

Aspirin and Hormone Therapy for Prostate Cancer

TO THE EDITOR: Abnormal liver-function tests have been reported in 5% of patients taking high-dose aspirin for rheumatoid arthritis or osteoarthritis.¹ A study of castrated rabbits revealed that serum levels of acetylsalicylic acid after oral aspirin administration were significantly higher than expected.² This effect was attributed to slow metabolism of aspirin as a result of low testosterone levels. In men with prostate cancer, this effect of aspirin on liver-function tests could have clinical importance because the antiandrogen component of hormone therapy is discontinued when liver-function tests become abnormal.

We investigated whether the use of low-dose aspirin affects liver-function tests, and thereby interferes with the ability to deliver a full course of hormone therapy, in 206 men with localized but high- or intermediate-risk prostate cancers who were enrolled in a randomized trial³ comparing radiation therapy alone with radiation therapy plus hormone therapy. Hormone therapy consisted of 6 months of a luteinizing hormone–releasing hormone (LHRH) agonist and the antiandrogen flutamide. A logistic-regression multivariable analysis⁴ was used to assess whether an association existed between commonly used drugs

Table 1. Relative Risk of Death According to Treatment and Selected Baseline Characteristics among 206 Men with Prostate Cancer.*

Covariate	No. of Men	No. of Deaths	Relative Risk of Death (95% CI)	P Value
Treatment				
Radiation therapy plus 6 mo of hormone therapy	73	16	1.00	—
Radiation therapy plus <6 mo of hormone therapy	29	14	3.50 (1.03–11.80)	0.04
Radiation therapy alone	104	44	6.10 (2.30–16.20)	<0.001
ACE-27 comorbidity score†				
No or minimal comorbidity	157	42	1.00	—
Moderate or severe comorbidity	49	32	38.00 (13.00–117.00)	<0.001
Interaction terms				
Treatment (radiation therapy) × comorbidity score	206	74	0.04 (0.01–0.14)	<0.001
Treatment (radiation therapy plus <6 mo of hormone therapy) × comorbidity score			0.10 (0.02–0.48)	0.004
Log PSA level‡	206	74	1.40 (1.00–2.00)	0.09
Gleason score on biopsy§				
5–6	57	17	1.00	—
7	119	39	0.90 (0.50–1.80)	0.85
8–10	30	18	1.90 (0.90–3.90)	0.08
2002 AJCC tumor category				
T1	99	29	1.00	—
T2	107	45	1.00 (0.60–1.60)	0.92
Age¶	206	74	1.07 (1.02–1.13)	0.007

* These results are from a multivariable Cox regression analysis⁵ of data for the 206 men in the study cohort. AJCC denotes the American Joint Committee on Cancer.

† Possible scores on the 27-item Adult Comorbidity Evaluation (ACE-27) are 0 (no comorbidity), 1 (minimal comorbidity), 2 (moderate comorbidity), and 3 (severe comorbidity).

‡ Relative risk for prostate-specific antigen (PSA) is given for each unit increase in nanograms per milliliter.

§ The Gleason score can range from 2 to 10, with higher scores indicating more aggressive disease.

¶ Relative risk for age is given for each unit increase in years.

(baby aspirin or atorvastatin) and the discontinuation of flutamide due to elevated values on liver-function tests. The use of baby aspirin was significantly associated with abnormal liver-function tests ($P=0.02$), whereas the use of atorvastatin was not ($P=0.13$). Flutamide was prematurely discontinued in 37% of aspirin users, as compared with 16% of nonusers, because of abnormal liver-function tests. Moreover, after a median follow-up period of 7.6 years and adjustment for known prognostic factors and interactions, and with men who completed 6 months of hormone therapy with both the LHRH agonist and flutamide as the comparison group, the risk of death was 3.5 times as high among men who completed 6 months of the LHRH agonist but discontinued flutamide early ($P=0.04$) and 6.1 times as high among men treated with radiation therapy alone ($P<0.001$) (Table 1). These data show that a commonly used drug can alter the tolerability of anticancer therapy.

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