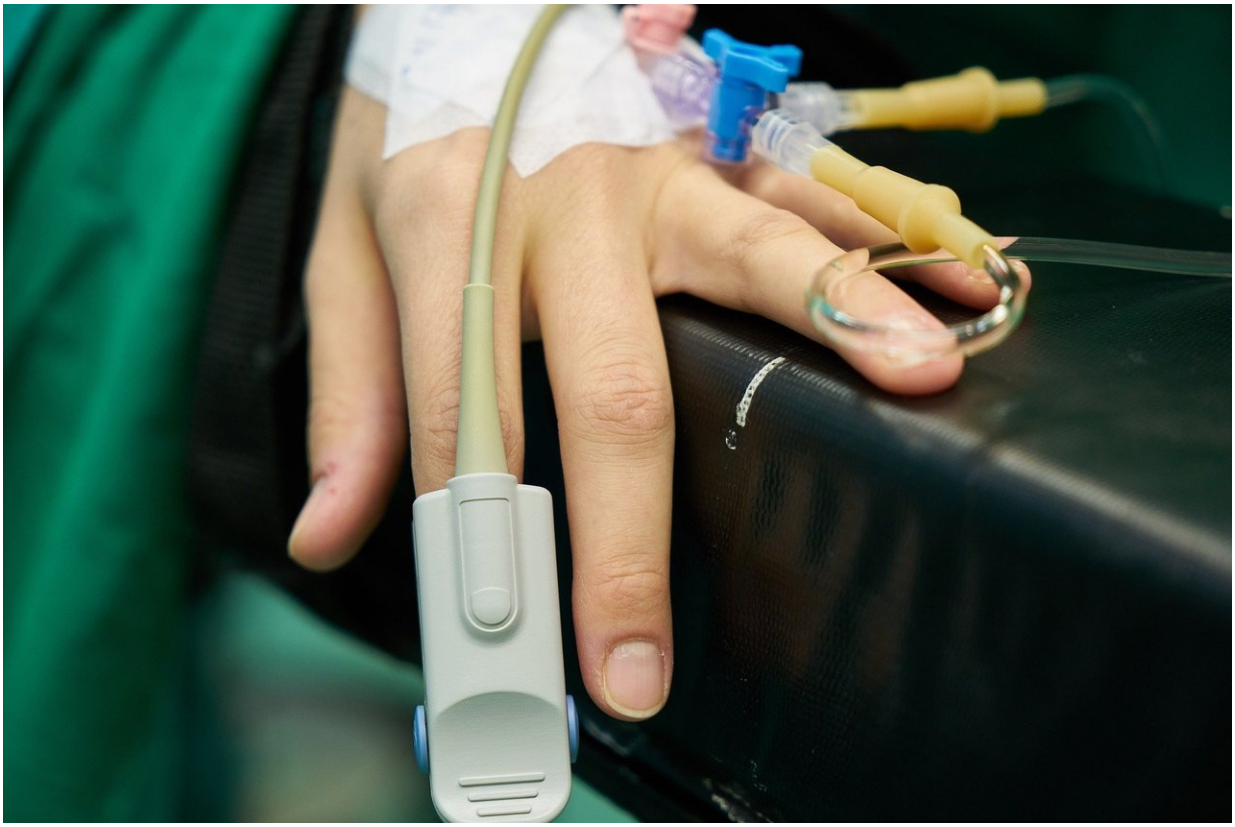
Accurately diagnosing genetic disease prevents cancer, saves lives

March 29 2018



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A single, upfront genomic test is more effective for detecting Lynch syndrome in colorectal cancer (CRC) patients than the traditional multiple, sequential testing approach, according to new clinical data

reported by The Ohio State University Comprehensive Cancer Center - Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC - James).

Researchers say offering this type of advanced genetic testing at the time of diagnosis could help guide and expedite treatment decisions for many patients who have CRC while simultaneously identifying the patients who are likely to have Lynch syndrome. This cancer-causing condition occurs when a person inherits a mutation in one of the DNA repair genes. Individuals with Lynch syndrome are much more likely to develop CRC, uterine, ovarian, stomach or other cancers than the general population.

For this study, researchers wanted to know if an upfront tumor-sequencing approach using a single test that screens for multiple mutations could replace the current multi-test screening approach commonly used to determine if a patient has Lynch syndrome.

To do this, researchers analyzed tumor samples from 419 CRC patients who participated in the Ohio Colorectal Cancer Prevention Initiative (OCCPI), a statewide research study to screen newly diagnosed CRC patients and their biological relatives for Lynch syndrome.

All OCCPI study participants had their tumor samples analyzed using the traditional multi-test genetic testing approach and the single, upfront genomic tumor-sequencing test approach in which a single tumor sample was analyzed for multiple mutations simultaneously.

Researchers compared results from the two screening methods and found that the upfront tumor-sequencing approach was more sensitive and more specific for detecting Lynch syndrome than the old, multiple-test model. Tumor sequencing resulted in a 10-percent improvement in Lynch syndrome detection rates while also providing important

information about treatment options for the patients.

They report their findings in the March 29, 2018, issue of the medical journal *JAMA Oncology*.

"Testing methods of the past would just point to a suspicion of Lynch syndrome, but they could not confirm the diagnosis without multiple additional tests, which slows down the diagnostic process and adds costs," says Heather Hampel, MS, CGC, corresponding author of the study and principal investigator of OCCPI. "This new approach points to the exact mutation patients were born with and does so through a single test. The mutation will need to be confirmed using a blood test but this requires a single mutation test which is less expensive than multi-gene panel testing. The previous method could sometimes require patients to get up to five individual tests before knowing if they had Lynch syndrome."

The study also showed the test had some unanticipated benefits. For example, eight patients (1.7%) with DYPD mutations were identified. Patients with this mutation are prone to severe toxic reactions to 5-FU chemotherapy, the most common chemotherapy used to treat CRC. Another eight patients were found to have mutations in different hereditary cancer susceptibility genes which is important information for the patient and their family members.

"Knowing this type of information ahead of time might be useful for oncologists who can select another drug or use lower doses to avoid these bad reactions. In addition, this test can also identify other potential hereditary cancer syndromes by looking at other known cancer susceptibility genes at the same time," said Hampel.

It was already known that upfront tumor testing could be used to accurately test for mutations in the three genes (BRAF, KRAS, and

NRAS) that help determine treatment options for patients with advanced stage colorectal cancer; using this same test to determine Lynch syndrome status is a new discovery.

Researchers say this is a step toward integrating upfront tumor testing as part of the standard of care for all CRC patients instead of reserving this testing for advanced-stage patients for whom standard therapies are not working.

"While this new test is more expensive, it will eliminate many other tests for a subset of patients so that it may be more cost-effective overall. If it is not now, it will certainly be in the future as the costs of tumor sequencing continue to decline," adds Hampel.

However, formal cost analysis studies will be necessary to determine if this is a cost-effective approach.

Provided by The Ohio State University Comprehensive Cancer Center