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Cancer Epidemiology, Biomarkers & Prevention

Null Results in Brief

Statin Use and Risk of Prostate Cancer in the Prospective Osteoporotic Fractures in Men (MrOS) Study

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Abstract

Background: Statins are a common medication for cholesterol control that may also have effects on cancer-related pathways. The evidence of an association between statins and prostate cancer risk remains ambiguous.

Methods: We examined statin use in a prospective cohort of 5,069 elderly U.S. men and the risk of incident total, low/high stage, and low/high grade prostate cancer diagnosed between 2000 and 2008. We used multivariate logistic regression models to estimate relative risks and 95% confidence intervals, adjusting for demographic and lifestyle characteristics.

Results: There was no evidence of an association between statin use and any of the prostate cancer endpoints (total, low/high stage, low/high grade prostate cancer), adjusting for age, study site, race, body mass index, marital status, family history of prostate cancer, number of comorbidities, physical activity, and smoking history.

Conclusions and Impact: In this study of elderly U.S. men, we observed a null association between statin use and risk of prostate cancer. *Cancer Epidemiol Biomarkers Prev; 21(10); 1886–8. ©2012 AACR.*

Background

Prostate cancer is the most common cancer among men in the United States and second leading cause of cancer death. Screening is controversial, and it remains a public health priority to identify prevention strategies for this common malignancy.

Statin medications inhibit f3-hydroxy-f3-methylglutaryl coA (HMG-CoA) reductase to lower plasma cholesterol levels and thereby reduce risk of coronary artery disease. Since the beginning of their use in 1987, statins have become the primary medication used to treat hyperlipidemia (1). Through inhibition of HMG-CoA reductase, statins block the mevalonate pathway, thus affecting regulation of cell cycle progression, proliferation and signaling pathways that can also influence tumor initiation or growth (2).

The evidence on statins and prostate cancer risk is inconsistent. A pooled analysis of 6 cohort studies published through 2007 observed no relationship between statin use and prostate cancer risk (RR = 0.98, 95% CI, 0.89 to 1.09, $I^2 = 38\%$; ref. 3). There have been no clinical trials specifically addressing statin assignment and the primary prevention of prostate cancer, however, a meta-analysis of clinical trials published through 2007 where prostate cancer was assessed as a secondary outcome reported no association (RR = 1.06, 95% CI, 0.93 to 1.20; ref. 3). In contrast, 6 of 10 cohort studies published after those combined analyses reported a statistically significant inverse association between statin use and prostate cancer risk (1, 4–8).

We examined the association of self-reported statin use and risk of incident total and high stage/grade prostate cancer in a prospective cohort of older men from the Osteoporotic Fractures in Men Study (MrOS).

Materials and Methods

The MrOS cohort includes 5,994 community dwelling, ambulatory men who were age 65 or older and living in 6 geographic regions of the United States in 2000 to 2002: Birmingham, Alabama; Minneapolis, Minnesota; Palo Alto, California; Pittsburgh, Pennsylvania; Portland, Oregon; and San Diego, California. The original goals of the MrOS trial were to identify risk factors and consequences of vertebral and non-vertebral fractures in older men. We excluded men with a self-reported history of PCa ($n = 708$) or any patient with missing statin data ($n = 217$) at baseline, leaving 5,069 men for analysis.

Multivariate logistic regression models were used to compute OR and 95% CI as estimates for the relative risk of prostate cancer associated with statin use. Current statin use (Yes/No) was assessed on the baseline questionnaire and defined as any use in the previous two weeks. Medication use in MrOS was verified by review of medication bottles by trained staff. Our main outcome

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was incident prostate cancer diagnosed between 2000 and 2008, and we also examined subcategories of low and high stage and low and high grade cancers given the known heterogeneity of the disease. Prostate cancer diagnoses were identified via self-report on tri-annual follow-up questionnaires, and medical and pathology records were collected and centrally adjudicated. We considered the following potential confounding factors in multivariate analyses: baseline age, race, body mass index (BMI), site, family history of prostate cancer, marital status, comorbid conditions, physical activity, and smoking history.

Results

Table 1 provides characteristics of the study population by statin use at baseline in 2000 to 2002. As anticipated, statin users had lower LDL, HDL, and total cholesterol, were more likely to be married, and have a smoking history and comorbidities (heart disease and diabetes). Twenty-seven percent of the men were using statins at baseline, and we identified 356 cases of incident prostate cancer during an average of 7 years of follow-up.

We observed no statistically significant associations for statin use at baseline and the outcomes of total ($P = 0.07$), low grade ($P = 0.49$), high grade ($P = 0.10$), low stage ($P = 0.29$), or high stage ($P = 0.12$) prostate cancer (Table 2). Further consideration of statin subtype (lipophilic vs. hydrophilic) did not alter these results (data not shown).

Discussion

This cohort study of older U.S. men provides no evidence of an association between statin use and the risk of incident overall, low/high stage, or low/high grade prostate cancer.

Strengths of this study include the prospective design, detailed comorbidity and demographic data, and central adjudication of all prostate cancer outcomes. Limitations of this study include the overall smaller and more homogenous sample size, and lack of data on duration or dose of statin usage or diet. Overall, this study is consistent with several other epidemiologic studies reporting null associations for statin use and prostate cancer outcomes. Potential reasons for the apparent discrepancy between

Table 1. Demographic characteristics of MrOS cohort by statin use, 2000 to 2002

	Statin user		
	No ($n = 3,692$)	**Yes ($n = 1,377$)**	***P***
Age (y, mean ± SD)	73.5 ± 5.9	73.1 ± 5.5	0.04
White (%)	90.5	91.4	0.32
BMI (kg/m^2, mean ±SD)	27.3 ± 3.9	27.7 ± 3.7	<0.001
Site (%)			
Birmingham	628 (17)	244 (17.7)	0.030
Minneapolis	571 (15.5)	192 (13.9)	
Palo Alto	589 (15.9)	244 (17.7)	
Pittsburgh	657 (17.8)	239 (17.4)	
Portland	633 (17.1)	196 (14.2)	
San Diego	614 (16.6)	262 (19.0)	
Married (%)	3009 (81.5)	1172 (85.1)	0.003
Some college or more (%)	2793 (75.7)	1064 (77.3)	0.23
Comorbid conditions (%)			
Diabetes	346 (9.4)	212 (15.4)	<0.001
Heart attack	291 (7.9)	422 (30.6)	<0.001
Hypertension	1438 (38.9)	752 (54.6)	<0.001
Chronic lung disease	377 (10.2)	152 (11.0)	0.39
Family history of prostate cancer (%)	472 (15.8)	199 (17.5)	0.18
Smoking status			
Past	2128 (57.6)	866 (62.9)	<0.001
Current	153 (4.1)	29 (2.1)	
Never	1411 (38.2)	481 (35.0)	
Physical activity (PASE score)	148.4 (70.3)	141.1 (64.9)	<0.001
LDL (mg/dL)	119.9 ± 30.8	97.8 ± 25.4	<0.001
HDL (mg/dL)	49.0 ± 15.2	47.8 ± 12.7	0.005
Total cholesterol (mg/dL)	198.9 ± 34.1	176.6 ± 29.1	<0.001
Prostate cancer (%)	6.5	8.1	0.05

PASE, physical activity scale for the elderly.

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Table 2. Multivariate relative risks of total, low/high stage, and low/high grade prostate cancer for current vs. nonuse of statins, among 5069 men in the MrOS cohort

	Cases (total *N*)	Age and site adjusted OR	95% CI	*P*	Cases (total *N*)	Multivariate OR[a]	95% CI	*P*
Total	356 (5069)	1.24	0.98–1.57	0.07	298 (4120)	1.07	0.82–1.40	0.63
Gleason <7	155 (4868)	1.13	0.80–1.61	0.49	135 (3957)	1.07	0.73–1.59	0.72
Gleason $\geq$ 7	195 (4908)	1.29	0.95–1.76	0.10	157 (3979)	1.04	0.73–1.50	0.82
Low stage (T1/T2)	252 (4965)	1.16	0.88–1.54	0.29	209 (4031)	1.00	0.73–1.37	0.99
High stage (T3/T4)	100 (4813)	1.40	0.92–2.13	0.12	86 (3908)	1.29	0.80–2.07	0.30

[a]$n = 4{,}120$ (298 cases) due to missing data for covariates; model additionally adjusted for race, BMI, marital status, family history of prostate cancer, number of comorbidities, physical activity, and smoking history.

this study and other prospective cohorts that have reported a marked reduction in risk for statin use and prostate cancer include differences in the study population (e.g., mean age = 74 years), residual confounding, and measurement error in the self-reported assessment of statins.

In conclusion, we observed no evidence that statins reduce the risk of incident prostate cancer or prostate cancer subtypes in this prospective cohort of U.S. men.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: J.M. Chan, J. Shannon, D.C. Bauer
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): N.A. Daniels, D.C. Bauer
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): J.M. Chan, S.L. Harrison, T.J. Wilt, D.C. Bauer
Writing, review, and/or revision of the manuscript: J.M. Chan, S.R. Bauer, N.A. Daniels, T.J. Wilt, J. Shannon, D.C. Bauer
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): S.R. Bauer

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