Patients With Prostate Cancer by Age



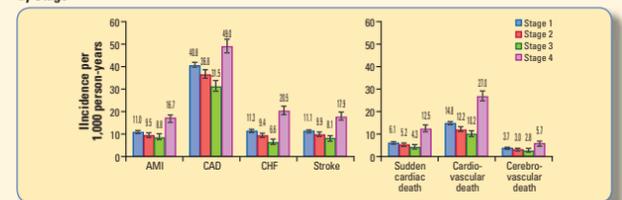
CAD = coronary artery disease; CHF = congestive heart failure; AMI = acute myocardial infarction.

Figure 3. Incidence of Cardiovascular and Cerebrovascular Events in Patients With Prostate Cancer by Previous Cardiovascular or Cerebrovascular Disease



CAD = coronary artery disease; CHF = congestive heart failure; AMI = acute myocardial infarction.

Figure 4. Incidence of Cardiovascular and Cerebrovascular Events in Patients With Prostate Cancer by Stage



CAD = coronary artery disease; CHF = congestive heart failure; AMI = acute myocardial infarction.

CONCLUSIONS

- Incidence rates for certain medical conditions derived from SEER-Medicare linked data in the over-65 population can aid in understanding results of oncology clinical trials, which often have limited long-term follow-up data on the nonexperimental arms of the trials.
- Age, cancer stage, and pre-existing cardiovascular or cerebrovascular diseases are important factors to take into account when evaluating incidence rates of cardiovascular events in men with prostate cancer.

LIMITATIONS

- Study sample is limited to persons aged 65 and older in the US.
- Data on services not covered by Medicare, including routine physical examinations and long-term care, are unavailable.
- Cardiovascular events are defined from claims data and death certificate data without medical record validation.
- There is an inability to ascertain from claims important cardiovascular risk factors such as obesity and smoking.

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CONFLICT OF INTEREST

RTI Health Solutions employees developed the analysis plan and conducted the analysis for this study. Employees of Ferring Pharmaceuticals reviewed and provided comments on the analysis plan and results. Ferring Pharmaceuticals provided funding for this analysis.

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