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Postoperative neurocognitive disorders in ambulatory surgery: a narrative review

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Running title: Postoperative neurocognitive disorders

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Abstract

Postoperative neurocognitive disorders (PoNCDs), such as postoperative delirium and cognitive dysfunction or decline can occur after surgery, especially in older patients. This significantly affects patient morbidity and surgical outcomes. Among various risk factors, recent studies have shown that preoperative frailty is associated with developing these conditions. Although the mechanisms underlying PoNCDs remain unclear, neuroinflammation appears to play an important role in their development. For the prevention and treatment of PoNCDs, medication modification, a balanced diet, and prehabilitation and rehabilitation programs have been suggested. The risk of developing PoNCDs is thought to be lower in ambulatory patients. However, owing to technological advancements, an increasing number of older and sicker patients are undergoing more complex surgeries and are often not closely monitored after discharge. Therefore, equal attention should be paid to all patient populations. This article presents an overview of PoNCDs and highlights issues of particular interest for ambulatory surgery.

Keywords: Ambulatory surgery; Cognitive dysfunction; Delirium; Outpatient; Perioperative neurocognitive disorders; Postoperative complications.
Introduction

Owing to advancements in various anesthetic techniques, such as regional anesthesia, and the
development of rapid-acting anesthetic agents, the number and scope of ambulatory anesthesia have
been steadily increasing [1]. Some advantages of ambulatory surgery include minimizing the
hospitalization period and avoiding unnecessary medical expenses. However, thorough preparation
and contingency plans are necessary to enable same-day postoperative discharge, which can burden
healthcare providers [2]. Therefore, adequately anticipating and addressing potential complications
is essential.

Anesthesia has been associated with cognitive changes for over a century [3]. However, it has only
recently been intensively investigated through animal experiments and clinical research with
objective testing. Many studies have suggested that anesthesia may have harmful consequences on
cognitive function [4-8].

One important postoperative neurocognitive disorder (PoNCD) is postoperative delirium (POD).
POD is an acute neuropsychiatric disorder that can occur starting on the first postoperative day and
is characterized by impaired perception, attention, and cognitive function [9,10]. Although mostly
transient and reversible, this condition can be a risk factor for developing dementia [11] and is
associated with postoperative cognitive dysfunction (POCD), another potential concern for surgical
patients. Even when symptoms are not immediately evident, a consistent decline in cognitive function
has been observed in the short-term (7 days) and medium-term (1–3 months) following anesthesia
and surgery [12].

POCD is distinct from POD [13]. While POD is relatively well-defined, conceptualizing POCD
remains challenging, even though the term has been defined according to the Diagnostic and
Statistical Manual for Mental Disorders, Fifth Edition (DSM-5), and the neurocognitive testing
methods used are heterogeneous. Patients with POCD experience cognitive decline compared to preoperative levels, which manifests as dysfunctions in memory, mental ability, language, and/or other cerebral functions [14,15]. These conditions not only compromise recovery from surgery and quality of life after surgery, but also potentially contribute to an elevated patient mortality rate [16,17].

Considering that characteristics of POD and POCD progression can occur even after ambulatory surgery and recognizing the subsequent rapid decline in the continuity of patient care post-discharge, these conditions are likely underdiagnosed. Therefore, we conducted a narrative review of the overall patterns of disease occurrence and preventive and treatment methods. This study aimed to gain a better understanding of these conditions, particularly in ambulatory surgery.
Nomenclature

After several meetings that began in 2014, the Working Group on Perioperative Cognitive Nomenclature, comprising experts from various disciplines, reached a consensus with the following recommendation: perioperative neurocognitive disorders (NCDs) be used as the comprehensive term for any impairment in cognitive function identified in the preoperative or postoperative period, including cognitive impairment diagnosed before surgery (described as NCDs), any form of acute event (POD), and cognitive decline diagnosed up to 30 d (delayed neurocognitive recovery) or 12 months (PoNCD) after the procedure [12]. Although these definitions are recommended, we were unable to follow the diagnostic and testing methods used by the Working Group for the terms POD and POCD as most of the included studies used different definitions and diagnostic methods. In this review, the term POCD is used to describe cognitive dysfunction from the late period of delayed neurocognitive recovery to the entire postoperative period in which NCDs can occur.

Frailty

Recent studies have reported that frailty in older patients increases the incidence of postoperative complications [18-21]. In addition, studies have reported that frailty status is a better predictor of patient mortality and complications, and prolonged hospital length of stay than chronological age [20]. Frailty is a term that describes a patient’s diminished ability to cope with physiologically stressful events, such as surgery. Frailty can be defined in several ways. Although no clear consensus exists, the Fried criteria, which assess unintentional weight loss, weakness or poor grip strength, self-reported exhaustion, low physical activity, and slow walking speed, have been widely used [22,23]. Brown et al. reported a frailty prevalence of 30.9% in a cohort of patients (>55 years old) scheduled to undergo cardiac surgery in 2016 [22]. In addition, a 2001 study conducted by Linda et al. reported
that the overall prevalence of frailty in a community-dwelling population was 6.9%, and the prevalence was proportional to age and higher in women [23].

Preoperative frailty is an important risk factor for POD. In a prospective observational pilot study of 55 patients undergoing coronary artery bypass graft surgery, Brown et al. reported that patients with preoperative frailty had a significantly higher incidence of POD than those without preoperative frailty (47.1% vs. 2.6%; P < 0.001) [22]. A prospective cohort study of 167 patients aged ≥ 65 years undergoing noncardiac surgery reported that patients determined to be frail or pre-frail were associated with increased odds of POD compared to healthy patients (odds ratio: 2.7, 97.5% CI: 1.0–7.3) [24]. These results suggest that the degree of frailty in elderly patients undergoing surgery should be assessed in advance.

**Neuroinflammation**

Surgical injury increases neuroinflammation and decreases neuronal growth, both of which are strongly associated with the development of POD and POCD [14]. This suggests that neuroinflammation plays an important role in both disorders, although the pathophysiology is not fully understood [25]. The hypothesis that surgical trauma disrupts the blood-brain barrier (BBB), leading to central nervous system (CNS) inflammation and subsequent functional impairment of neuronal activity, resulting in POCD has received increasing attention [13]. Further studies of these mechanisms may increase our understanding of the pathogenesis of POD and POCD and improve prevention and treatment strategies.

Cells injured at the site of surgery release substances known as damage-associated molecular patterns (DAMPs). These DAMPs bind to receptors on the cell membrane of bone marrow-derived monocytes (BMDMs) and activate nuclear factor kappa B (NF-kB), which enters the nucleus and triggers
upregulation of inflammatory cytokines, such as interleukin (IL)-1, tumor necrosis factor-α (TNF-α), and IL-6. This further activates NF-κB, which in turn promotes the synthesis of prostaglandins. Prostaglandins alter the permeability of the BBB and allow BMDMs to enter the CNS and activate dormant microglia, which in turn promotes the release of IL-1 and TNF-α from BMDMs. As a result, BMDMs are present in the CNS and continue to secrete pro-inflammatory cytokines, leading to neuroinflammation [13]. Animal studies have reported that modulating the release of substances that act at each of these stages can reduce the risk of POCD. For example, inhibiting NF-kB and pro-inflammatory cytokines [26,27] or depleting BMDMs [28] has been reported to reduce POCD. These findings could lead to the development of treatments for POCD.

Studies on epigenetic mechanisms [14] and the gut-brain axis [29] to better understand the mechanism of neuroinflammation after anesthesia and surgery have also been conducted. In particular, cognitive dysfunction following surgery can persist over a long period, and changes in the epigenetic profile have been suggested as a possible cause. Epigenetics has been implicated in cognitive impairment for many reasons, including exposure to inflammation in the hippocampus due to general anesthesia, hypotension, hypoxia, psychotropic drugs, and surgery. Early studies have suggested that these factors may induce epigenetic dysfunction in the brain because chromatin remodeling is required for the transcription and expression of genes involved in memory, which may be particularly important in older patients [14]. Epigenetic modulators may be promising targets for mitigating the neurotoxic effects of anesthetics on the brain. However, further studies on whether anesthetics cause epigenetic changes are needed.

**Preoperative assessment of neurocognitive disorders**

Preoperative cognitive impairment is an important risk factor for POD and POCD [30,31]. However, existing pre-anesthesia assessment systems do not include cognitive testing as part of routine
preoperative patient evaluations [23]. The proportion of elderly patients undergoing ambulatory surgery continues to increase, and the prevalence of cognitive impairment in elderly patients increases with age. In a study of 1465 patients undergoing ambulatory surgery in 2019, Sherman et al. reported that 6.4% of participants aged 65–75 years, 13.4% of participants aged 76–85 years, and 19.3% of participants aged ≥ 86 years had cognitive impairment [32]. Given that preoperative cognitive impairment is associated with increased postoperative mortality and morbidity and the development of delirium [23] and POCD cannot be diagnosed unless the patient undergoes formal cognitive function testing before and after surgery [33], cognitive screening should be conducted during the pre-anesthesia assessment. Indeed, the American College of Surgeons and the American Geriatrics Society recommend preoperative screening for neurocognitive impairment to establish baseline cognitive levels [15].

Screening tools for preoperative cognitive testing should be adapted to clinical practice and should be highly reproducible. Screening tools include the Montreal Cognitive Assessment (MoCA), Mini-Mental State Examination (MMSE), and Mini-Cog; however, the MoCA and MMSE are complex and require standardized test forms, which limits their feasibility in busy clinical settings [19,34]. The Mini-Cog test, on the other hand, is simple to administer and does not require a standardized template [20,35]. Several studies have explored it as a tool for pre-anesthetic cognitive assessments [23,34,36]. The Mini-Cog test consists of two components: items that assess memory, such as word recall, and a clock drawing test that evaluates cognitive domains such as language, fine motor skills, and executive function [35]. Patients are asked to listen to three unrelated words and immediately recall them. They are then asked to draw an analog clock as required by the evaluator and, after drawing the clock, recall the three words again. The patient receives one point per word the patient can recall, and the clock drawing test is scored as normal or abnormal. If the delayed word recall score is 0 out of 3, or if the score is 1 or 2 and the clock drawing test result is abnormal, the test...
is scored as positive for a possible diagnosis of dementia. If the delayed word recall score is 3, or if the score is 1 or 2 and the clock drawing test result is normal, the test is negative (indicating the absence of dementia) [34]. The Mini-Cog test is a cognitive stratification test, not a diagnostic test [37]. Providers who identify it in the pre-anesthesia assessment can share this information in the electronic medical record to allow for more individualized care before and after surgery.

POD

POD is a serious problem that increases the incidence of postoperative complications [38] and represents a decrease in cerebral responses due to one or more pathophysiological stressors [39]. The DSM-5 provides the following revised diagnostic criteria for delirium: 1) an impairment of attention and awareness that occurs over a short period (hours to days), with rapid changes in baseline status and frequent fluctuations in severity throughout the day; 2) additional cognitive impairment (loss of memory and orientation) that cannot be explained by a pre-existing, ongoing neurocognitive disorder and does not result in a severely depressed level of arousal, such as a coma; and 3) the condition does not result from other medical conditions (e.g., substance intoxication or withdrawal) or exposure to toxic substances. POD occurs when the antecedent factors of surgery and anesthesia interact with a patient’s vulnerability to delirium [40]; therefore, assessing the preoperative status of patients scheduled for surgery and individualizing the approach for those at high risk for POD are important for reducing the incidence of delirium and improving patient outcomes [41].

Epidemiology

The effects of anesthesia and surgery on patients have long been studied, particularly in elderly patients and inpatients undergoing noncardiac and cardiac surgery. Although relatively few studies have been conducted on outpatients, concern about PoNCDs in older patients undergoing ambulatory
surgery is growing owing to the aging population and the expansion of the scope of ambulatory surgery.

In one study, Aya et al. investigated the incidence of POD in 141 patients after undergoing ambulatory surgery [11]. The authors identified the occurrence of delirium via phone calls 3–5 days after surgery. In this study, two patients (1.4%) developed POD, which is a significantly lower incidence than that found in inpatients (up to 60%) [9]. One explanation is that many risk factors for POD, including unfamiliar surroundings, separation from family, and sleep deprivation, are not present for patients undergoing ambulatory surgery. Therefore, outpatients may have a lower risk of developing POD than inpatients.

Prevention and treatment

Preventive measures and pharmacological management should be optimized to reduce the incidence and severity of POD. Some medications used during the perioperative period have central anticholinergic activity as their primary mechanism of action, which may be a risk factor for POD. These medications include cimetidine, corticosteroids, diphenhydramine, belladonna, promethazine, warfarin, narcotics, benzodiazepines, and antiparkinsonian drugs [42]. For older patients, avoiding these medications or using lower dosages is advised to minimize the risk of delirium. Among these medications, benzodiazepines, morphine, and anticholinergics are the three most commonly associated with delirium [43]. In a prospective cohort study conducted by Duprey et al. on adults ≥ 70 years without dementia undergoing major elective surgery, postoperative hospital benzodiazepine use (adjusted hazard ratio: 3.23, 95% CI: 2.10–4.99) was associated with a higher incidence of POD [44]. Furthermore, patients with substance abuse such as alcohol or illicit substance withdrawal may require specific treatment strategies that differ from those for other types of delirium in elderly patients.
postoperative patients. For former alcoholics, thiamine should be administered to manage Korsakoff’s psychosis.

Hemodynamic stability, adequate oxygenation, acid-base balance, and electrolyte regulation should be maintained intraoperatively [45]. A Cochrane Review in 2016 found that multi-component interventions reduced the incidence of delirium compared to usual care in non-intensive care unit patients (RR: 0.69, 95% CI: 0.59–0.81; 1950 patients; moderate quality evidence) [46]. These interventions include an orientation protocol that repeatedly orients patients to their surroundings and care team members, a sleep protocol to provide uninterrupted nighttime sleep, an early mobilization protocol for daily ambulation and range of motion, a vision protocol to facilitate access to visual aids, and a hearing protocol to provide amplifying devices and other hearing aids. These interventions have been found to reduce delirium by 10–15% in terms of both duration and total episodes, although hospital length of stay was not affected [45].

Certain practices should be avoided to minimize the risk of delirium exacerbation. For example, dehydration and hypovolemia should be prevented [45] as they can worsen delirium symptoms. Nonessential catheters, such as Foley catheters, nasogastric tubes, or multiple intravenous access lines, should also be avoided [47]. Finally, attention should be paid to the risk of self-harm as patients with mixed motor or hyperactive delirium may inadvertently pull tubes, drains, or lines and those with hypoactive delirium may begin wandering.

In terms of medications, olanzapine has been reported to decrease the incidence of POD by 75.6%, even after the administration of all types of anesthesia [48]. However, the guidelines of the European Society of Anaesthesiology and Intensive Care Medicine do not recommend the use of any drugs as a prophylactic measure to reduce the incidence of POD [41]. For POD prevention, only
intraoperative or postoperative dexmedetomidine should be considered with caution owing to side effects, such as bradycardia and hypotension [41].

In addition, prehabilitation interventions have recently been investigated. These may include a combination of exercise programs, nutritional support, psychological counseling, and education regarding upcoming surgery [49]. One study investigated the impact of preoperative cognitive training on POD [50] and found promising results for decreasing the incidence of delirium. However, multiple barriers to the implementation of these programs exist, including preoperative time commitment, technical issues, and participants feeling overwhelmed [51]. Therefore, further research is required to find the ideal type of intervention and its timing and duration. Despite various attempts, completely preventing POD has not been possible. However, these interventions can be applied not only to prevent POD but also to treat it.

Neuroleptic agents such as haloperidol have been found to be effective in the pharmacological treatment of POD [9,52]. For postoperative treatment in the intensive care unit, a loading dose of 2 mg of intravenous haloperidol is administered, with repeated doses every 15–20 min as long as the agitation persists. The dose should be doubled in cases of severe agitation [53]. In the surgical ward, oral, intramuscular, or intravenous administration of an initial dose of 1 to 2 mg haloperidol is recommended, followed by maintenance doses of 0.25 to 0.5 mg every 4 h [54]. Atypical antipsychotics, such as risperidone, can also be considered [13]. In the case of delirium caused by sedative or analgesic withdrawal, a systematic tapering of the medications and the introduction of an α2 agonist such as dexmedetomidine can help reduce concurrent sedative and analgesic requirements [53]. Delirium caused by central anticholinergic syndrome, in which anticholinergic medications block muscarinic cholinergic receptors in the brain, can be managed with the intravenous administration of physostigmine at a dose of 10–30 mg/kg [55].
POCD

The incidence of POCD is significantly lower in ambulatory surgery than in inpatient surgery [2]. However, because older patients are more likely to have preexisting cognitive impairment [32] and surgery in elderly patients can result in rapid cognitive decline [36,56], prevention and treatment of POCD should not be neglected despite the low incidence. To evaluate for the development of POCD, baseline cognitive function needs to be assessed preoperatively. This can then be compared with the postoperative state. However, no clear consensus regarding the level of cognitive decline that is clinically significant has been reached [33].

Increased mortality, decreased quality of life, and labor market withdrawal associated with POCD have been addressed in several studies [23,33,57]. Steinmetz et al. reported a long-term prognostic study of patients undergoing noncardiac surgery with a median follow-up of 8.5 years [38]. The risk of leaving the labor market prematurely for disability reasons was higher in patients with POCD at 1 week postoperatively (hazard ratio: 2.26, 95% CI: 1.24–4.12; P = 0.01). These patients were found to receive social transfer payments for a more extended time during the observational period (prevalence ratio: 1.45, 95% CI: 1.03–2.04; P = 0.03). This is an example of the impact of POCD on socioeconomic status. Bickel et al. studied the causal relationship between POD and cognitive impairment, functional impairment, and death in 200 patients aged > 60 years who underwent hip surgery [58]. POD occurred in 41 patients, 53.8% of which had cognitive impairment 38 months after discharge, whereas only 4.4% of patients without POD developed cognitive impairment. This suggests that POD adversely affects the preservation of cognitive function and provides important evidence for the need for proactive prevention of POD.
Epidemiology

Considering that patients undergoing ambulatory surgery are generally in better physical condition and the intensity of ambulatory surgery is milder, POCD that occurs after ambulatory surgery may significantly impact patients’ social lives. Canet et al. examined 372 patients aged > 60 years who underwent minor surgery under general anesthesia. They reported that 16 of 164 inpatients (9.8%) developed POCD; however, the incidence was significantly lower in outpatients (5 of 141 outpatients, 3.5%) [59]. However, studies on whether this relationship occurs in hospitalized patients undergoing ambulatory surgery are lacking; thus, further research is needed.

Prevention and treatment

Ambulatory surgery has emerged as a favorable option for elderly patients undergoing minor surgical procedures with promising implications for reducing POCD. Canet et al. demonstrated that elderly patients who chose ambulatory surgery and thus avoided hospitalization experienced less cognitive dysfunction in the first postoperative week, likely benefiting from recovering in a less-stressful setting than the hospital [59,60]. The lower incidence of POCD in ambulatory surgery may be explained by the lower incidence of risk factors for POD, such as noise, bright lights, restraints, and sleep deprivation [61]. These factors, which are not often encountered at home, increase the incidence of POD, which is a strong independent predictor of POCD [58].

The use of opioids also presents potential challenges in POCD. Opioid-related side effects, such as sedation and hallucinations, can trigger, exacerbate, or imitate the symptoms of delirium, such as disorientation and hypoactive motor and cognitive functions [9]. However, a reduction in opioid administration may not prevent these complications. For example, a randomized controlled trial (RCT) comparing low (10 µg/kg) and high (50 µg/kg) doses of fentanyl revealed that low doses were associated with higher rates of POCD one week after surgery (23.6% vs. 13.7%, respectively; P =
0.03) [62]. However, no significant differences were observed at 3 and 12 months postoperatively. In contrast, the mode of opioid administration may have a stronger association. A prospective cohort study of elderly patients undergoing noncardiac surgery found that those treated solely with oral opioids had a significantly reduced likelihood of experiencing delayed neurocognitive recovery compared to patients treated with intravenous opioids through a patient-controlled system (odds ratio: 0.22, 95% CI: 0.06–0.80; P = 0.02) [63]. These findings underscore the complex relationship between opioids and postoperative cognitive outcomes and support the need for further exploration and careful consideration of opioid use in pain management while minimizing the risk of cognitive complications.

Another RCT focused on dexamethasone dosage found that higher doses increased the incidence of POCD in the early postoperative period (0 vs. 0.1 mg/kg vs. 0.2 mg/kg of dexamethasone: 22.3% vs. 20.6% vs. 31.4%; P = 0.003) [64]. However, the dose of dexamethasone used in clinical practice rarely reaches the levels associated with increased risk (0.2 mg/kg).

Additionally, a study focusing on sevoflurane found that seven days after surgery, the incidence of POCD did not differ between the sevoflurane and propofol groups (29.7% vs. 33.3%; P > 0.05) [60]. However, a significant difference in the severity of POCD was found between the two groups, with sevoflurane anesthesia showing a more pronounced impact on cognitive function than propofol anesthesia (P < 0.01). The type of inhaled anesthetic used may have affected the incidence of POCD.

In a pilot study comparing isoflurane and desflurane in patients receiving spinal anesthesia, those who received spinal anesthesia and isoflurane had a higher incidence of POCD than those who received spinal anesthesia alone or spinal anesthesia plus desflurane [65]. These findings suggest that isoflurane and desflurane may have different effects on POCD; however, this was a pilot study and the combined use of spinal and inhaled anesthesia is not common.
In a study comparing the effects of propofol, dexmedetomidine, and midazolam sedation on POCD in elderly patients, propofol sedation demonstrated a significant advantage in terms of short-term POCD [66]. The incidence of POCD 7 days after surgery was significantly lower in the propofol group compared to the dexmedetomidine and midazolam groups (propofol vs. dexmedetomidine: 18.2% vs. 40.0%, $\chi^2 = 6.346, P = 0.012$; propofol vs. midazolam: 18.2% vs. 51.9%, $\chi^2 = 13.603, P < 0.001$). However, no significant differences in POCD incidence were found at the one-year postoperative retest (propofol vs. dexmedetomidine: 10.6% vs. 14.0%, $\chi^2 = 0.230, P = 0.631$; propofol vs. midazolam: 10.6% vs. 14.9%, $\chi^2 = 0.382, P = 0.536$). A prospective cohort study revealed that benzodiazepine use before surgery was associated with a lower risk of cognitive dysfunction one week after surgery in elderly patients [67]. However, the blood concentrations of benzodiazepines at the time of neuropsychological testing did not explain this cognitive dysfunction; it was more attributed to patient age. The timing of benzodiazepine administration may be more relevant in POCD.

General approaches for the treatment of POD may also be applied to POCD. Addressing underlying medical conditions; sleep management; medication review; cognitive stimulation (reading, solving puzzles, learning new skills); physical activity; nutrition with a balanced diet containing essential nutrients, omega-3 fatty acids, and antioxidants; and avoidance of polypharmacy may support brain health [9,68-70].

Several drugs have been investigated for the prevention and treatment of POCD. In an RCT involving cardiac surgery patients, the administration of ketamine was found to attenuate POCD one week after surgery (Placebo vs. ketamine: 21/26 vs. 7/26, $P < 0.001$) [71]. This effect is believed to be related to the anti-inflammatory activity of the drug. Another RCT investigating the effects of intraoperative lidocaine administration demonstrated a lower incidence of cognitive dysfunction in the early postoperative period (9 days postoperatively) [72]. More recent meta-analysis research also reported...
that intravenous lidocaine could attenuate the overall incidence of POCD and its severity in the short term (< 30 days) [73].

In addition to medications, cognitive interventions, such as cognitive training, stimulation, and rehabilitation, capitalize on the plasticity of the brain to enhance cognitive function after general anesthesia. These interventions aim to enhance cognitive function through repetitive training on specific tasks targeting cognitive domains, which can be achieved through traditional (verbal and pen-and-paper) or computerized interventions, as well as cognitively stimulating activities such as board games, word searches, or discussions related to current news stories [74]. These interventions have shown positive effects in healthy older individuals and those with mild cognitive impairment and heart failure, improving subjective and overall cognition [75]. The impact of postoperative cognitive rehabilitation after general anesthesia has demonstrated some efficacy, particularly in cognitive function targeting memory [74].
Conclusion

Table 1 summarizes POD and POCD in ambulatory surgery. PoNCDs are significant complications that can adversely affect a patient’s mental and cognitive wellbeing. The stress of surgery and anesthesia on the patient may contribute to the development of the disease, and the presence of POD increases the incidence of POCD. In particular, frailty in elderly patients significantly increases the risk of POD, and neuroinflammation plays a vital role in POCD development. Although the risk of developing POD or POCD is considered low in ambulatory surgery, healthcare professionals should be mindful of these potential adverse effects, mitigate the risks associated with PoNCDs, and improve patient outcomes by implementing appropriate preventive measures and pharmacological management strategies. Evaluating cognitive function during ambulatory surgery as a preventive measure for POD and POCD is also important. The incidence of PoNCDs in the ambulatory surgery patient population may be underestimated, as these patients are often not monitored for these specific conditions after discharge. Further studies are thus needed to overcome these limitations.

Patients and their caregivers communicating any cognitive changes to the healthcare team is essential as early intervention can lead to better outcomes. For severe cases or cases in which symptoms persist or worsen, referral to a neurologist or cognitive specialist is warranted for further evaluation and treatment.
References


Table 1. Comparison of POD and POCD in ambulatory surgery

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>POD</th>
<th>POCD</th>
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<tbody>
<tr>
<td></td>
<td>• Lower incidence</td>
<td>• Lower incidence</td>
</tr>
<tr>
<td></td>
<td>• Appears immediately after surgery or in the following hours/days</td>
<td>• No universal definition and tests</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Appears days or months after surgery</td>
</tr>
<tr>
<td>Pathophysiology</td>
<td>Unclear, neuroinflammation has been suggested</td>
<td></td>
</tr>
<tr>
<td>Assessment tool</td>
<td>Confusion Assessment Method</td>
<td>MoCA, MMSE, Mini-Cog test</td>
</tr>
<tr>
<td>Risk factors-causes</td>
<td>Advanced age, preexisting cognitive impairment, medical comorbidities, benzodiazepines, ketamine, opioids, frailty, insufficient pain control, unrecognized hypoxia, pneumonia, urinary retention, hypoglycemia</td>
<td>POD and its risk factors</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Diabetes, dehydration, dexamethasone, inhaled anesthetics</td>
</tr>
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<td></td>
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<tr>
<td>Prevention/treatments</td>
<td>• Prehabilitation</td>
<td>• Address medical conditions, sleep management, medication review, cognitive stimulation, physical activity, balanced diet, avoid polypharmacy</td>
</tr>
<tr>
<td></td>
<td>• Intraoperative management</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(maintain hemodynamic stability, adequate oxygenation, acid-base balance, and electrolytes)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Multicomponent interventions, avoid non-essential catheters</td>
<td>• Cognitive rehabilitation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Studied medications (e.g., ketamine, lidocaine)</td>
</tr>
</tbody>
</table>
• Studied medications (e.g.,
  olanzapine, haloperidol,
  risperidone, dexmedetomidine)

POD: postoperative delirium, POCD: postoperative cognitive dysfunction, MoCA: Montreal Cognitive Assessment, MMSE: Mini-Mental State Examination.