Study finds elevated risk of rare blood cancers after chemotherapy for most solid tumors

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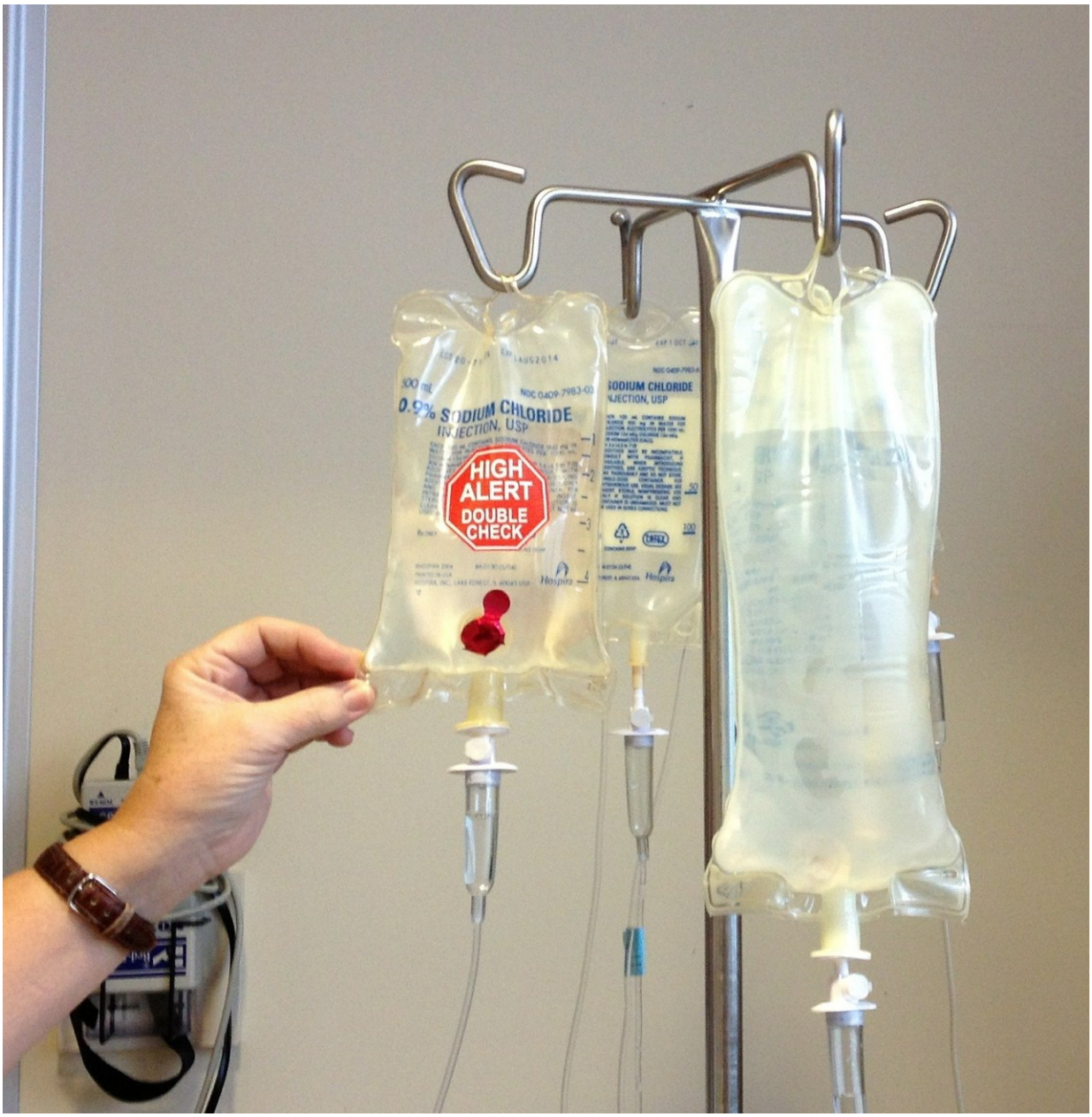

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Findings from a new study by researchers at the National Cancer Institute (NCI) show that patients treated with chemotherapy for most solid tumors during 2000-2014 experienced an increased risk of therapy-

related myelodysplastic syndrome/acute myeloid leukemia (tMDS/AML). The study, which used U.S. population-based cancer registry data from NCI's Surveillance, Epidemiology, and End Results (SEER) program and treatment information from the SEER-Medicare database, was published December 20, 2018, in *JAMA Oncology*. NCI is part of the National Institutes of Health.

Advances in treatment over the last several decades have resulted in improved survival for patients with many types of cancer. However, survivors may be at increased risk of developing a subsequent treatment-related cancer. In this study, researchers aimed to quantify the risk of developing tMDS/AML, a rare but often fatal blood cancer, in patients treated with chemotherapy.

"We've known for a long time that the development of myeloid leukemia is a very rare adverse effect of some types of cancer treatments that damage cells," said Lindsay Morton, Ph.D., lead author of the study and a senior investigator in NCI's Division of Cancer Epidemiology and Genetics. "There have been many changes in cancer treatment over time, including the introduction of new chemotherapy drugs and drug combinations, but we didn't know what the risk of therapy-related leukemia looked like for patients since these changes were made."

Because tMDS/AML is rare, most data on the disease have come from case series, case-control studies, and clinical trials, which often include a relatively small number of tMDS/AML cases. In this study, investigators brought a population-based data approach to the research, with a much larger sample size and prospective data from long-term patient follow-up.

To this end, they analyzed SEER registry data on more than 700,000 patients age 20-84 in the United States with solid tumors who were diagnosed and treated with initial chemotherapy during 2000-2013 and

survived at least one year after diagnosis. Of these patients, 1,619 developed tMDS/AML through 2014. When the researchers analyzed the risk of tMDS/AML by original cancer type, they found that risk was increased by 1.5-fold to more than 10-fold for 22 of the 23 solid cancer types investigated (all except colon cancer).

These findings expand the groups of survivors at risk of tMDS/AML following treatment with chemotherapy because, in the past, excess risks were established only after chemotherapy for cancers of the lung, ovary, breast, soft tissue, testis, and brain/central nervous system. In the present analysis, cumulative incidence of tMDS/AML was less than 1 percent at 10 years after chemotherapy for most solid cancer types. However, prognosis following tMDS/AML diagnosis was very poor.

Because information on the specific chemotherapy agents was not available in the SEER registry data, the researchers used the SEER-Medicare linked database to examine the patterns of use of specific chemotherapy agents during the same time period. Among 165,000 patients in the SEER-Medicare database who received initial chemotherapy for a first primary solid cancer during the study period, 2000-2013, there was a substantial rise in use of platinum-based chemotherapy agents, from 57 percent of patients in 2000-2001, to 81 percent of patients in 2012-2013. Platinum-based chemotherapy agents are known to increase risk of tMDS/AML.

"The most important message from this study is that, while advances in cancer treatment approaches have improved the prognosis for many types of cancer, the number of patients at risk of developing rare, therapy-related leukemia after cancer chemotherapy in the modern treatment era has markedly expanded," Dr. Morton said. "Assessments of treatment risks and benefits should balance these risks and other adverse effects of chemotherapy against potential gains in survival following treatment for the initial solid cancer."

The researchers wrote that their study shows that continued efforts to minimize exposure to leukemia-causing chemotherapy agents and to develop effective and less toxic chemotherapeutic approaches are critical going forward.

More information: *JAMA Oncology* (2018). DOI: 10.1001/jamaoncol.2018.5625