Blood test can predict prognosis in deadly brain cancer

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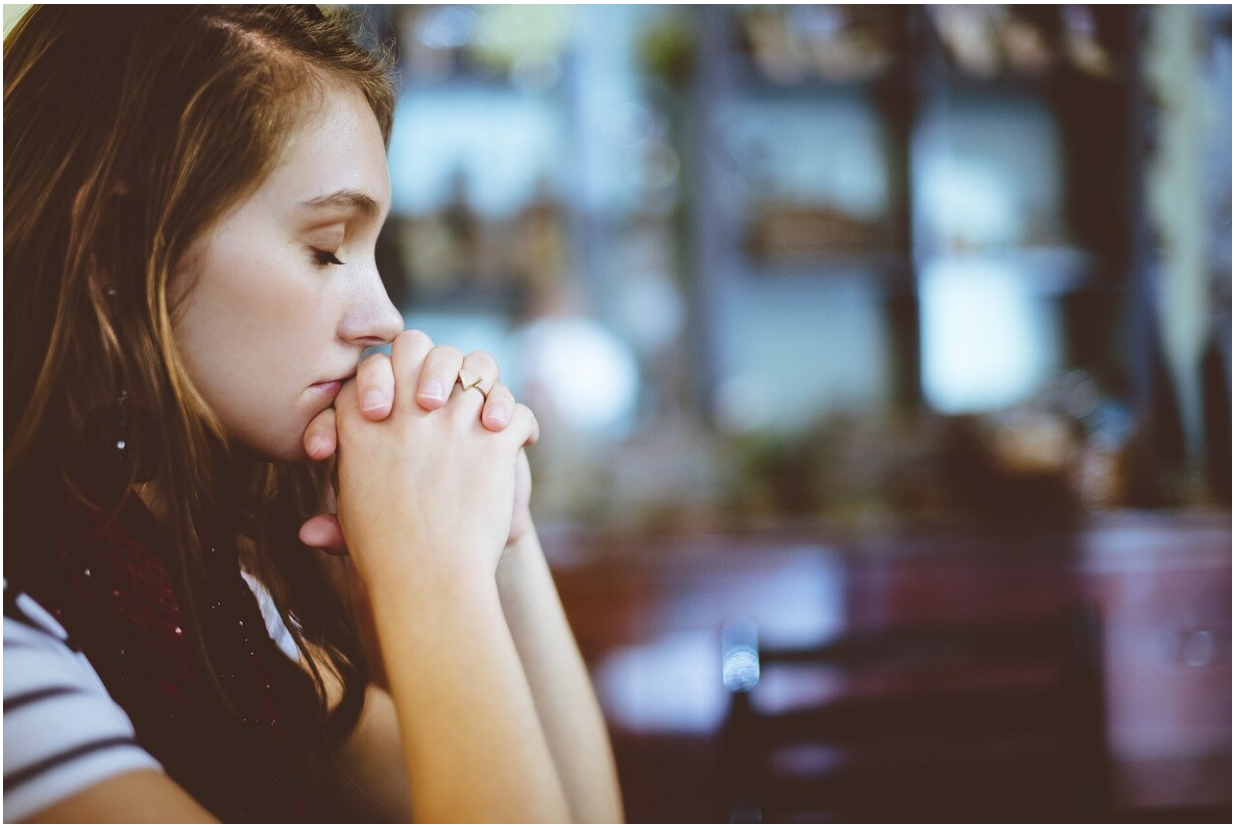

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A blood test that measures the amount of cell-free DNA (cfDNA) in the bloodstream—called a liquid biopsy—correlates with how patients will progress after they are diagnosed with glioblastoma (GBM), the deadliest

and most common primary brain tumor in adults. In a new study, researchers from the Abramson Cancer Center of the University of Pennsylvania are the first to show that patients with a higher concentration of cfDNA—circulating DNA that cancer and other cells shed into the blood—have a shorter progression-free survival than patients with less cfDNA, and that cfDNA spikes in patients either at the time of or just before their disease progresses. The team also compared genetic sequencing of solid tissue biopsies in GBM side-by-side with the liquid biopsies and found that while both biopsies detected genetic mutations in more than half of patients, none of those mutations overlapped, meaning liquid biopsy may provide complementary information about the molecular or genetic makeup of each tumor. *Clinical Cancer Research*, a journal of the American Association for Cancer Research, published the findings today.

"Doctors have begun using liquid biopsies more frequently to monitor certain cancers—particularly lung cancer—in recent years as research has shown their effectiveness in other disease sites. But until now, there has been little focus on the clinical utility of liquid biopsy in brain tumors," said the study's senior author Erica L. Carpenter, MBA, Ph.D., director of the Liquid Biopsy Laboratory and a research assistant professor of Medicine at Penn.

The findings may eventually prove impactful for GBM patients. The disease is particularly aggressive, and while most estimates show there are around 11,000 new cases each year, the five-year survival rate is between five and 10 percent. One of the challenges in treating GBM is that monitoring imaging can be an inaccurate way to detect disease progression. Moreover, the tumors themselves are usually heterogeneous—meaning that different parts of the tumor contain different genetic mutations—which means treatments focused on only one target are ineffective or only partially effective. Another problem is that trying to track these mutations over time can be difficult, since

getting a new tissue sample requires a repeat brain surgery. While most patients do have their tumors surgically removed after initial diagnosis, additional procedures to monitor their disease over the course of treatment can be difficult and are invasive for patients. These issues are especially difficult in patients who experience a recurrence, since when GBM comes back, it often returns with a vastly different genetic makeup.

"If our findings are validated by further studies, it would mean that these patients may be able to get a simple blood test that would give us a more accurate assessment than imaging of whether their disease has progressed or not, as well as more data on the mutations in their tumors," said the study's lead author Stephen J. Bagley, MD, MSCE, an assistant professor of Hematology-Oncology in Penn's Perelman School of Medicine.

This study included 42 patients with newly diagnosed GBM. They had blood tests at diagnosis, before surgery, and at regular intervals throughout their standard of care chemotherapy and radiation. The 28 patients with a lower concentration of cfDNA pre-surgery—defined as cfDNA that was below the average of the total group—had almost double the progression free survival (median 9.5 months) compared with the 14 patients with higher concentrations (median 4.9 months). In a sub-analysis of 20 patients, liquid biopsy detected at least one mutation in 11 patients, and all of those mutations were different than what was detected in analysis of each patient's solid tumor biopsy.

The authors say the detection of additional mutations is especially exciting, since effective therapy for GBM will ultimately require combination therapies due to the heterogeneity of the tumor.

"If liquid biopsy can give us a more comprehensive view of the molecular profile of the tumor, we can potentially pick more effective

combinations for each patient," Bagley said.

The authors say this work is more hypothesis-generating than practice-changing at this point since the cohort of patients is relatively small. However, they've continued to enroll patients and plan to perform a larger analysis in the future. They also plan to perform tumor DNA sequencing on multiple different samples of the resected tumors of each patient to learn about the full molecular profile of each.

More information: Stephen Bagley et al. Clinical utility of plasma cell-free DNA in adult patients with newly diagnosed glioblastoma - a pilot prospective study, *Clinical Cancer Research* (2019). DOI: 10.1158/1078-0432.CCR-19-2533

Provided by Perelman School of Medicine at the University of Pennsylvania

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