How does COVID-19 affect patients with cancer? Largest U.S. study shares first results

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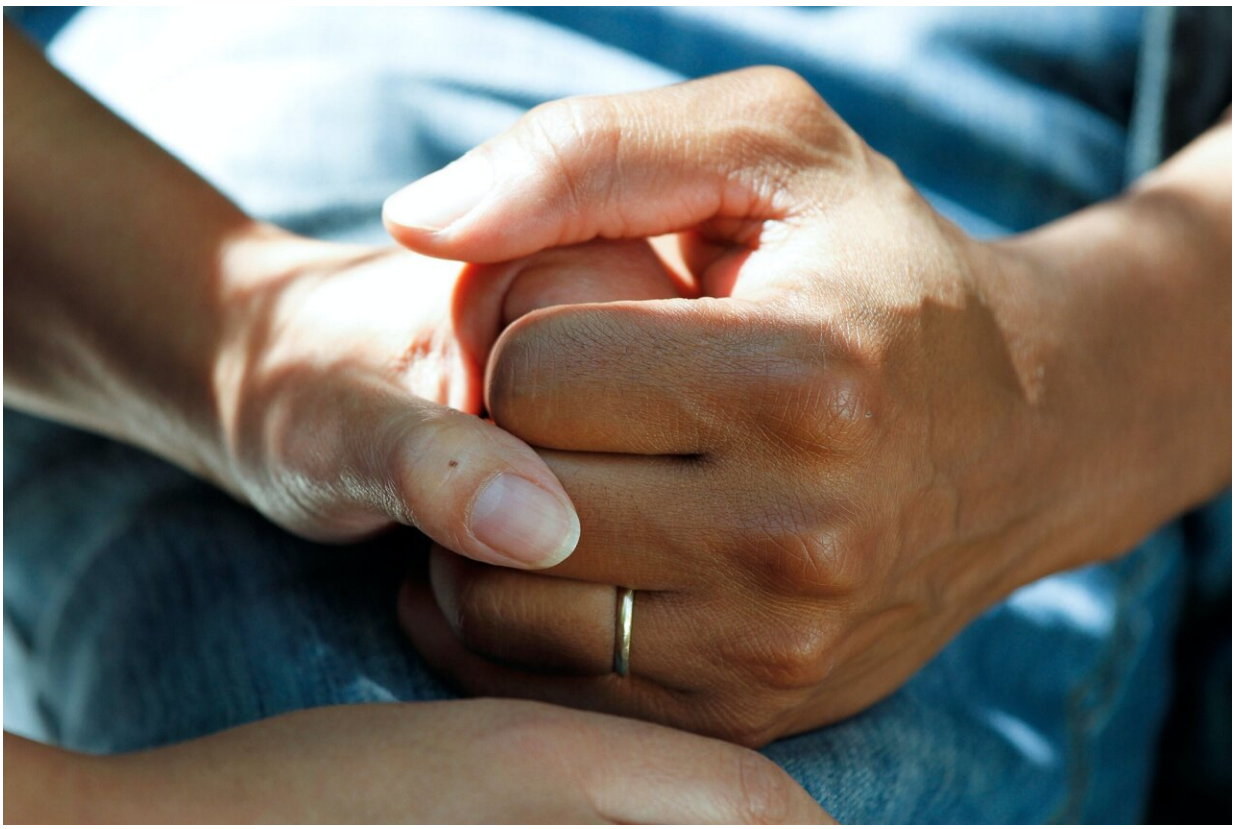

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In the largest study of its kind to date, researchers analyzing national data from more than 63,000 patients with cancer and a positive COVID-19

diagnosis report an increased risk of death among those who were older, male, had a higher number of comorbidities, and had hematologic cancers and recent chemotherapy treatments.

These findings were shared in an oral presentation June 4 at the annual meeting of the American Society of Clinical Oncology by University of Alabama at Birmingham Assistant Professor Noha Sharafeldin, MBBCh, Ph.D. Sharafeldin is a medical doctor and epidemiologist in the Division of Hematology and Oncology and member of UAB's Institute for Cancer Outcomes and Survivorship and the O'Neal Comprehensive Cancer Center.

A more detailed journal article was published simultaneously in the society's *Journal of Clinical Oncology*.

The results are one of the first major publications from the National COVID Cohort Collaborative, known as N3C. UAB and 54 other clinical institutions nationwide have contributed de-identified electronic health record data from 6.2 million patients from 49 states to a secure, cloud-based database to enable first-of-its-kind research. The N3C began curating data in January 2020, and its database contains patient records dating back to 2018. Among the 6 billion rows of data collected are more than 2 million positive COVID diagnoses and more than 400,000 patients with a cancer diagnosis.

'A scale that has not been possible before'

"People in the cancer world are very eager to get more information about the effects of COVID-19 in general and the interaction with specific cancer types and cancer treatments," Sharafeldin said.

Previous studies in relatively small cohorts have found variation in risk for patients with cancer.

"The N3C contains a huge amount of data that has allowed us to investigate these questions at a scale that has not been possible before, using real-world clinical data," Sharafeldin said. "The strength of this first report is that it demonstrates the utility of resources like N3C and the collaborative research that has made it possible. There are other cancer/COVID patient cohorts out there, but nothing the size of N3C, or with the same level of representation of patients from across the country."

From its founding, N3C leadership has encouraged researchers interested in COVID-19's effects on particular health conditions to form clinical domain teams. Along with Umit Topaloglu, Ph.D., an informatician from Wake Forest University, and Benjamin Bates, M.D., a clinician at Rutgers University, Sharafeldin is co-leading the N3C Oncology Domain Team.

"We started by simply investigating the feasibility of answering these questions we had about COVID's effects on patients with cancer using N3C's data resources," Sharafeldin said. "As we went along, the oncology domain team started expanding to include biostatisticians, bioinformatics and analysis experts, and researchers in machine learning and other advanced applications, as well as clinicians—all under the umbrella of being interested in cancer."

No. 1 question: Can it be done?

One of the strengths of N3C has been its harmonization of data from a wide range of different electronic medical records systems and hospital databases. Sharafeldin and the Oncology Domain Team first had to create their cancer cohort from the mass of data by defining terms and making sense of diagnostic codes and diagnosis timelines.

"You could have a patient who was just diagnosed, or one who had been

diagnosed many years before and was a survivor," Sharafeldin said. "They could be in remission or receiving end-of-life care."

There have been a lot of challenges handling real-world data that researchers needed to navigate, including identifying the primary site of a patient's cancer and defining categories of cancer treatment.

"We have many questions, but we thought the No. 1 question to answer first was whether we could curate and describe a cancer cohort and examine mortality risk in our cohort," Sharafeldin said. "Cancer patients are already a vulnerable population; we wanted to identify factors that put these patients at increased risk."

In her presentation and the accompanying manuscript, the Oncology Domain Team shared findings on those risk factors.

Study findings

From a total of 398,579 adult patients with cancer identified in the N3C cohort, 63,413 (15.9 percent) were diagnosed as COVID-positive. The most common represented cancers were skin (13.8 percent), breast (13.7 percent), prostate (10.6 percent), hematologic (10.5 percent) and GI cancers (10 percent). COVID-19 positivity was significantly associated with increased risk of all-cause mortality. Among COVID-positive patients, several characteristics were associated with an increased risk of all-cause mortality:

- age 65 or older
- male gender
- residents of the Southern or Western United States
- adjusted Charlson Comorbidity Index score of 4 or greater
- patients with hematologic malignancies
- patients with multi-tumor sites

- patients who had recent (within 30 days) chemotherapy treatment

"Age, male sex and increasing comorbidities have been found to be important risk factors for the population in general, and that stayed consistent in our cohort as well," Sharafeldin said.

Consistent with previous literature (including this June 2020 paper in *The Lancet* and this February 2021 paper in *Annals of Oncology*), patients with hematological malignancies had higher mortality, while the N3C dataset confirmed that "patients who received recent immunotherapies or targeted therapies did not have higher risk of overall mortality," Sharafeldin and her co-authors wrote in their *Journal of Clinical Oncology* manuscript.

Going forward, the researchers aim to dig deeper into the data to "provide further insights into the effects of COVID-19 including effects of vaccinations on cancer outcomes and the ability to continue specific cancer treatments," they wrote.

"We want to look deeper in patient records and take a more nuanced look at treatments," Sharafeldin explained. "Future studies of the cohort will provide insights into the evolving effect of COVID-19 on patients with cancer and guide clinical management."

'People interested in every aspect'

The long-distance collaborations and rapid time frame for the work have been tiring at times, Sharafeldin says, but also invigorating.

"It has been very collaborative and enjoyable and open," she said, noting that the team includes everyone from full professors to graduate trainees. "Generally, you need to know someone, to have connections and mentors and a healthy network to get access to this type of data and be successful.

With N3C, you just have to be willing to share your skills."

Sharafeldin encourages other scientists, whatever their expertise, to visit the N3C website and engage with others around their area of interest. "There is a large diversity in the N3C domain teams covering a wide range of clinical interests," Sharafeldin said.

The recognition at ASCO and publication in a top-tier journal are some of the highest-profile results from N3C so far, which has everyone involved in the project excited, Sharafeldin says.

"So many people have volunteered their time and worked on this," Sharafeldin said. In addition to researchers and clinicians, there are specialists in programming and data analysis and database architecture from private companies and institutes.

"Within every domain team, there are logic and data liaisons from N3C and experts in how the cohort is being created to help us navigate and provide consistent support, in addition to a knowledge store where researchers are sharing workflows and technical help," she said.

"The beauty of N3C is that it's this really open environment, and if you are willing to lend your time and expertise, you can make a real difference," Sharafeldin said. "Throughout this pandemic, everyone has wanted to contribute and help. Once you get an opportunity to do that, it's very exciting."

More information: Noha Sharafeldin et al, Outcomes of COVID-19 in Patients With Cancer: Report From the National COVID Cohort Collaborative (N3C), *Journal of Clinical Oncology* (2021). DOI: 10.1200/JCO.21.01074

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