

# Postoperative cognitive dysfunction

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## Abstract

Postoperative cognitive dysfunction (POCD) refers to a deterioration in cognition noted to occur after surgery and anesthesia. Recent studies have demonstrated a number of correlates and risk factors for this condition, although much remains to be elucidated in terms of the true incidence, etiology, prevention, and treatment.

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## Introduction and context

Physicians have long recognized that certain patients develop postoperative cognitive dysfunction (POCD) [1], especially after cardiac surgery [2]. Recently, as investigators have begun to examine the incidence of POCD after major non-cardiac, non-carotid, non-neurosurgical procedures, certain risk factors have been identified. Monk and colleagues [3] studied 1064 patients aged 18 years and older before and after non-cardiac surgery and found that POCD was present at hospital discharge in 117 (36.6%) young (18 to 39 years), 112 (30.4%) middle-aged (40 to 59 years), and 138 (41.4%) elderly (60 years and older) patients. The difference in incidence was significant between the age groups themselves and between each age group and 210 age-matched (but not disease-matched) controls. At 3 months after surgery, the presence of POCD, while similar between young and middle-aged patients and age-matched controls, was significantly higher in older patients as compared with older controls ( $P < 0.001$ ).

The independent risk factors for POCD at 3 months identified by Monk and colleagues [3] included older age (perhaps owing to a diminution in cognitive reserve [4]), lower level of education, history of previous cerebrovascular accident without residual impairment, and presence of POCD at hospital discharge. Postoperative delirium and increased use of opioid analgesics correlated with POCD at hospital discharge but not at 3

months. Patients who had POCD were also at increased risk of death in the first year after surgery.

Other risk factors for the development of POCD include major but not minor surgery [5,6], a history of alcohol abuse in older patients [7], and postoperative changes in thyroid hormones [8] as demonstrated by the occurrence of the euthyroid sick syndrome – reduced serum T3 and T4 concentrations without an increase in thyroid-stimulating hormone secretion – within hours after major surgery. Modifications in thyroid hormone functioning may take place as a result of the psychophysical stress caused by surgery and the reduced conversion of T4 into T3 by a liver engaged in the metabolism of anesthetic drugs. As there is a possible association between thyroid abnormalities and Alzheimer disease because of the interrelationship between thyroid hormones and the cholinergic system, which is selectively affected in Alzheimer disease, postoperative changes in thyroid hormones may play a role in the pathogenesis of POCD.

Bickel and colleagues [9], in their study of 200 patients, 60 years and older, undergoing hip surgery, reported that postoperative delirium was a strong independent predictor of the development of subsequent cognitive impairment, subjective memory decline, and the need for long-term care. A similar correlation was noted by Rudolph and colleagues [10] between delirium and early (7 days) but not late (3 months) POCD in 1218 patients,

60 years and older, undergoing elective non-cardiac surgery. Kat and colleagues [11] also reported that the risk of dementia or mild cognitive impairment in 112 hip surgery patients, 70 years and older, at 30 months after discharge was almost doubled in patients who had postoperative delirium (77.8%) as compared with at-risk patients who had not developed delirium (40.9%). Cerebral trauma (even in the absence of symptoms) [12] and preoperative cognitive decline [13] have also been reported to be risk factors for the development of postoperative delirium and POCD in the elderly.

Tan and colleagues [14] investigated 103 patients who had POCD and 103 cognitively normal controls and reported that POCD was induced by the use of patient self-controlled intravenous analgesia (PCIA). A history of cerebral trauma was an independent risk factor for POCD induced by the use of PCIA, but a high education level seemed to be protective. This relationship was also noted by the International Study of Postoperative Cognitive Dysfunction [15]. Gögenur and colleagues [16], in their study of the cognitive function in 36 patients before and 4 days after major abdominal surgery, reported that POCD was associated with inferior sleep quality and more awakenings, but not with postoperative disturbances in circadian rhythm.

Interestingly, what has not been shown to correlate with the development of POCD is whether the patient had regional or general anesthesia [17–19]. Deeper levels of general anesthesia, as assessed by the use of the bispectral index (median of 50.7 versus 38.9), however, were associated with better cognitive function, especially the ability to process information, 4 to 6 weeks after surgery [20].

Most of the studies of POCD, however, have methodological difficulties, as pointed out by Newman and colleagues [21] in their review of more than 40 studies. The definition used to classify individuals as having POCD was not standardized among investigators, nor was there uniformity in the number, range, and diversity of neuropsychological tests, their sensitivity to change and learning, and the intervals between testing. There was also no standardization in experimental design with variations in the type of surgery and anesthesia, presence or absence of controls, type of controls, and statistical methods used to analyze the data, all of which make comparisons among studies very difficult. A majority of the studies were also underpowered.

### Recent advances

A significant limitation of the studies of POCD is that they do not include a standardized preoperative

neurological examination in addition to the neuropsychological testing. This makes it almost impossible to separate out the relationship between surgery and anesthesia and subsequent cognitive decline and death from the cognitive decline and death that occur among older adults without surgery. The relationship between aging and cognitive decline and mortality rate in the absence of surgery was demonstrated almost a decade ago [22]. More recently, Inzitari and colleagues [23] developed a 15-minute neurological examination to elicit subtle but clinically detectable neurological abnormalities (SNAs), defined as abnormalities demonstrated in the absence of patient complaints and not associated with any neurological disease. Follow-up examination at 4 and 8 years revealed that patients who had three or more SNAs at initial evaluation had an increased risk of cognitive decline, cerebrovascular events, and death, possibly because the SNAs signaled a concomitant decline in cognitive reserve [4]. The authors did not track which patients had surgery and anesthesia during the follow-up period.

In light of the demonstration by Inzitari and colleagues [23] of the progression of neurological deterioration, it is essential that future studies of POCD include a uniform neurological examination of all patients and control subjects. The neurological examination must have good inter-rater agreement and reproducibility. Without prior knowledge of SNAs, it is impossible to assign causation to the cognitive dysfunction that may occur after surgery and anesthesia. Is it the normal progression of a condition, however subtle, that is present preoperatively; is it the effect of surgery and anesthesia alone; or have surgery and anesthesia worked in some way to hasten the progression of the preoperatively present condition? Clearly, whatever else the experimental protocols include to achieve uniformity and facilitate interstudy comparison (age- and disease-matched controls in every study and uniformity of operation, anesthesia, neuropsychological tests, testing intervals, statistical analysis, and control subjects), neurological examination for both gross and subtle neurological abnormalities must be included too.

### Implications for clinical practice

Even in the absence of POCD study protocols, preoperative information about SNAs would facilitate the discussion of informed consent when older adults are contemplating surgical procedures as neurological abnormalities, even in the absence of overt symptoms, have been correlated with POCD [3]. Thus it may be advisable for an SNA 'score' as developed by Inzitari and colleagues [23] with their brief neurological

examination, to be included with the other vital signs measured in older adults before surgery.

It is important to note that the studies of POCD are, as yet, in their infancy. Until research protocols achieve sufficient power and uniformity, it will be difficult to draw conclusions applicable to patient care. As suggested by Newman and colleagues [21], the very term POCD as a binary definition of what may be, in reality, a continuous process may require modification to reflect the necessity of examining cognitive change as a continuum that marches through discrete events such as surgery and anesthesia. This will necessarily influence the methodology by which changes in test performance are analyzed.

While central nervous system dysfunction after surgery and anesthesia has been demonstrated to occur, especially in older adults, it is important to bear in mind that, as Silverstein and colleagues [24] point out, any illness requiring hospitalization may be associated with cognitive decline. This introduces the possibility that cognitive decline occurs as a concomitant of generalized illness rather than being causally related to surgery and anesthesia and speaks to the need for not only age-matched controls but also disease-matched and hospitalization-matched clinical cohorts as well. In addition, the observation made by a number of investigators that cognitive decline itself increases the risk of mortality in older adults [25,26] further confounds interpretation of the correlation between POCD and mortality reported by Monk and colleagues [3].

Newman and colleagues [21] also direct our attention to the problem inherent in conducting adequately-powered studies in this era of scarce health care resources. They suggest that investigators develop a consensus regarding the experimental protocols to enable them to pool data across studies to achieve power in secondary analyses.

Even in the absence of uniform, adequately-powered studies of POCD, clinicians can work to mitigate some of the risk factors associated with POCD. For example, postoperative delirium [27], a correlate of POCD, is associated with increased intraoperative blood loss and postoperative transfusions, a postoperative hematocrit of less than 30%, and severe postoperative pain. The Hospital Elder Life Program has developed interventions to decrease the incidence and severity of delirium. These include the frequent presentation of orienting information, physical activity, cognitive stimulation activities, use of visual aids and auditory amplifying devices, sleep inducement through nonpharmacological methods, assistance with alimentation, geriatric-psychiatric

consultations, and patient and family education. The risk of delirium has been shown to be reduced using these techniques [28,29].

### Abbreviations

PCIA, patient self-controlled intravenous analgesia; POCD, postoperative cognitive dysfunction; SNA, subtle neurological abnormality.

### Competing interests

The author declares that she has no competing interests.

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