Re: The Association Between Statins and Cancer Incidence in a Veterans Population

I was pleased to read the article by Farwell et al. (1) reporting on statins and cancer. By comparing cancer incidence rates in statin users (irrespective of antihypertensive drug use) and antihypertensive drug users, the investigators likely limited detection bias that can arise in studies in which opportunity for exposure and outcome detection both depend on accessing medical care. For prostate cancer, detection bias has become of particular concern in epidemiological studies after the introduction of prostate-specific antigen (PSA) screening. Detection bias could arise when men who seek medical care are screened for both elevated cholesterol and PSA: compared with men who test negative, men who test positive for elevated cholesterol are more likely to be prescribed a statin, and men who test positive for elevated PSA are more likely to undergo biopsy examination. Consequently, men with prostate cancer who take a statin would be more likely diagnosed when their disease is organ confined, whereas men with prostate cancer who do not take a statin would be more likely diagnosed when their disease is advanced. Thus, statin use would appear associated positively with total and early disease and inversely with advanced disease.

Farwell et al. (1) reported a slight inverse association between statins and prostate cancer (relative risk = 0.90, 95% confidence interval = 0.81 to 0.99) but no trend across dose. These findings are somewhat different than for lung and colorectal cancers, which were moderately inversely associated (1). I am concerned that Journal readers may be left with the impression that there is little, if any, evidence that statins influence the development of prostate cancer.

What Farwell et al. (1) did not address is the growing literature on statins and prostate cancer with a worse prognosis. Five prospective studies and a clinic-based case-control study support an inverse association between statins, especially long-duration statin use, and advanced or high-grade prostate cancer, whereas one hospital-based case-control study reported no association [see references in (2–4)]. Other epidemiological studies and statin trials in which cancer was a safety outcome [see references in (5)] did not evaluate stage and grade.

The possibility of detection bias was considered in the US prospective studies [see references in (2)] by taking into account the notable difference between statin users and nonusers in the proportion of men who had a screening PSA test. This bias was likely reduced in the clinic-based case-control study (6) by including men who had a PSA test in the past year as control subjects. Further support that the inverse association is not solely due to detection bias comes from a study in Finland (7), where PSA screening is not common, and, thus, the correlation of cholesterol screening leading to statin use with PSA screening leading to biopsy may be lower. At this time, there is no compelling evidence to refute that statins may protect against advanced or high-grade prostate cancer, but detection bias cannot be ruled out as an explanation. Given a great strength of the study by Farwell et al. (1)—limited detection bias—I am eager to know the association between statin use and advanced prostate cancer in this study.

ELIZABETH A. PLATZ

References

Notes
Correspondence to: Elizabeth A. Platz, ScD, MPH, Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health; the James Buchanan Brady Urological Institute and the Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins Medical Institutions, 615 N Wolfe St, Rm E6132, Baltimore, MD 21205 (e-mail: eplatz@jhsp.h.edu).
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