Aspirin shows promise for colon cancer patients

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Men and women who were diagnosed with colorectal cancer and began regular use of aspirin had a lower risk of overall and colorectal cancer death compared to patients not using aspirin, according to a study in the August 12 issue of *JAMA*.

Numerous prospective, observational studies demonstrate that regular aspirin use is associated with a lower risk of colorectal adenoma (a benign tumor) or cancer. Aspirin is likely, at least in part, to prevent colorectal neoplasia (tumor growth) through inhibition of cyclooxygenase-2 (COX-2; an enzyme), which promotes inflammation and cell proliferation, and is overexpressed in the majority of human colorectal cancers, according to background information in the article. However, the influence of aspirin on survival after diagnosis of colorectal cancer has been unknown.

Andrew T. Chan, M.D., M.P.H., of Massachusetts General Hospital and Harvard Medical School, Boston, and colleagues studied the association between aspirin use and survival among 1,279 men and women with nonmetastatic (stage I, II, and III) colorectal cancer who were participating in 2 large prospective cohort studies (Nurses' Health Study [NHS] and the Health Professionals Follow-up Study [HPFS]) that were initiated (in 1980 and 1986, respectively) prior to cancer diagnosis and followed up through June 1, 2008.

"Within these cohorts, we previously have demonstrated that regular aspirin use was associated with a reduction in the subsequent risk of developing an initial primary colorectal cancer, particularly tumors with COX-2 overexpression. Because these participants have provided biennially updated data on aspirin use, we had a unique opportunity to extend these findings by examining the influence of prediagnosis and postdiagnosis aspirin use on the survival of patients with established colorectal cancer," the authors write.

For participants who were alive through the end of follow-up, the median (midpoint) time of follow-up from date of diagnosis was 11.8 years. There were 193 total deaths (35 percent) and 81 colorectal cancer-specific deaths (15 percent) among 549 participants who regularly used aspirin after colorectal cancer diagnosis, compared with 287 (39 percent) total and 141 (19 percent) colorectal cancer-specific deaths among 730 participants who did not use aspirin. For the entire cohort, the overall 5-year survival was 88 percent for participants who used aspirin compared with 83 percent for those who did not. The corresponding 10-year survival rates were 74 percent and 69 percent.

Regular use of aspirin after diagnosis was associated with a significant reduction in risk of colorectal cancer-specific death and a reduction in overall mortality. Compared with nonusers, regular aspirin use after diagnosis was associated with a 29 percent lower risk for colorectal-specific mortality and a 21 percent lower risk for overall mortality. Because the prognosis among stage I participants is generally favorable, the researchers also examined the influence of aspirin use among those diagnosed with stage II or III disease and observed similar results.

Among the 719 participants who did not use aspirin before diagnosis, initiation of use postdiagnosis was associated with a 47 percent lower risk for colorectal cancer-specific mortality and a 32 percent lower risk of overall mortality. In contrast, among participants who were using aspirin before diagnosis, continuation of aspirin use postdiagnosis was not associated with a significant reduction in colorectal cancer-specific survival or overall survival.

Among participants with COX-2-positive tumors, regular aspirin use after diagnosis was associated with a 61 percent lower risk of colorectal cancer-specific death and 38 percent lower risk of overall mortality, whereas postdiagnosis aspirin use was

not associated with lower risk of either colorectal cancer-specific or overall mortality for those with COX-2-negative tumors. "This supports the hypothesis that COX-2-positive tumors may be relatively sensitive to the anticancer effect of aspirin, whereas COX-2-negative tumors may be relatively aspirin-resistant. Moreover, it potentially explains the observation that the benefit of postdiagnosis aspirin use on patient survival was not apparent among patients who used aspirin prior to cancer diagnosis," the researchers note.

"These results suggest that aspirin may influence the biology of established colorectal tumors in addition to preventing their occurrence. Our data also highlight the potential for using COX-2 or related markers to tailor aspirin use among patients with newly diagnosed colorectal cancer. Nonetheless, because our data are observational, routine use of aspirin or related agents as cancer therapy cannot be recommended, especially in light of concerns over their related toxicities, such as gastrointestinal bleeding. Further studies among patients with colorectal cancer, including placebo-controlled trials of aspirin or related agents as adjuncts to other routine therapies, are required."

More information: *JAMA*. 2009;302[6]:649-659.

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