Aspirin Use and the Risk of Lethal Prostate Cancer in the Physicians' Health Study

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We have no conflicts of interest to report.

Funding Acknowledgments:

1. Prostate Cancer Foundation
2. National Cancer Institute CA34944, CA40360, CA141298, CA167552, HL26490, HL34595

Background

Regular aspirin use likely confers protection against some malignancies including prostate cancer, but its impact on lethal prostate cancer is particularly unclear. Given the clinical importance of lethal disease, our objective was to investigate the association between regular aspirin use and (1) risk of lethal prostate cancer in a large prospective cohort, and (2) survival after prostate cancer diagnosis among patients only.

Methods

In 1981-82, The Physicians' Health Study randomized 22,071 disease-free male physicians to aspirin, beta-carotene, both medications, or placebo. The trial ended in 1988, but annual questionnaires have obtained aspirin use, prostate cancer diagnoses, and outcomes through 2009 for all participants, and through 2015 for prostate cancer patients.

Regular aspirin use was defined as >3 tablets per week. Lethal prostate cancer was defined as metastases or prostate cancer death. Cox proportional hazards models estimated age- and multivariate-adjusted hazard ratios (HR) for (1) *risk analysis:* regular aspirin use (updated until initial prostate cancer diagnosis for prostate cancer patients) and risk of lethal prostate cancer among all participants; and (2) *survival analysis:* regular aspirin use after diagnosis and post-diagnostic survival to lethality among men diagnosed initially with non-metastatic prostate cancer.

Secondary risk and survival analyses stratified on year of prostate cancer diagnosis (pre-PSA era: before 1992 vs. PSA era: 1992 and later). An additional secondary survival analysis stratified on clinical stage at diagnosis (T1 vs. T2-T4).

Results

Risk analysis: 519 men developed lethal prostate cancer by 2009. Current and past regular aspirin use were associated with decreased risk of lethal prostate cancer (current: 0.70, 0.54-091; past: 0.51, 0.38-0.67) compared to never use. Stopping use closer to diagnosis was associated with a stronger inverse relation among past users. Associations were stronger for prostate cancer cases diagnosed before the introduction of widespread PSA testing in 1992.

Survival analysis: 409 men diagnosed with non-metastatic prostate cancer developed lethal disease by 2015. Post-diagnostic aspirin use was associated with improved survival for lethal prostate cancer (0.73, 0.55-0.97) and overall mortality (0.78, 0.67-0.92). We were unable to assess the effect of aspirin dose. Associations were stronger for prostate cancer cases diagnosed before 1992, and for cases diagnosed with more advanced disease (T2-T4).

Conclusions

In this prospective study of 22,071 physicians, regular aspirin use was associated with a decreased risk of lethal prostate cancer among all participants. Post diagnosis use was associated with improved survival after prostate cancer diagnosis. Aspirin may inhibit prostate cancer progression, thus prolonging cancer-specific and overall survival. A randomized trial of aspirin at time of prostate cancer diagnosis should be considered.