Personalized Blood Test Can Detect Colon Cancer Recurrence Sooner Than Scans

Tests for circulating tumor DNA can help predict which patients are more likely to relapse.

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A personalized liquid biopsy test that detects circulating tumor DNA (ctDNA) in the blood can help identify which colorectal cancer patients are more likely to relapse after surgery, according to research presented at the virtual American Society of Clinical Oncology Gastrointestinal Cancers Symposium.

The “tumor-informed” blood test, known as Signatera, detected molecular residual disease, or evidence of remaining cancer, eight months before CT scans showed recurrence. Detecting residual cancer early could help doctors tailor treatment after surgery.

Tenna Henriksen, a PhD candidate at Aarhus University in Denmark, and colleagues conducted a study to determine whether repeated ctDNA testing after surgery could identify colorectal cancer patients at high risk for recurrence, assess the effectiveness of adjuvant (post-surgery) chemotherapy and detect relapse sooner than radiological imaging.

Around 20% to 30% of people with colorectal cancer relapse after surgery, and earlier detection of recurrence could increase the proportion of patients able to receive curative treatment, leading to improved survival, Henriksen noted as background.

The study included 260 people with Stage I to III colorectal cancer, the largest cohort yet assessed using ctDNA testing. All participants underwent surgery to remove their tumors, and nearly two thirds (165) then received adjuvant chemotherapy; 48 (18%) eventually relapsed.

The patients’ tumor DNA was sequenced to identify mutations, and a customized Signatera ctDNA test was designed to track tumor-specific mutations in each patient’s blood samples over time.

Unlike a standard liquid biopsy test, Signatera is not intended to match patients with a particular therapy, but rather it is used to detect and quantify how much cancer is left in the body, detect recurrence earlier and help optimize treatment decisions, according to test manufacturer Natera. In addition to colorectal cancer, the test has also been clinically validated for non-small-cell lung

cancer, breast cancer and bladder cancer.

The researchers collected blood samples at various time points—before and after surgery and every three months thereafter—over a median follow-up period of about 30 months. CT scans were done at one year and three years after surgery.

Post-surgery ctDNA status was assessed for 218 people prior to adjuvant chemotherapy. Twenty people were found to have molecular residual disease (MRD) according to the test. Within this subgroup, 15 people (75%) relapsed. In contrast, just 14% of the 198 people found to be MRD negative experienced recurrence.

Among the subset of patients who received adjuvant chemotherapy, 83% of those who tested MRD positive on the ctDNA test experienced recurrence, compared with 13% of those with MRD negative tests.

People with detectable ctDNA immediately after surgery had a high risk of recurrence, Henriksen said. After that, the risk increased over time in patients who tested MRD positive (reaching 89%) but decreased in those who tested MRD negative (falling to 3%). However, with more follow-up time, some people who initially tested MRD negative later became MRD positive.

Results from the ctDNA tests were compared against those from a more frequently used test for a tumor biomarker known as carcinoembryonic antigen (CEA). While testing positive for ctDNA right after surgery was significantly associated with reduction in relapse-free survival, this was not the case for a positive CEA test. Over time, repeated ctDNA testing predicted recurrence better than repeated CEA tests. What's more, ctDNA monitoring detected MRD a median of 8.1 months before recurrence was seen on a scan.

Based on these findings, the researchers concluded that ctDNA analysis can predict the risk of colon cancer recurrence and is a more reliable biomarker for treatment response monitoring. The study also showed that post-surgery chemotherapy can cure some MRD positive patients.

Another research team conducted a related study in which 122 people with Stage II or III colorectal cancer were monitored before and after surgery using the Signatera ctDNA test. Again, patients who tested MRD positive after surgery had a significantly higher relapse rate than those who were MRD negative.

"Through this study, we are able to demonstrate that serial ctDNA testing can detect molecular residual disease a median of eight months ahead of clinical relapse, with significant potential to improve patient care," Claus Lindbjerg Andersen, PhD, of Aarhus University, the senior author of the Danish study, said in a Natera press release.

Two larger clinical trials are underway to further assess the Signatera test for people with colorectal cancer. In the IMPROVE-IT study, people with Stage I or low-risk Stage II cancer who test MRD positive will receive adjuvant chemotherapy and those who test MRD negative will not. In IMPROVE-IT2, patients who test MRD positive will undergo more frequent radiological imaging and

receive intensified treatment.

Click here to read the study abstract.

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