Cholesterol levels, not statins, influence colorectal cancer risk

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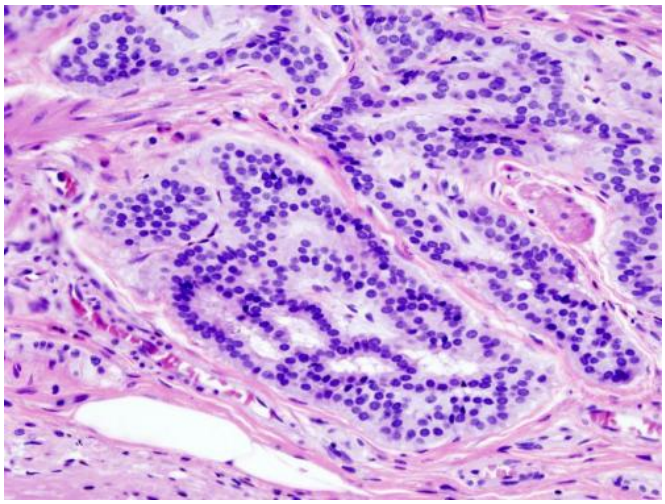

Cancer — Histopathologic image of colonic carcinoid.
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Long-term use of the cholesterol-lowering drugs known as statins does not appear to decrease a patient's risk of colorectal cancer, suggests a new, large case-control study from Penn Medicine researchers published this week in *PLOS Medicine*. The observational analysis of over 100,000 patients' medical records suggests it is cholesterol levels that influence risk, not the much-debated statins, and that "indication bias" may explain the link between the widely-used cardiovascular drugs and risk. Such bias occurs when the indication (high cholesterol, in this case) being treated with a drug is also associated with the outcome of interest (colorectal cancer).

"There appears to be an artificially protective effect of statins," said Ronac Mamtani, MD, MSCE, an assistant professor of Hematology/Oncology from the Perelman School of Medicine at the University of Pennsylvania and the Abramson Cancer Center, and lead author of the study. "Although the risk of colorectal cancer was lower in statin users versus non-users, when we compared those who continued statin therapy versus those who discontinued the therapy, such that each group shared the same indication for statin therapy, there was no difference in risk."

Both statin use and high cholesterol have been linked to a lower colorectal cancer risk, but it has remained unclear which may be responsible for the apparent beneficial effects.

Blood cholesterol levels were inversely related to colorectal cancer risk: the higher the cholesterol level, the lower the risk for patients, regardless of statin use, the authors found. The researchers also found that an unexplained drop in cholesterol levels one year before a cancer diagnosis increased the risk of cancer in both statin users and non-users.

The findings point to a bigger role of cholesterol levels on cancer risk that could potentially serve as a blood biomarker to help diagnosis colorectal cancer earlier.

Ben Boursi, MD, a postdoctoral fellow in the Perelman School of Medicine, and Yu-Xiao Yang, MD, MSCE, an associate professor of Medicine and Epidemiology at Penn, are senior authors on the paper.

Statins are a common cholesterol-lowering treatment strategy for the management of patients at risk for coronary heart disease. Previous studies have also shown a potential reduction in cancer risk for people who take the drugs; however, they did not account for the blood cholesterol level on cancer risk, the authors said.

In the new study, the researchers compared statin use and blood cholesterol level between 22,163 patients with colorectal cancer and 86,538 patients without colorectal cancer (controls) from a database of electronic records of over 10 million patients from primary care practices in the United

Kingdom.

They confirmed findings from previous studies that showed a decreased risk of colorectal cancer in statin users compared to non-users. However, they found that the difference in the risk of colorectal cancer was not significantly different between those patients who continued statin therapy and those who discontinued (OR, 0.98; 95% CI, 0.79-1.22). Furthermore, for every 1 mmol/L (~38.6 mg/dl) increase in total cholesterol level, authors observed a 10 percent decreased risk of colorectal cancer.

Additionally, they observed that decreases in total serum cholesterol (>1 mmol/L) at least a year before the cancer diagnosis were associated with 1.25-fold and 2.36-fold increased risk of colorectal cancer in users and nonusers, respectively.

"Together, these data demonstrate a complex association between statins, cholesterol, and colorectal cancer," Mamtani said. "While unexplained decreases in blood total cholesterol should alert physicians to consider colon cancer as one potential explanation, future studies are needed to determine the utility of blood cholesterol as a marker for early detection of colon cancer."

More information: Mamtani R, Lewis JD, Scott FI, Ahmad T, Goldberg DS, Datta J, et al. (2016) Disentangling the Association between Statins, Cholesterol, and Colorectal Cancer: A Nested Case-Control Study. *PLOS Medicine*, 13(4): e1002007. journals.plos.org/plosmedicine … journal.pmed.1002007

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