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Risk of Myocardial Infarction or Diabetes During Androgen Deprivation Therapy for Prostate Cancer: Does Comorbidity Influence Risk?

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Abstract

Background—Androgen deprivation therapy for prostate cancer is associated with cardiovascular disease and diabetes. Some data suggest that men with certain conditions may be more susceptible to developing cardiovascular disease than others.

Objective—Assess whether the risk of myocardial infarction or diabetes during androgen deprivation therapy is modified by specific baseline comorbidities.

Design, Settings and Participants—Population-based observational study of 185,106 U.S. men aged 66 years diagnosed with local/regional prostate cancer from 1992 to 2007. We assessed comorbidities monthly over the follow-up period.

Outcome Measurement and Analysis—Cox proportional hazards models with time varying variables assessing incident diabetes or myocardial infarction.

Results and limitations—Overall, 49.9% received androgen deprivation therapy during follow-up. Among men with no comorbidities, androgen deprivation therapy was associated with an increase in the adjusted hazard of myocardial infarction (adjusted hazard ratio [AHR]=1.09, 95% confidence interval [CI]=1.02–1.16) and diabetes (AHR=1.33, 95% CI=1.27–1.39). Risk of myocardial infarction and diabetes were similarly increased among men with and without specific comorbid illnesses (all P for interactions >.10 with one exception). Previous myocardial infarction, congestive heart failure, peripheral arterial disease, stroke, hypertension, chronic obstructive pulmonary disease, and renal disease were associated with new myocardial infarction and diabetes, and obesity and rheumatologic disease were also associated with diabetes. Limitations include the observational study design, reliance on administrative data to ascertain outcomes, and lack of information on risk factors such as smoking and family history.

Conclusions—Traditional risk factors for myocardial infarction and diabetes were also associated with developing these conditions during androgen deprivation therapy but did not significantly modify the risk attributable to androgen deprivation therapy. Strategies to screen and

prevent diabetes and cardiovascular disease in men with prostate cancer should be similar to those recommended for the general population.

Keywords

prostate cancer; myocardial infarction; diabetes

Introduction

Androgen deprivation therapy (ADT) is increasingly being prescribed for the treatment of local or regional prostate cancer,[1,2] a setting for which long-term data on the benefits and risks are limited. Recent research suggests that ADT is associated with an increased risk of diabetes and cardiovascular disease.[3–6] Some data suggest that men with certain conditions may be more susceptible to developing cardiovascular disease than others. For example, one study found an increased risk of all-cause mortality associated with neoadjuvant hormonal therapy for prostate cancer, but only in the subgroup of 256 men with known coronary artery disease resulting in heart failure or myocardial infarction.[7] Another observational study identified an increased risk of mortality associated with hormonal therapy among men with a history of myocardial infarction or stroke.[8]

We examined a large population-based cohort of men with prostate cancer to identify whether men who are older or have specific baseline comorbidities have increased risk for developing diabetes and myocardial infarction during ADT relative to men without these conditions who received ADT. These analyses may inform recommendations for screening, risk modification, or specific interventions to prevent diabetes and/or cardiovascular disease for men who require ADT.

Methods

Data

We used Surveillance, Epidemiology, and End Results (SEER)-Medicare data for this analysis.[9] The SEER program of the National Cancer Institute collects uniformly reported data from population-based cancer registries covering approximately 28% of the U.S. population.[10] For each incident cancer, SEER registrars collect data on patient demographics, tumor characteristics, and primary treatment. These data are linked with Medicare administrative data (successfully linking more than 94% of SEER patients diagnosed at age ≥ 65).[9]

Cohort

We identified men aged ≥ 65 years with a first diagnosis of prostate cancer during 1992–2007 who were continuously enrolled in Parts A and B of fee-for-service Medicare as of 1 year before diagnosis (N=249,977). We excluded 3,372 men diagnosed at death or autopsy, 6,411 men with no administrative claims from 45 days before diagnosis through 195 days after diagnosis (because we were concerned about incomplete data), and 55,086 men with metastatic disease or unknown stage at diagnosis. The final cohort included 185,106 men with local/regional prostate cancer.

Diabetes and myocardial infarction

As described previously,[3, 4] we identified myocardial infarction and diabetes using diagnosis and procedure codes (Appendix). Acute myocardial infarction was identified if a man was hospitalized with a primary diagnosis of acute myocardial infarction.[11–13] Diabetes was identified if there were two or more outpatient visits with a primary or

secondary diagnosis code or one hospitalization with a primary diagnosis of diabetes. [12,14,15]

For diabetes, we ascertained risk of incident, not prevalent, disease. Men who met the criteria for diagnosis of diabetes beginning 12 months before through 6 months after diagnosis were considered to have prevalent disease and were excluded from the diabetes analyses. Incident diabetes was defined among other men beginning at least 6 months after diagnosis.

Androgen deprivation therapy

We used administrative data to ascertain receipt of ADT, including gonadotropin releasing hormone (GnRH) agonists and bilateral orchiectomy (Appendix). Because most doses were for 3- or 4-month equivalent doses and since men may have persistent hypogonadism for prolonged periods after GnRH agonist discontinuation,[16,17] men were considered continuously treated for 6 months after each dose of GnRH agonist.

Patient age and comorbid illness

We characterized each man's age at diagnosis of prostate cancer. We characterized comorbid illness during the 12 months before diagnosis and throughout the study period using the Klabunde modification[18] of the Charlson score.[19] The Charlson score assesses the prevalence of 12 conditions that were found to be associated with mortality in a cancer population:[19] myocardial infarction, congestive heart failure, peripheral vascular disease, stroke, chronic obstructive pulmonary disease, dementia, paralysis, diabetes, chronic renal insufficiency, liver disease, peptic ulcer disease, rheumatologic disease. We also coded two additional risk factors for cardiovascular disease that are not included in the Charlson score: hypertension (International Classification of Disease 9th Edition (ICD-9) diagnosis codes 401–405.99) and obesity (ICD-9 diagnosis codes 278, 278.0, 278.00, 278.01, 278.02) using the Klabunde algorithm. We characterized the presence or absence of each of the above conditions throughout the study period. Specifically, we assessed for evidence of each comorbidity (using the Klabunde algorithm) on a month-by-month basis. Thus, our comorbidity variables were time varying. Once a patient met criteria, that comorbidity was considered present through the rest of the follow up.

Other independent variables

We documented each patient's race, Hispanic ethnicity, marital status, year of diagnosis, tumor grade and stage, type of primary treatment (surgery, radiation, or neither [Appendix]), SEER region, urban residence, census-tract level income and education (categorized in quartiles within registries). Prostate specific antigen values were not available. Variables were categorized as in Table 1.

Analyses

Men were censored on December 31, 2009 (the last date for which data were available) or sooner if they died or disenrolled from Parts A and B of fee-for-service Medicare. We used two separate Cox proportional hazard models to assess the associations of ADT, patient age, and comorbidity on developing (1) myocardial infarction or (2) diabetes. These models included time-varying variables for use of ADT and comorbidity, as described above. Diabetes was not included in the diabetes model (because patients with prevalent diabetes were excluded from that analysis). We included interaction terms for ADT by age and each comorbidity, adjusting analyses for the other patient characteristics in Table 1. In both analyses, men were followed until developing an event of interest or censoring. We also used the Cox proportional hazard models to estimate the adjusted rate of myocardial

infarction or diabetes at 1 year for patients who were and were not on ADT with and without each comorbidity, setting all other characteristics to that of the average (for continuous variables) or most common (for categorical variables) value.

All tests of statistical significance were two-sided; analyses were conducted with SAS statistical software, version 9.2 (SAS Institute, Inc., Cary, North Carolina). The study used pre-existing data without identifiers and was deemed exempt by the Harvard Medical School Human Subjects Committee.

Results

Among 185,106 men with local/regional prostate cancer, 49.9% received ADT at some time after their prostate cancer diagnosis. Table 1 shows use of ADT by patient characteristics, including comorbidity. Of these, 47.8% received GnRH agonists, 2.2% underwent orchiectomy, and 0.7% received both treatments. Among men treated with ADT, the median duration of treatment was 450 days (interquartile range 96–804).

Myocardial infarction

Table 2 shows the adjusted hazard ratio for myocardial infarction for each comorbidity, stratified by receipt of ADT. Also shown is the number of men per 1000 person years having myocardial infarction within 1 year for each group. Among men with no comorbidities, ADT was associated with an increase in the risk of myocardial infarction (adjusted hazard ratio [AHR]=1.09, 95% confidence interval [CI]=1.02–1.16). For men not on ADT, several comorbidities were associated with an increased risk of myocardial infarction, including a previous myocardial infarction, congestive heart failure, peripheral arterial disease, stroke, hypertension, chronic obstructive pulmonary disease, renal disease, and peptic ulcer disease (Table 2). Other than for peptic ulcer disease (P for interaction=0.04), the same comorbidities were also associated with increased risk of myocardial infarction for men on ADT ($P>0.10$ for all interactions), with generally similar hazard ratios attributed to the comorbidity.

The risk of myocardial infarction was associated with increasing age for men on ADT (AHR=1.032 per year, 95% CI=1.027–1.036) and for men not on ADT (AHR=1.027, 95% CI=1.020–1.034). A test for differential effect (i.e., interaction) between age and ADT was not significant ($P=.22$).

Diabetes

The cohort at risk for diabetes included 155,574 men without diabetes at baseline. Among these men, 49.2% received ADT during follow up. Table 3 shows the AHRs for diabetes by comorbidity stratified by receipt of ADT. Among men with no comorbidities, ADT was associated with an increase in the risk of diabetes (AHR=1.34, 95% CI=1.29–1.40). Among men not on ADT, myocardial infarction, congestive heart failure, peripheral arterial disease, stroke, hypertension, obesity, chronic obstructive pulmonary disease, and renal disease were all associated with incident diabetes. Men with dementia had a slightly lower risk of being diagnosed with diabetes. The risk of diabetes by comorbidity was generally similar for men on ADT, although the elevated risk was not statistically significant for stroke, hypertension, chronic obstructive pulmonary disease, renal disease, and peptic ulcer disease, and was significant for rheumatologic disease (P for all interactions $>.10$).

We observed a decreased risk of diabetes associated with increasing age (AHR=0.982 per year, 95% CI=0.979–0.988). As for myocardial infarction, we did not find evidence to conclude that the effect of age differed for men on ADT (AHR=.982, 95% CI=.979-.985) from men not on ADT (AHR=.978, 95% CI=.973-.983; P for interaction=.60).

Table 4 shows the expected number of myocardial infarctions or incident cases of diabetes per 1000 men by 1 year by comorbidity. These estimates incorporate the increased risk associated with ADT, and for most conditions, the risks are similarly elevated for the ADT vs. no ADT group.

Discussion

We studied a large population-based cohort of men with local or regional cancers to identify whether the association of ADT with myocardial infarction or diabetes varied by baseline comorbidities or age. As before,[3,4] we observed that ADT was associated with an increased risk of myocardial infarction and diabetes. However, we found no evidence to suggest that this risk was modified by the presence of existing comorbid illness, although we observed that a number of comorbidities, including traditional risk factors, were also associated with these outcomes. These findings are important because they suggest that decisions to use ADT should not be determined based on the presence or absence of underlying risk factors. In addition, our findings suggest that strategies to reduce risk of myocardial infarction and diabetes among prostate cancer patients receiving ADT should be similar to those for the general population.

Some previous studies have suggested that men with coronary artery disease associated with heart failure[7] or a prior history of myocardial infarction or stroke[8] may be at higher risk of developing cardiovascular disease when treated with ADT. These prior studies included men treated at a single center or its affiliated sites and had relatively small numbers of individuals with these comorbidities at baseline. Our findings provide some reassurance that although ADT is associated with cardiovascular and diabetes risk, the relative risks are not greater in specific populations, and thus should not lead to withholding of these medications in men who stand to benefit. This is particularly important for high-risk tumors in men undergoing radiation where overall survival benefits have been demonstrated.[20–24] Nevertheless, although relative risks were not modified by comorbidity, absolute risks may still differ depending on a patient's baseline risk. For example, if a man's 10-year risk of diabetes was 10%, with a relative hazard ratio of 1.33, their 10-year risk would increase to 13.3%, an absolute risk of 3.3% (number needed to harm=30). If the 10-year risk was 30%, it would increase to 39.9%, an absolute risk of 9.9% (number needed to harm=10). This underscores the need to select patients for therapy who are most likely to benefit, and avoid ADT in settings where there is no compelling evidence for benefit. Additional clinical trials are needed to help determine the overall benefits versus risks for ADT for primary treatment of local/regional prostate cancer and the treatment of biochemical recurrence following surgery and/or radiation therapy. Importantly, our findings also suggest that efforts aimed at risk modification, including smoking cessation, healthy diet, exercise, weight loss, and management of existing comorbidities are important to reduce morbidity and mortality associated with cardiovascular disease and diabetes, for all men, regardless of prostate cancer diagnosis or treatment with ADT.[25]

We observed higher risk for myocardial infarction associated with known risk factors including hypertension, renal insufficiency, and other cardiovascular disease, including prior myocardial infarction, congestive heart failure, peripheral arterial disease, and stroke. We also observed an increased risk of myocardial infarction associated with chronic obstructive pulmonary disease, a smoking-related condition that has been associated with increased risk of cardiovascular disease.[26] Surprisingly, we did not observe an increased risk of myocardial infarction among patients with diabetes or obesity, but diabetes and obesity were both highly correlated with several of the other comorbidities we studied, and obesity is very likely to be incompletely ascertained in administrative data.

The comorbidities associated with an increased risk for diabetes included obesity, hypertension, and myocardial infarction, congestive heart failure, and stroke. These conditions often track together, and our study design did not allow us to identify causal associations in one direction or the other. We also saw increased risk associated with chronic obstructive pulmonary disease and rheumatologic disease, which are often treated with corticosteroids, which can predispose individuals to diabetes. We saw a lower risk of diabetes among patients with dementia, possibly because such patients undergo fewer blood tests and screening for diabetes.

We also assessed whether older patients were more or less likely than younger patients to have adverse events on ADT, and we found no differences. We did observe an increased risk of myocardial infarction associated with increasing age. Surprisingly, we saw a decreased risk of diabetes associated with increasing age. The risk of diabetes in general increases with increasing age, particularly age >45.[27] Our cohort included men aged >65 years who were receiving regular health care in general. Many of the men who were likely to develop diabetes may have already had it identified earlier in their follow up.

Our study has some limitations. First, we identified disease outcomes and comorbidities using diagnosis codes in administrative data. Although we applied codes and algorithms used by others,[11–15] there may be some error. Second, some conditions are coded less reliably in administrative data than others. The low prevalence of obesity (4%) for example, is surely due to under-coding of this condition, which is present in about one-third of Americans.[28] Third, we had no information on certain important risk factors for the conditions we studied, including family history of cardiovascular disease or diabetes and smoking status. Fourth, SEER-Medicare data did not include information about oral medications during the study period, and therefore we could not ascertain use of oral antiandrogens. Treatment with antiandrogen monotherapy is not approved for prostate cancer in the U.S., so few men likely received such therapy. Other data suggest that the effects of oral antiandrogen do not substantially modify the effects of GnRH agonists on the outcomes studied.[3] Finally, we studied older men living in areas with SEER registries, so we cannot be certain that our findings generalize to younger men and men in other areas. Nevertheless, older men account for the majority of prostate cancer diagnoses, and the SEER areas represent 28% of the U.S. population.

Conclusions

In conclusion, ADT was associated with an increased risk of myocardial infarction and diabetes, and the risk did not vary by the presence or absence of comorbid illnesses. Traditional risk factors were associated with developing these conditions regardless of ADT use. These observations suggest that strategies to screen and prevent diabetes and cardiovascular disease in men with prostate cancer should be similar to those recommended for the general population.

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Appendix

Diagnosis or Procedure	ICD-9 Diagnosis	HCPCS	CPT	ICD-9 Procedure	Comments
Diabetes and Myocardial Infarction					
Diabetes[4, 12, 14, 15]					
Diabetes mellitus	250.xx				Required two or more outpatient encounters with a primary or secondary diagnosis code or one hospitalization with a primary diagnosis of diabetes
Diabetic polyneuropathy	357.2				
Diabetic retinopathy	362.0–362.0x				
Diabetic cataract	366.41				
Acute myocardial infarction [4, 11–13]	410.xx except 410.x2				Required an inpatient admission with a primary diagnosis of acute myocardial infarction
Androgen Deprivation Therapy*					
Leuprolide injection		J9217, J9218, J9219, J1950			
Goserelin injection		J9202			
Triptorelin injection		J3315			
Orchiectomy			54520, 54521, 54522, 54530, 54535, 54690, 49510	62.3, 62.4, 62.41, 62.42	
Primary Treatment**					
Radical prostatectomy*			55810–55815, 55840–55845	60.5	
Radiation therapy*	V58.0, V67.1, V66.1		77261–77431, 77499, 77750–77799	92.2–92.29	

* 54 of the 185,106 men were treated with abiraterone; because of the very small numbers, it was not assessed.

** Radical prostatectomy and radiation therapy were identified based on claims in the 6 months after diagnosis or data from the SEER data indicating use of these treatments.[29,30]

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Table 1

Patient characteristics and receipt of androgen deprivation therapy

	N (%)	% who received androgen deprivation therapy during follow-up
Total	185,106	49.9
Age in years		
66–69	45,844 (25)	37.3
70–74	58,450 (32)	46.6
75–79	45,379 (25)	56.1
80–84	24,036 (13)	63.4
85	11,397 (6)	64.2
<i>Comorbidity</i>		
Prior myocardial infarction	7859 (4)	53.8
Congestive heart failure	36,994 (20)	59.1
Peripheral vascular disease	23,817 (13)	56.9
Stroke	30,648 (17)	55.7
Obesity	7046 (4)	54.2
Hypertension	56,449 (31)	52.8
Chronic obstructive pulmonary disease	35,321 (19)	55.7
Diabetes	26,339 (14)	56.0
Chronic renal insufficiency	24,588 (13)	57.8
Liver disease	1927 (1)	55.5
Peptic ulcer disease	8553 (5)	55.8
Rheumatologic disease	4043 (2)	53.9
Dementia	9988 (5)	57.6
Paralysis	4957 (3)	56.1
Race		
White	157,064 (85)	49.4
Black	16,502 (9)	50.4
Other	7285 (4)	55.5
Unknown	4255 (2)	54.5
Hispanic ethnicity		
No	170,613 (92)	49.7
Yes	9266 (5)	52.9
Unknown	5227 (3)	52.1
Marital status		
Unmarried	37,085 (20)	51.0
Married	127,939 (69)	48.5
Unknown	20,082 (11)	57.0
Residence*		
Major metropolitan area	104,884 (57)	49.5
Metropolitan county	51,784 (28)	49.2

	N (%)	% who received androgen deprivation therapy during follow-up
Urban	10,878 (6)	52.4
Less urban	14,420 (8)	52.3
Rural	3140 (2)	53.8
SEER region		
San Francisco	8296 (4)	47.1
Connecticut	14,672 (8)	54.0
Detroit	21,547 (12)	46.2
Hawaii	3279 (2)	56.9
Iowa	14,904 (8)	52.4
New Mexico	6196 (3)	41.2
Seattle	14,100 (8)	42.0
Utah	8338 (5)	42.1
Atlanta	6759 (4)	37.7
San Jose	5050 (3)	60.5
Los Angeles	16,656 (9)	49.1
Rural Georgia	540 (0)	39.6
Great California	22,995 (12)	46.5
Kentucky	9557 (5)	52.0
Louisiana	10,260 (6)	56.8
New Jersey	21,957 (12)	61.1
Median household income in census tract of residence		
Quartile 1 (lowest)	45,872 (25)	52.9
Quartile 2	45,946 (25)	50.8
Quartile 3	46,072 (25)	48.9
Quartile 4 (high)	46,077 (25)	47.0
Unknown	1139 (1)	44.9
% high school graduates in census tract of residence		
Quartile 1 (lowest)	46,124 (25)	52.6
Quartile 2	46,005 (25)	50.6
Quartile 3	46,002 (25)	49.4
Quartile 4 (high)	45,836 (25)	47.1
Unknown	1139 (1)	44.9
Tumor grade (Gleason)		
Well differentiated (2–4)	8265 (4)	34.5
Moderately differentiated (5–7*)	108,475 (59)	43.4
Poorly differentiated/undifferentiated (8–10)	62,389 (34)	63.6
Unknown	5977 (3)	45.0
Tumor size		
T1 (clinically inapparent)	78,522 (42)	43.6
T2 (organ confined)	96,792 (52)	53.8
T3 (extracapsular or seminal vesicle invasion)	5824 (3)	66.5

	N (%)	% who received androgen deprivation therapy during follow-up
T4 (invading bladder and/or rectum)	3892 (2)	55.1
Unknown	76 (0)	65.8
Primary treatment received in the 6 months after diagnosis		
Radical prostatectomy	28,662 (15)	24.1
Radiation therapy	83,022 (45)	57.2
Neither radical prostatectomy or radiation	73,422 (40)	51.7

SEER=Surveillance, Epidemiology, and End Results

Gleason grade 7 was categorized as moderately differentiated before January 1, 2003 and as poorly differentiated as of January 1, 2003.

Table 2

Adjusted Risk of Myocardial Infarction by Comorbidity with and without Androgen Deprivation Therapy

Characteristic	Adjusted hazard ratio for association of comorbidity with myocardial infarction with or without ADT (95% CI)*		P value for interaction of comorbidity by ADT
	No ADT	ADT	
No comorbidity	1.00	1.09 (1.02–1.16)	-
<i>Comorbidity</i>			
Myocardial infarction	1.72 (1.51–1.97)	1.75 (1.41–2.16)	.92
Congestive heart failure	2.00 (1.88–2.13)	2.15 (1.94–2.39)	.23
Peripheral arterial disease	1.39 (1.30–1.50)	1.41 (1.24–1.59)	.91
Stroke	1.29 (1.20–1.38)	1.44 (1.27–1.62)	.13
Hypertension	1.08 (1.03–1.14)	1.17 (1.06–1.29)	.16
Obesity	0.97 (0.84 to 1.11)	0.93 (0.71–1.22)	.96
Chronic obstructive pulmonary disease	1.14 (1.07–1.22)	1.19 (1.06–1.33)	.56
Diabetes	1.03 (0.96–1.11)	0.98 (0.85–1.12)	.47
Chronic renal insufficiency	1.63 (1.51–1.76)	1.51 (1.31–1.74)	.36
Liver disease	0.93 (0.66–1.30)	0.79 (0.41–1.52)	.69
Peptic ulcer disease	1.14 (1.01–1.28)	0.86 (0.68–1.09)	.04
Rheumatologic disease	1.03 (0.87–1.21)	0.91 (0.65–1.28)	.55
Dementia	0.97 (0.85–1.11)	0.78 (0.60–1.01)	.14
Paralysis	1.17 (0.99–1.38)	1.27 (0.96–1.68)	.61

* Adjusting for all variables in Table 1.

ADT=androgen deprivation therapy

Table 3

Adjusted Risk of Developing Diabetes by Comorbidity with and without Androgen Deprivation Therapy

Characteristic	Adjusted hazard ratio for association of comorbidity with myocardial infarction with or without ADT (95% CI)*		P value for interaction of comorbidity by ADT
	No ADT	ADT	
No comorbidity	1.00	1.33 (1.27–1.39)	-
<i>Comorbidity</i>			
Myocardial infarction	1.29 (1.25–1.35)	1.32 (1.24–1.42)	.58
Congestive heart failure	1.34 (1.27–1.42)	1.35 (1.23–1.48)	.94
Peripheral arterial disease	1.15 (1.08–1.22)	1.07 (0.95–1.19)	.26
Stroke	1.13 (1.07–1.20)	1.09 (0.98–1.22)	.60
Hypertension	1.16 (1.11–1.20)	1.18 (1.10–1.26)	.57
Obesity	2.03 (1.86–2.21)	2.06 (1.74–2.44)	.85
Chronic obstructive pulmonary disease	1.14 (1.08–1.19)	1.08 (0.99–1.18)	.32
Chronic renal insufficiency	1.19 (1.10–1.28)	1.06 (0.92–1.22)	.17
Liver disease	1.09 (0.85–1.40)	1.32 (0.89–1.98)	.42
Peptic ulcer disease	0.96 (0.87–1.06)	1.12 (0.94–1.34)	.13
Rheumatologic disease	1.12 (0.98–1.27)	1.26 (1.00–1.59)	.39
Dementia	0.79 (0.69–0.90)	0.85 (0.68–1.06)	.57
Paralysis	0.94 (0.81–1.11)	0.89 (0.67–1.20)	.75

* Adjusting for all variables in Table 1 (except diabetes).

ADT=androgen deprivation therapy

Table 4

Expected number of patients per 1000 with outcome by 1 year by comorbidity and ADT status *

Characteristic	Expected number of patients per 1000 men with myocardial infarction by 1 year		Expected number of patients per 1000 men with incident diabetes by 1 year	
	No ADT	ADT	No ADT	ADT
No comorbidity	9.0	9.8	23.9	31.7
<i>Comorbidity</i>				
Myocardial infarction	15.4	17.0	30.1	41.7
Congestive heart failure	17.9	20.9	31.9	42.4
Peripheral arterial disease	12.5	13.7	27.3	33.7
Stroke	11.6	14.0	26.9	34.6
Hypertension	9.7	11.4	27.5	37.3
Obesity	8.7	9.1	47.8	64.3
Chronic obstructive pulmonary disease	10.2	11.6	27.0	34.2
Diabetes	9.3	9.5	--	--
Chronic renal insufficiency	14.6	14.7	28.2	33.5
Liver disease	8.3	7.7	26.0	41.7
Peptic ulcer disease	10.2	8.4	22.9	35.5
Rheumatologic disease	9.2	8.9	26.7	39.7
Dementia	8.7	7.6	18.9	26.9
Paralysis	10.5	12.4	22.6	28.4

* Predictions account for ADT effect as well as comorbidity effect. Predictions are from the Cox proportional hazard models that include all variables in Table 1.

ADT=androgen deprivation therapy