

## JAMA Insights

## Cognitive Decline Associated With Anesthesia and Surgery in Older Patients

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**In the last decade**, the population aged 65 years and older increased by 34.2% in the US and now accounts for a disproportionate number of surgical procedures requiring anesthesia. Among these patients, aging causes a number of changes in the brain that may contribute to decreased cognitive reserve, susceptibility to the stresses of surgery and anesthesia, and increased risk of neurologic injury such as postoperative neurocognitive disorders (PNDs).<sup>1</sup>

*Postoperative neurocognitive disorders* is an overarching term that includes postoperative delirium, an acute state of confusion and inattention; and postoperative cognitive dysfunction (POCD), a prolonged state of cognitive impairment that predominantly affects higher-level cognitive skills and memory. Delirium and POCD previously were considered distinct entities, but recent data suggest an underlying relationship between them for the patient whose brain may be vulnerable to cognitive decline after the stressors of surgery and anesthesia. Proposed potential mechanisms for postoperative neurocognitive decline are speculative but include neuroinflammation as a result of perioperative stress, vascular disorders, or the acceleration of neurocognitive decline in patients with a previously undiagnosed neurodegenerative disorder, such as preclinical dementia. According to a study of patients who underwent noncardiac surgery, covert stroke occurred in 7% of 1114 older patients ( $\geq 65$  years) after surgery and was associated with an increased risk of postoperative delirium and long-term cognitive deficits.<sup>2</sup>

Among patients aged 65 years and older, up to an estimated 65% experience delirium and 10% develop long-term cognitive decline after noncardiac surgery.<sup>1</sup> Complications associated with delirium include longer hospitalization, more days with mechanical ventilation, and functional decline. After discharge from the hospital, patients who develop postoperative delirium are at increased risk of worsening functional and psychological health, progressive cognitive decline, dementia, and death. Although not as extensively studied as delirium, POCD is associated with a decrease in quality of life, loss of function, and increased mortality.

### Perioperative Care

Postoperative neurocognitive disorders develop through a complex interaction between a patient's baseline vulnerability and other risk factors.<sup>1</sup> Commonly cited nonmodifiable risk factors for PNDs include age; compromised higher-level cognitive skills; procedure characteristics such as invasiveness, duration, and urgency; and postoperative admission to an intensive care unit. The presence of these risk factors should trigger a detailed evaluation of the patient and a thorough conversation with the patient, their family or caregivers, and the perioperative team. Before the patient undergoes elective surgery, clinicians should perform a full health assessment to address and optimize modifiable risk factors for PNDs. Preoperative modifiable risk factors represent a spectrum of risks often associated with but not necessarily causative of PNDs. Moreover, the relationship between the duration of an intervention to ameliorate risk and its clinical influence is largely unknown. However, multicomponent targeted reduction of preoperative risk is recommended because most of these interventions will at least benefit the overall health of the patient.

Although there are no compelling medical, pharmacologic, or intraoperative interventions, patient-specific prehabilitation programs and care pathways could limit both the incidence and severity of PND.<sup>3</sup> Among patients aged 65 years and older, avoiding medications such as benzodiazepines, centrally acting cholinergics, meperidine, phenothiazines, and antipsychotics during the perioperative period decreases the risk of cognitive changes.

Adopting preoperative recommendations for healthy lifestyles, such as the World Health Organization guidelines for risk reduction of cognitive decline and dementia, is a reasonable strategy for increasing the resilience of patients to the stresses of surgery and anesthesia. The strongest recommendations focus on physical activity, tobacco cessation, nutrition, and management of hypertension and diabetes. Incorporating the fundamentals of prehabilitation into even more comprehensive systems of care that implement targeted, multicomponent, evidence-based methods such as the Hospital Elder Life Program is a robust approach to decrease risk. In a 2019 study,<sup>4</sup> 3 universal protocols (orientation, cognitive stimulation, and mobilization) were implemented along with targeted protocols based on specific risk factors for each patient. Among 281 patients older than 70 years, this tailored, family-involved program reduced postoperative delirium, with rates of 19.4% in the control group vs 2.6% in the intervention group. Moreover, physical and cognitive function was improved in the intervention group compared with the control group at 30 days after discharge.<sup>4</sup> Another targeted prehabilitation study in which 699 older adult participants ( $\geq 60$  years) used preoperative cognitive exercises targeting memory, speed, attention, flexibility, and problem-solving functions resulted in decreased delirium incidence, with rates of 13.2% in the intervention group vs 23.0% in the control group.<sup>5</sup>

In recognition of the distinct care needs of older surgical patients, several organizations, including the American College of Surgeons National Surgical Quality Improvement Program, American Geriatrics Society, and European Society of Anaesthesiology and Intensive Care, have published guidelines that recommend specific practices for perioperative care of older adults. Despite the evidence that supports these recommendations, there is a gap in their integration into pathways of care for patients. In a study that surveyed 1737 US anesthesiologists, preoperative screening for frailty and dementia, preoperative geriatric consultation, and postoperative screening for delirium were reported for less than 10% of surgical cases.<sup>6</sup> A feasibility study of 61 older patients ( $\geq 60$  years) found that when a cognitive prehabilitation program was prescribed, only 17% completed the training; they reported "feeling overwhelmed" by the activities, having "technical issues" with training, and being overburdened with the time commitment.<sup>7</sup>

In the context of a direct connection between anesthesia and brain health, studies have failed to show a meaningful difference between regional and general anesthesia. Moreover, when anesthetic agents are compared, there is no compelling evidence to suggest that a specific anesthetic agent is indicated or is to be avoided regarding cognitive outcomes after general anesthesia. One area of controversy is the use of a processed electroencephalogram (EEG) monitor to minimize the anesthetic dose during surgery. Although

**Perioperative risk factors and targeted interventions for postoperative neurocognitive disorders****Functional status and baseline frailty score**

Hearing and vision aids made available; exercise programs

**Depression**

Treatment and counseling

**Hypertension**

Cardiac evaluation; appropriate perioperative hemodynamic management

**Sleep disorders**

Optimization of physical environment (eg, sleep hygiene, sleep protocol); treatment of obstructive sleep apnea

**Glycemia**

Perioperative glycemic control; diabetes control

**Alcohol and other substance use/dependence**

Treatment of alcohol and substance use disorders; monitoring for substance withdrawal syndromes

**Medication**

Cessation of nonessential medications; review of essential medications; monitoring for polypharmacy and potential interactions

**Nutritional status**

Perioperative nutritional plan; supplementation if indicated; shortened fluid fast considered, clear liquids encouraged up to 2 h before surgery; dentures made available; resumption of diet as early as feasible

**Perioperative pain**

Directed pain history; ongoing education regarding safe and effective use of institutional treatment options; multimodal, individualized pain control; vigilant dose titration

**Family and social support system**

If concerns, referral to a social worker and/or pastoral care

several studies have been performed, the literature does not give a clear answer about whether the incidence of postoperative neurocognitive decline is affected by anesthesia titrated to an EEG metric. In a meta-analysis published in 2018,<sup>8</sup> MacKenzie et al concluded that the use of EEG-guided anesthetic depth "was associated with a decrease in postoperative delirium." However, in a randomized clinical

trial of 1232 patients published in 2019, Wildes et al<sup>9</sup> concluded "EEG-guided anesthetic administration, compared with usual care, did not decrease the incidence of postoperative delirium."<sup>9</sup> Further investigation is needed, but a prevailing hypothesis may be that there is a subset of cognitively frail patients who are uniquely susceptible to the adverse effects of an anesthetic overdose and might benefit from EEG-guided anesthetic depth.

**Future Concerns**

Anesthesia and surgery are shown to be associated with a modest acceleration in the rate of cognitive decline in older patients. How this acceleration might be magnified in the patient already on a steep trajectory of cognitive decline, such as one with presymptomatic Alzheimer disease and related dementia, is unknown. Some evidence suggests that anesthetics may increase cerebral  $\beta$ -amyloid deposits, a hallmark of Alzheimer disease. A study from 2014 of 24 901 patients aged 50 years and older observed an increase in the incidence of dementia and a reduced interval to dementia diagnosis after anesthesia and surgery.<sup>10</sup> In addition, even though the knowledge base for this clinical scenario is limited, if the association between anesthesia and surgery and acceleration of neurocognitive decline in a patient with a vulnerable brain is real, it does not appear dependent on whether general or regional anesthesia is used, suggesting that care pathways for these patients should be organized around factors such as comorbidities, the underlying condition necessitating surgery, or the inflammatory responses caused by surgery or major illness.

**Conclusions**

Advances in surgery and anesthesia can improve function and quality of life for older patients, but not without potential risk to brain health. Postoperative neurocognitive decline is a meaningful concern to patients and represents a significant and expanding challenge to health care in the US and worldwide. Surgeons and anesthesiologists should assess, discuss, and optimize associated potential risks for each patient before surgery. Best practices and interventions can begin before surgery and extend well into the recovery period. To be most effective, these strategies require family engagement and the involvement of an interdisciplinary health care team and comprehensive systems of care.

**ARTICLE INFORMATION**

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