Immune-boosting cancer treatment may pose cardiovascular risk

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A type of cancer treatment used to boost the body's immune system may worsen inflammation in the arteries that distribute blood from the heart, according to a small study.

The research, published Sept. 8 in the American Heart Association (AHA) journal *Circulation*, found increased inflammation in the large arteries of 20 Austrians with melanoma immediately following treatment with immune checkpoint inhibitors. The drugs are a type of cancer treatment known as immunotherapy because they strengthen the ability of the body's immune system to attack cancer cells.

"The study provides evidence that [immune checkpoint inhibitor] therapy aggravates present atherosclerosis and treating physicians should consider potential complications here," said study senior author Dr. Marcus Hacker, of the division of nuclear medicine at the Medical University of Vienna.

Immunotherapy has been shown to be effective for many people with cancers resistant to chemotherapy and radiation. Immune checkpoint inhibitors work by thwarting the part of the body's immune system that keeps it from responding too strongly, to protect healthy cells from being destroyed. Drugs that block immune checkpoints make it easier for the body's infection-fighting T-cells to kill cancer cells. But side effects include potential cardiovascular damage.

People who have cancer are generally at greater risk of dying from cardiovascular disease than the general population. A 2019 study in the *European Heart Journal* found that over nearly 40 years, more than 1 in 10 cancer survivors in the United States died from some form of cardiovascular disease, most often from heart disease. According to American Cancer Society statistics, there are about 17 million U.S. cancer survivors.

While the new study looked at people with just one type of tumor, Hacker said his team has since expanded its investigation to lymphoma patients, finding similar results that have not yet been published. What's needed next, he said, are studies that look at whether the increased arterial inflammation in people receiving immune checkpoint inhibitors leads to heart problems later in life.

A larger study that tracks patients for 10 or 20 years would be a logical next step, said Carolyn Miller Reilly, a professor at Emory University's Nell Hodgson Woodruff School of Nursing in Atlanta. She co-authored a recent AHA scientific statement about the intersection of cardiovascular medicine and cancer treatments—an emerging field known as cardio-oncology.

"The changes they are showing here are not going to immediately demonstrate adverse events," said Reilly, who was not involved in the new research. "It's not like we're going to give this drug, and a

month later the patient is going to have a heart attack. But it's going to cause plaque buildup that can become more unstable. Long-term, we may see the development of cardiovascular disease."

The study does not suggest cancer patients—even those with pre-existing cardiovascular disease—should forego immune checkpoint inhibitor therapy, she added, noting that inflammation had worsened most in those with the mildest plaque buildup. "I would not withhold this treatment as the benefits outweigh the risk."

Instead, she said, oncologists may wish to consider strategies to mitigate any impact on the heart and consult with a cardio-oncologist to evaluate a specific patient's cardiovascular disease risk.

Reilly often teaches about the need for lifestyle changes to control risk factors for cancer and heart disease by optimizing weight, decreasing cholesterol levels, eating a healthy diet, exercising and maintaining good blood pressure control. "Cancer and heart disease have all the same risk factors," she said.

In some cases, medications may also be useful, Hacker said.

"If our study results can be replicated in prospective settings, we should think about future combination therapies with atherosclerosis-stabilizing agents like statins to potentially protect patients at cardiovascular risk from unfortunate events after therapy."