

Blood analyses may predict risk of delirium in older surgical patients

6 May 2016

Delirium, or sudden severe confusion due to rapid changes in brain function that can occur with physical or mental illness, affects 15% to 53% of older surgical patients. New research led by investigators at Beth Israel Deaconess Medical Center (BIDMC) may now help clinicians assess an individual patient's risk of developing post-operative delirium, enabling preventive measures to safeguard their health. Published online today in the journal *Biological Psychiatry*, the research also provides insights into the potential mechanisms involved in the development of delirium, which could lead to new therapeutic strategies.

Delirium in older surgical patients has been linked with longer hospital stays, greater postoperative complications, and higher rates of discharge to nursing homes. In the United States, health care costs attributable to [delirium](#) are upwards of \$164 billion annually, yet there are no established biological markers to guide the diagnosis or management of the condition.

To look for potential blood-based markers of delirium, a team led by senior investigators Towia Libermann, PhD and Edward Marcantonio, MD, SM, both of BIDMC, screened plasma from adults without dementia aged 70 and older undergoing major non-cardiac surgery using data from the Successful Aging after Elective Surgery Study. Of the 566 patients enrolled, 24 percent experienced delirium. Plasma was collected at four time points: preoperatively (PREOP), in the postanesthesia care unit (PACU), on postoperative day 2 (POD2) and at a 1-month follow-up appointment (PO1MO).

High levels of a protein called C-reactive protein (CRP), which has been linked to inflammation and infection, emerged from an analysis of more than 100 proteins as being strongly linked to delirium. Compared with patients without delirium, those with delirium had significantly higher plasma CRP levels at PREOP, PACU, and POD2, but not at PO1MO.

Although the relationship between CRP and delirium has been previously reported, this study is the first to document and analyze CRP levels before onset of symptoms.

"Our findings demonstrate that, in patients who go on to develop delirium, CRP levels in blood are slightly increased before surgery and further increase after surgery relative to patients who do not develop delirium," said Libermann, who is Director of the Genomics, Proteomics, Bioinformatics and Systems Biology Center at BIDMC and Associate Professor of Medicine at Harvard Medical School (HMS). Further, he noted that increased plasma CRP levels are linked to various clinical conditions, which means that CRP is not a highly specific marker for delirium. To identify more selective delirium markers, the investigators are planning to expand their search to include metabolites, lipids and less abundant proteins in the blood. "We anticipate that the most specific delirium biomarkers will be found at very low concentrations and not among the most common proteins," Libermann explained.

Uncovering such markers may provide clues regarding the mechanisms that underlie the development of delirium. "We speculate that, despite the heterogeneity of patients and delirium, common mechanisms are shared by all patients developing postoperative delirium and that a pre-inflammatory state as reflected by slightly increased levels of CRP even before surgery predisposes patients to a more pronounced inflammatory response upon surgery that increases the likelihood of delirium," said Libermann.

"From a clinical standpoint, our findings suggest that CRP could be used to risk stratify patients before surgery, enabling proactive interventions that target patients at risk for developing postoperative delirium," said Sarinnapha Vasunilashorn, PhD, co-lead author and postdoctoral fellow in the Division of General

Medicine at Primary Care at BIDMC and HMS.

Marcantonio, a board-certified geriatrician who is Section Chief for Research in the Division of General Medicine and Primary Care at BIDMC and Professor of Medicine at HMS, added, "This is a great example of translational research using the combined efforts of a top-notch patient-oriented research team and the innovative laboratory expertise of Dr. Libermann and co-lead author Dr. Simon Dillon to make an important discovery that will ultimately have a positive impact on how we care for [patients](#)."

Provided by Beth Israel Deaconess Medical Center

APA citation: Blood analyses may predict risk of delirium in older surgical patients (2016, May 6) retrieved 20 November 2022 from <https://medicalxpress.com/news/2016-05-blood-analyses-delirium-older-surgical.html>

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