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Perioperative cognitive trajectory in adults

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Editor's key points

- Postoperative cognitive decline is recognized as a major impact of surgery.
- Cognitive impairment appears to be affected adversely by other postoperative complications, including ongoing pain.
- In the absence of such complications, the elderly can be expected to resume their preoperative cognitive trajectory, and may even experience cognitive improvement if surgery results in alleviation of significant symptoms.

Summary. Approximately a quarter of a billion people undergo surgery every year hoping that the operation will alleviate symptoms, cure diseases, and improve quality-of-life. A concern has arisen that, despite the benefits of surgery, elderly patients might suffer neurological injury from surgery and general anaesthesia leading to persistent cognitive decline. However, many studies of postoperative cognition have had methodological weaknesses, including lack of suitable control groups, dissociation of cognitive outcomes from surgical outcomes, sub-optimal statistical techniques, and absence of longitudinal preoperative cognitive assessments. Emerging evidence suggests that after early cognitive decline, most patients return to their preoperative cognitive trajectories within 3 months of surgery; some even experience subsequent cognitive improvement. In this review, we summarize the scientific literature on perioperative cognition. We propose that the most important determinants of the postoperative cognitive trajectory are the preoperative cognitive trajectory, the success of the surgery, and events in the perioperative period. Postoperative complications, ongoing inflammation, and chronic pain are probably modifiable risk factors for persistent postoperative cognitive decline. When surgery is successful with minimal perioperative physiological perturbations, elderly patients can expect cognition to follow its preoperative course. Furthermore, when surgery alleviates symptoms and enhances quality-of-life, postoperative cognitive improvement is a possible and desirable outcome.

Keywords: anesthesia recovery period; postoperative period, cognition; preoperative period

For the last 60 yr, there has been a strong perception that many elderly patients experience persistent cognitive decline that is directly attributable to surgery and general anaesthesia.[1] Particular surgeries, most notably, cardiac surgery and major orthopaedic surgery, have been associated with persistent postoperative cognitive decline (POCD) in up to 50% of patients.[2 3] Based on limited clinical data[4] and laboratory experimentation,[5–9] it has been hypothesized that surgery and anaesthesia could either accelerate the onset of or even cause dementia.[8] If these concerns regarding persistent POCD were proved to be true, we would face a growing public health problem as an increasing number of elderly patients underwent elective surgeries. Older patients and their families would need to factor in the risk of persistent POCD when deciding whether or not to proceed with elective surgical procedures.

There is strong evidence to suggest that pain and inflammation carry a cognitive burden;[10–15] people who have chronic inflammatory states or unremitting pain may suffer from accelerated cognitive decline.[16–19] Acute postoperative pain and inflammation probably also affect cognition and might exacerbate or cause delirium, which is a well-defined, common, and clinically important postoperative complication.[20–23] Furthermore, with ongoing pain or inflammation, cognition may be impaired for several weeks after surgery,[20 24 25] analogous to the cognitive impairment that occurs after acute medical illnesses. However, recent research suggests that this initial POCD usually resolves within months of surgery.[20 26 27]

The scientific study of POCD has been compromised by the lack of a consensus definition of POCD and by conflicting data regarding its time course and clinical impact. The medical literature in this area is permeated with data from studies with key methodological limitations, highlighted in a recent review,[28] including retrospective designs,[29] unsuitable or lack of non-surgical control groups,[2 3 30] failure to detect pre-existing cognitive impairment,[2 3 30–44] missing information on preoperative cognitive trajectories,[2 3 26 30–44] insufficient long-term follow-up,[31 33 34 43] and suboptimal statistical analyses.[26 45] Interestingly, emerging studies that have addressed some of these limitations have found that when surgery is successful, quality-of-life, functional status, and cognition might all improve in the intermediate term.[11 15 42 46 47] Resolution of pain and inflammation might be important prerequisites for

postoperative cognitive improvement (POCI), which might occur even with older patients as the brain retains neuroplastic potential throughout life.[11 14 48–50] Mounting evidence suggests that for many patients, after transient POCD, intermediate-term cognitive trajectories are likely to be unchanged or even improved compared with preoperative trajectories.[51–53] As such, the authors of this review believe that a paradigm shift regarding postoperative cognition is warranted. We propose that when surgery alleviates symptoms and enhances quality-of-life, POCI is a possible and desirable outcome.

In this review, we shall address whether there is a vulnerable subgroup of patients who might be afflicted with long-lasting cognitive decline and, conversely, whether some patients may exhibit cognitive improvement after recovery from surgery. From the outset it is necessary to qualify that the published literature can be interpreted in various ways, and currently there is a range of views surrounding the clinical relevance of persistent POCD. In the last few years, several clinical review articles and expert commentaries on POCD and postoperative dementia have been published.[27 28 54–63] While consensus on many issues is emerging, some of the emphases and nuances expressed in scientific reviews differ from our opinions. Reading some of these pertinent review articles might help to enrich perspectives on this controversial topic.

Limitations of POCD research

(1) Aging, even during the fifth decade of life, is associated with measurable cognitive decline[64] and an increasing incidence of dementia. The prevalence of Alzheimer's dementia alone in people over 60 is >5%,[65 66] and an estimated one-third of people over 85 have Alzheimer's.[67 68] Thus, any study that follows older people longitudinally will observe cognitive decline and incident dementia. If patients are followed after a surgical event without an age-appropriate control group, cognitive decline, incident dementia, or both might be incorrectly attributed to the surgery (Table 1).[41]

(2) Critical illness after surgery is often associated with multi-organ dysfunction, including neurological impairment.[69] Certain critical care diagnoses have been independently linked to a consequent diagnosis of dementia.[70] When patients suffer a serious postoperative complication, such as pneumonia or acute renal failure, subsequent persistent cognitive decline, or incident dementia might be ascribed to the surgery, whereas the root cause of brain injury might be the pathological processes associated with critical illness.

(3) Underlying comorbidities, such as vascular disease, are associated with cognitive decline and dementia.[27 41 71] Cognitive decline, incident dementia, or both may be wrongly attributed to a surgical event, rather than to other risk factors.[27 41]

(4) A lack of a consensus definition for POCD leads to marked discrepancies in the quoted incidence (e.g. from 5 to 50%) depending on the arbitrary diagnostic criteria that have been used.[3 26] For example, a very liberal criterion that has been used is a standard deviation (SD) decline in any of several administered cognitive tests, regardless of whether or not patients improve in any of the other cognitive tests. With such a permissive definition, it is likely that POCD would be diagnosed purely by chance in about a third of all patients.[72]

(5) Studies often correct for the learning effect of repeat cognitive testing based on measured learning in a 'control' group. However, this assumes that learning in surgical patients is relatively uniform and patients undergoing surgical procedures will learn as effectively as controls in a non-surgical group. It is unlikely that this assumption is appropriate as patients who are preparing for or recovering from surgery are less likely to learn as efficiently as a control group. Correcting for learning based on a non-surgical control group could lead to an over-estimate of the extent or incidence of POCD. This limitation was made salient in a study by Evered and colleagues,[73] which enrolled four cohorts: patients undergoing cardiac surgery, patients undergoing orthopaedic surgery, a control group undergoing coronary angiography, and a second control group not undergoing any procedure. Using the results in the non-procedural control group to correct for learning, this study found that at 3 months the cohort that underwent coronary angiography (i.e. no surgery and no general anaesthesia) had the highest incidence of cognitive decline. These results demonstrate that correcting for learning in a surgical (or procedural) group according to learning in a non-surgical control group could lead to an artificial diagnosis of POCD. Figure 1 illustrates the limitation of previous approaches used to correct for learning. Alternative statistical approaches, like mixed effects models, have been used in studies of POCD and are probably more robust than methods that rely on correction for learning based on a non-procedural control group.[27 29 36]

(6) Preoperative cognitive trajectories are likely to determine postoperative cognitive trajectories. For example, a patient assessed at a single point in time could be on many different cognitive trajectories making a single preoperative test suboptimal for assessing the cognitive trajectory (Fig. 2). There is compelling evidence that patients who have declining trajectories before surgery, such as those who have mild cognitive impairment (MCI) or early dementia, are more likely to decline cognitively after surgery, at least acutely.[20 29 74]

These barriers to POCD research leave us in a quandary regarding the exact nature of POCD. While most researchers would agree that cognitive dysfunction often occurs in the short term following surgery, manifesting either as delirium or a subtler problem, the limitations of many existing studies generate scepticism regarding the hypothesis that persistent POCD is a common occurrence.