

# Researchers ID blood protein that sheds light on common, post-operative complication

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Delirium, a common syndrome among older adults, particularly in those who have recently undergone surgery, critically ill patients in the ICU, and in older patients with multiple health issues, is a form of acute confusion that is characterized by poor attention, disorientation, impaired memory, delusions, and abrupt changes in mood and behavior. Moreover, patients who experience delirium are at increased risk of long term cognitive decline. Recently, clinicians and scientists have recognized that delirium is one of the first signs of COVID-19 infection in older patients and that it occurs frequently in patients with severe COVID-19 disease.

In a new study led by an interdisciplinary team of gerontologists, geriatricians, precision medicine experts, and bioinformaticians at Beth Israel Deaconess Medical Center (BIDMC), researchers identified a single protein present in the blood that is associated with increased risk of post-operative delirium. The finding, published in the *Journal of Gerontology: Medical Sciences*, sheds light on a potential pathophysiological mechanism underlying delirium and paves the way for a non-invasive, cost-effective test to guide prediction, diagnosis and monitoring of delirium. While further study is needed, pre-operative blood tests for these proteins could help physicians determine which patients are at higher risk for developing delirium.

"Delirium is associated with more complications, longer hospitalizations, increased risk of long-term cognitive decline, dementia and mortality, and costs the U.S. healthcare system an estimated \$182 billion each

year," said first author Sarinnapha Vasunilashorn, Ph.D., Assistant Professor of Medicine at BIDMC and Harvard Medical School (HMS).

"Despite its pervasiveness, delirium remains a clinical diagnosis with no established tests to diagnose the condition," said co-senior author Towia Libermann, Ph.D., Director of the BIDMC Genomics, Proteomics, Bioinformatics and Systems Biology Center. "The discovery of a reliable biomarker could change that."

Vasunilashorn, also a member of the Department of Epidemiology at the Harvard T.H. Chan School of Public Health, and colleagues used a cutting edge proteomics platform, SOMAScan—a large-scale quantitative analysis of the expression levels of proteins—to evaluate proteins present in the blood from a patient cohort called SAGES (Successful Aging after Elective Surgery). Sponsored by the National Institute on Aging, SAGES follows 560 noncardiac surgical patients ages 70 and older with the goal of identifying novel biomarkers of delirium and its associated long-term cognitive outcomes.

"SAGES participants have been very generous with their time, participating in interviews to test their memory and thinking, and also donate small amounts of blood, before and immediately after their major elective surgery," said co-senior author Edward Marcantonio, MD, Section Chief for Research in the Division of General Medicine at BIDMC and Professor of Medicine at HMS. "We are now analyzing this stored blood with novel techniques, such as SOMAScan, to understand the biological basis of delirium, an incredibly challenging clinical problem."

The researchers' analysis of more than 1,300 proteins revealed a single protein (known as chitinase-3-like-protein-1, or CHI3L1/YKL-40) that was present at higher concentrations in the blood both before and after surgery in patients who experienced delirium as compared with patients

who did not develop postoperative delirium. This protein—itsself linked to aging and age-related conditions including Alzheimer's disease—plays a critical role in the body's type 2 [immune response](#).

The team also found that patients who had high pre-operative levels of the protein CHI3L1/YKL-40 combined with high post-operative levels of an immune-related protein called interleukin-6 (or IL-6) were at increased risk of delirium.

"Our study specifically highlights the involvement of this highly specific immune activating [protein](#) in postoperative delirium, which may also play a role in COVID-19 associated delirium," said Libermann, who is also an Associate Professor of Medicine at Harvard Medical School. "In addition to providing a promising candidate for a delirium biomarker, our findings suggest a possible link between [delirium](#), aging and Alzheimer's disease."

**More information:** Sarinnapha M Vasunilashorn et al, Proteome-Wide Analysis using SOMAscan Identifies and Validates Chitinase-3-Like Protein 1 as a Risk and Disease Marker of Delirium Among Older Adults Undergoing Major Elective Surgery, *The Journals of Gerontology: Series A* (2021). [DOI: 10.1093/gerona/glaa326](https://doi.org/10.1093/gerona/glaa326)

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