Postoperative Delirium: Risk Assessment, Prevention, Detection, and Management

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ABSTRACT

There is strong evidence to support prevention of postoperative delirium through comprehensive geriatric assessment and multicomponent nonpharmacologic interventions. Risk assessment must be accompanied by communication of the risk to the patient, caregivers, and perioperative interdisciplinary team to engage all in evidence-based prevention interventions. However, once postoperative delirium has developed, efforts should be focused on prevention of short- and long-term adverse effects.

RÉSUMÉ

Des données probantes solides appuient la prévention du délire postopératoire en recourant à une évaluation gériatrique complète et à des interventions non pharmacologiques à plusieurs composantes. L'évaluation des risques doit s'accompagner d'une communication du risque au patient, aux soignants et à l'équipe interdisciplinaire périopératoire afin que tous participent aux interventions de prévention fondées sur des données probantes. Toutefois, une fois que le délire postopératoire s'est installé, les efforts doivent être axés sur la prévention des effets indésirables à court et à long terme.

Background

Delirium is an acute disorder of attention, awareness, and cognition that tends to fluctuate in severity during the course of a day and is usually triggered by an underlying medical illness, drugs, or surgery.¹ Postoperative delirium has been defined as that which occurs within 1 week postprocedure or until discharge from hospital, whichever occurs first.²

The incidence of postoperative delirium varies widely, between 5 and 50%, depending on the type of surgery.³ Postoperative delirium is linked to adverse outcomes, including increased lengths of stay, mortality, and institutionalization.⁴ It is also associated with patient and caregiver distress.^{5,6} Beyond the

perioperative period, postoperative delirium is associated with clinically meaningful impairment in functional recovery at up to 18 months⁷; moreover, symptoms can persist for 6 months in one-third of patients.⁸

The European Society of Anaesthesiology and American Geriatrics Society offer evidence-based guidelines for postoperative delirium management, and the Association of Anaesthetists provide guidelines on the perioperative care of people with dementia.^{3,9,10} The purpose of this review is to explore the current evidence and rationale for the prevention, detection, and management of postoperative delirium in older adults in the inpatient surgical ward setting.

Why Is It Important to Assess Cognition Preoperatively?

The most common independent risk factor for delirium is preexisting cognitive impairment.⁴ Preoperative cognitive screening serves to document baseline cognitive performance so as to anticipate and better manage postoperative delirium and postoperative cognitive dysfunction (POCD).¹¹ The risk of delirium is linearly and strongly related to preoperative cognitive performance level.¹² Persons who develop postoperative delirium also have greater long-term cognitive decline as compared with those who do not develop delirium.¹³ Screening for cognitive impairment can be done quickly using tools validated for preoperative use and associated with increased risk of postoperative delirium, such as the Mini-Cog.^{14,15} The Mini-Cog test, which is widely available for online use,¹⁶ includes a clock drawing task to command with the clock face already provided, and a 3-word recall task (<https://mini-cog.com/>).

Who Is at Risk for Developing Postoperative Delirium?

Overall, 30–40% of cases of delirium are considered preventable, and, thus, knowledge of associated risk factors is important to identify persons at increased risk for postoperative delirium.¹⁷ Preexisting cognitive impairment is a major risk factor for postoperative delirium (odds ratio [OR] = 2.7; 95% confidence interval [CI]: 1.9–3.8).¹⁸ Additional risk factors include increasing age, auditory and visual impairment, frailty, functional impairment, polypharmacy, psychotropic use, depression, illness severity, as well as alcohol and substance misuse.^{18,19} Frailty is a decrease in physiological reserve across multiple organ systems leading to increased vulnerability to external stressors, such as surgery.²⁰ Although comprehensive geriatric assessment (CGA) is the gold standard method for diagnosing frailty, there are numerous frailty screening tools validated for use in the surgical setting.²¹ Functional decline is a new loss of independence in self-care activities or as deterioration in self-care skills, measured on an activities of daily living (ADL) scale (e.g., feeding, bathing, grooming, using the toilet, transferring, and walking) and/or on an instrumental activities of daily living (IADL) scale (e.g., using the telephone, grocery shopping, using transportation, cooking, housekeeping, taking medications, and handling finances).^{22,23} Illness severity is also associated with increased risk for postoperative delirium. As such, persons with acute admissions for injurious falls, hip fracture, active infections, underlying metabolic derangements including anemia and renal insufficiency are at risk for postoperative delirium.¹⁹ Furthermore, the type of surgery is relevant, with a greater risk for postoperative delirium associated with hip fracture and aortic vascular procedures.²⁴ On the other hand, caregiver support is

associated with a lower risk for postoperative delirium (OR = 0.69; 95% CI: 0.52–0.91).¹⁸

Validated delirium prediction rules for elective noncardiac and cardiac surgery can be used to inform risk assessment.^{25,26}

What Are Optimal Strategies to Prevent Postoperative Delirium?

Nonpharmacologic Delirium Prevention

The CGA is a multidimensional, interdisciplinary, diagnostic process to determine the medical, psychological, and functional capabilities of a frail older person to develop a coordinated and integrated plan for treatment and follow-up.²⁷ A systematic review found that CGA reduces rates of postoperative delirium (relative risk [RR] = 0.75; 95% CI: 0.60–0.94).²⁸

Another systematic review found that multicomponent nonpharmacologic interventions reduce the incidence of delirium in hospitalized patients (RR = 0.53; 95% CI: 0.41–0.69).²⁹ A well-studied risk mitigation model is the Hospital Elder Life Program (HELP). HELP includes core intervention protocols to target delirium risk factors and include for daily visits, orientation, therapeutic activities, sleep enhancement, early mobilization, vision and hearing adaptation, fluid repletion, and feeding assistance to reduce delirium (OR = 0.47; 95% CI: 0.37–0.59, 14 studies, 3,605 patients).³⁰ Strategies to address modifiable risk factors for delirium include optimizing sleep–wake cycles via natural light exposure during daytime, promoting safe mobility in hospital including avoiding physical restraints, mitigation of sensory impairment with eyeglasses and hearing aids/amplifiers, avoiding unnecessary psychoactive drugs, limiting alcohol use, and using interpreters to enhance communication.¹⁷ In the surgical setting, additional measures include protocols for bowel routine, early removal of urinary catheters, monitoring for common postoperative complications, and pain management.³¹ While opioids may precipitate delirium, poorly controlled pain may also precipitate delirium.³² Thus, postoperative pain protocols should use regularly scheduled acetaminophen which has been shown to reduce total opioid consumption in the postoperative period.³³ In most HELP studies, the multicomponent interventions are carried out by trained volunteers and hospital staff. When these interventions are delivered by family members, the number needed to treat to prevent 1 case of postoperative delirium was 5.9 (95% CI: 4.2–11.1).³⁴

Fluid fasting for more than 6 h is an independent risk factor for postoperative delirium (OR = 10.6; 95% CI: 1.4–78.6).³⁵ Thus, when the surgery is elective, patients at higher risk for delirium should be prioritized for surgery earlier in the day to reduce unanticipated prolonged preoperative fasting, sleep alteration, and interruption of medication schedules.

Cognitive Prehabilitation

The goal of cognitive prehabilitation is to increase cognitive reserve before surgery such as through preoperative cognitive exercise. An observational study demonstrated higher cognitive activity participation was associated with lower incidence of postoperative delirium.³⁶ A randomized trial of using electronic, tablet-based preoperative cognitive exercise targeting memory, speed, attention, flexibility, and problem-solving functions showed the intervention lowered delirium risk in patients who were at least minimally compliant.³⁷

Pharmacologic Delirium Prevention

While a systematic review of randomized trials showed that second-generation antipsychotics compared with placebo may lower the incidence of postoperative delirium (RR = 0.36; 95% CI: 0.26–0.50)³⁸, the largest of these trials also showed that second-generation antipsychotics were associated with a longer duration and greater severity of symptoms when delirium occurred.³⁹

Melatonin, a natural hormone produced by the pineal gland, is involved in sleep–wake cycle regulation. Ramelteon is a selective type 1 and type 2 melatonin receptor agonist, though not yet available in Canada. While a metaanalysis found that perioperative melatonin or ramelteon administration conferred a lower risk of developing postoperative delirium, the associated evidence was limited as only three of the six studies were randomized trials and had conflicting results.⁴⁰ Thus, the current evidence does not support routine use of melatonin or ramelteon for the prevention of postoperative delirium.

Metaanalyses have demonstrated that haloperidol (RR = 0.94; 95% CI: 0.77–1.16) and ketamine (RR = 0.83; 95% CI: 0.25–2.80) do not prevent delirium.^{38,41} There have also been negative delirium prevention trials of cholinesterase inhibitors, gabapentin, and tryptophan in surgical populations.^{42–44} Single randomized trials favoring pharmacotherapy to prevent postoperative delirium include parecoxib in joint replacement, methylprednisolone in hip fracture, intravenous acetaminophen in cardiac surgery, aripiprazole in neurosurgery, and thiamine in gastrointestinal surgery, but require replication before widespread adoption.^{45–49}

Thus, the current evidence does not support routine use of second-generation antipsychotics or haloperidol for the prevention of postoperative delirium; multicomponent nonpharmacologic prevention interventions, therefore, remain the optimal strategy to decrease the risk of postoperative delirium.

Intraoperative Delirium Prevention Strategies

Intraoperative interventions such as anesthesia type, multimodal pain management, dexmedetomidine, temperature regulation, transfusion, and hemodynamic targets are beyond the scope of this review. For the internist and hospitalist, of utmost importance

is the communication of delirium risk to the anesthesiologist to inform intraoperative risk reduction strategies.

Special Considerations in Hip Fracture Care

Hip fractures are common in older adults and are a marker of frailty. Consequently, this population is at high risk for postoperative delirium which may necessitate care processes tailored to meet the needs of frailty. For hip fracture care in particular, a systematic review showed there was a reduction in the incidence of postoperative delirium with early CGA (RR = 0.81; 95% CI: 0.69–0.94).⁵⁰ CGA was defined as a multidisciplinary, multicomponent intervention addressing multiple health domains to develop a coordinated, person-centered management plan and care took place either on a geriatrics or orthopedics ward. Accelerated hip fracture repair surgery, defined as the goal of surgery within 6 h of diagnosis, in the HIP ATTACK trial showed a reduction in the secondary outcome of postoperative delirium (OR = 0.72; 95% CI: 0.58–0.92) with absolute risk reduction in this outcome of 3% [95% CI: 1–5].⁵¹ Because uncontrolled pain as well as opioids are associated with delirium, peripheral nerve blocks can address both factors. A systematic review assessing preoperative use of fascia iliaca blocks found a significant reduction in the secondary outcome of postoperative delirium.⁵²

How Is Postoperative Delirium Detected?

The clinical presentation of delirium is variable. Motoric subtypes range from hypoactive (lethargic, withdrawn, decreased motor activity) to hyperactive (restlessness, irritable, agitated, or combative), or a mix of both forms. Of the three motor subtypes, the hypoactive form following surgery is associated with worse prognosis including 6-month mortality, likely due to delay in symptom recognition.^{53,54} Hypoactive delirium may be missed because the patient is too withdrawn and the symptoms are misinterpreted as depression or fatigue, recognition requires a longitudinal perspective with an understanding of shift from baseline, and clinicians mistakenly believe that hyperactive symptoms must be present in delirium.⁵⁵ Identifying delirium allows the clinician to address modifiable contributing factors in a timely manner, counsel and comfort caregivers to understand the clinical course, inform prognostication, and plan for follow-up.

The reference standard for delirium is the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5).¹ Delirium is often underrecognized by clinicians when using only routine observations, and as such, brief screening tools have been developed.⁵⁶ Validated screening tools with reasonable psychometric properties include the short form of the Confusion Assessment Method (CAM) (positive likelihood ratio [LR] = 9.6; 95% CI: 5.8–16.0 and negative LR = 0.16; 95% CI: 0.09–0.29) and the 4 “A”s Test (4AT) (sensitivity = 87%; 95% CI: 77–93,

and specificity = 83%; 95% CI: 73–89).^{57,58} In Canada, the most commonly used screening tool is the short form of the CAM which is based on the presence of four core features of delirium: acute onset and fluctuating course of symptoms, inattention, and either disorganized thinking or altered level of consciousness.⁵⁹ The CAM requires specific training in rating each of the features, including formal testing of attention, and must incorporate history from informants plus review of medical records.⁵⁹ The 4AT comprises four items: (i) alertness, (ii) Abbreviated Mental Test-4, (iii) attention (months backwards test), and (iv) acute change or fluctuating course. The advantage of the 4AT is that item scoring also accounts for patients who may not be able to undergo cognitive testing because of reduced arousal, such as in hypoactive delirium.⁶⁰

How Does Postoperative Delirium Differ from POCD?

The core features of postoperative delirium are characterized by acute, fluctuating changes in cognition with inattention and either disorganized thought processes or changes in mental status.¹ In contrast, POCD is a research construct defined as “new cognitive impairment arising after a surgical procedure.”^{2,61} The incidence of POCD following noncardiac surgery is 12–21%.^{2,62} Unlike delirium, which can be diagnosed during bedside clinical assessment, determination of POCD requires presurgical and postsurgical psychometric testing, and does not require a subjective or functional complaint.^{61,62} As such, postoperative delirium is a type of perioperative neurocognitive disorder that is distinct from POCD.²

What Is the Optimal Management of Postoperative Delirium?

While delirium is a diagnosis in the DSM-5, it is better viewed as a set of symptoms that result from predisposing and precipitating factors. Optimal management of postoperative delirium thus requires identification of contributing factors followed by management of treatable precipitants. Potentially modifiable precipitants may include medications, withdrawal from held medications or other substances, infection, electrolyte abnormalities, or other complications such as myocardial infarction or venous thrombosis. The evaluation should at a minimum include a history (substance use, medication list and changes), physical examination looking for common postoperative complications (vital signs, urinary retention, constipation, volume status, surgical incision site, asymmetric leg swelling), and investigations focused on the postoperative setting (electrolytes, complete blood count, glucose, troponin, calcium, ECG; and infectious work-up like chest x-ray, blood cultures, procedure-specific infection imaging, urine analysis).

Brain imaging is not a routine part of the evaluation and its use should be informed based on clinical judgment.^{19,31}

Careful medication review for culprit medications should be linked with the goal of tapering, discontinuing, and/or substituting with alternatives when possible. Increased delirium risk is associated with sedative-hypnotics such as benzodiazepines (OR 3.0, 95% CI 1.3–6.8), anticholinergic medications such as antihistamines (OR 1.8, 95% CI 0.7–4.5), meperidine (OR 2.7, 95% CI 1.3–5.5), and dihydropyridines in cardiac surgery (OR 2.4, 95% CI 1.0–5.8).^{32,63} Benzodiazepines are associated with longer duration of a first episode of delirium.⁶⁴

There are three Cochrane systematic reviews of different drug classes in the treatment of delirium. Antipsychotics do not reduce delirium severity (SMD –1.08, 95% CI: –2.55–0.39) and do not resolve symptoms (RR = 0.95; 95% CI: 0.30–2.98) when compared to placebo.⁶⁵ There is insufficient evidence to determine whether benzodiazepines are effective.⁶⁶ There is no difference in delirium duration to support the use of cholinesterase inhibitors.⁶⁷ Thus, because of the low risk of adverse events, reinforcement of the nonpharmacological methods used for delirium prevention is recommended as a first step in delirium management. Family members can serve as a reorienting and reassuring stimulus and may reduce the duration of delirium.^{31,68}

In the scenario where there are refractory distressing psychotic symptoms (such as hallucinations or delusions) or the symptoms of delirium imminently threaten the administration or maintenance of life-sustaining medical care (such as mechanical ventilation or dialysis catheters), expert opinion suggests the use of antipsychotics at the lowest effective dose for the shortest possible duration.¹⁷

At care transitions, documentation of delirium should be in the discharge summary communication to the primary care provider to screen for cognitive deficits postdischarge.¹¹

Summary

In summary, there is strong evidence to support prevention through CGA and multicomponent nonpharmacologic interventions. Risk assessment must be accompanied by communication of the risk to the patient, caregivers, and perioperative interdisciplinary team to engage all in evidence-based prevention interventions. However, once postoperative delirium has developed, aside from addressing precipitating causes, there are limited drug management strategies. Because postoperative delirium is associated with short- and long-term adverse effects, efforts should be focused on prevention.

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