

Perioperative Brain Health

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KEY POINTS

- Perioperative cognitive disorder is an overarching term that includes postoperative delirium, delayed neurocognitive recovery, and postoperative neurocognitive disorder.
- The preoperative visit is essential in identifying risk factors for initiation of risk-reduction strategies. The most consistent risk factors are old age and preoperative cognitive impairment.
- High-risk patients should have their baseline cognitive function established with a validated tool such as the Mini-Cog. They should also be informed of the risks of perioperative neurocognitive disorders as part of the consenting process.
- Intraoperative goals are to maintain cerebral perfusion and to minimise neurotoxic insults. This is achieved by avoiding significant physiological disturbances and excessive depth of anaesthesia.
- Postoperative goals are to optimise analgesia and facilitate reorientation. Postoperative delirium should be managed by excluding reversible causes and using nonpharmacological measures.

INTRODUCTION

Perioperative brain health refers to cognitive recovery after surgery and anaesthesia, which depends on both one's cognitive reserve and the extent of surgical or anaesthetic insults to the brain.¹ It is of particular concern to both patients and caregivers because it fundamentally changes one's identity and drastically impacts one's quality of life.²

The Brain Health Initiative was created by the American Society of Anaesthesiologists with the goal of optimising cognitive recovery and perioperative experience, especially for older adults undergoing surgery.³ Older adults 65 years of age or above are disproportionately represented amongst patients undergoing surgery and anaesthesia.⁴ Physiological changes that occur with ageing diminish the body's reserve, thereby rendering it more vulnerable to perioperative insults.

Perioperative care bundles that focus on brain health are emerging. Principles follow those of Perioperative Medicine and divide perioperative care into the preoperative, intraoperative, and postoperative phases. The perioperative care team consists of not only the anaesthesiologist, surgeon, and neurogeriatrician but also the patient's primary care physician and other allied health members.

BACKGROUND

Definition and Epidemiology

Perioperative neurocognitive disorder is an overarching term that describes the cognitive changes identified in the perioperative period.³ It is defined with reference to the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (DSM-5),⁵ and is

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further classified into postoperative delirium, delayed neurocognitive recovery, and postoperative neurocognitive disorder, according to the duration of onset after surgery and anaesthesia (Figure 1).⁶

Postoperative delirium refers to changes in attention, cognition, and awareness within 7 days that have an acute onset with fluctuating course. Behavioural disturbances may coexist, which range from hyperactivity that manifests as agitation to hypoactivity that manifests as somnolence.

Neurocognitive disorder refers to significant decline from previous level of activities in at least 1 of the 6 cognitive domains: executive function, complex attention, social cognition, learning and memory, language, and perceptual motor function. It is classified as *delayed neurocognitive recovery* when it occurs within 30 days and *postoperative neurocognitive disorder* when it occurs within 12 months.

Postoperative delirium is estimated to occur in up to 65% of older patients,⁷ while delayed neurocognitive disorder and postoperative neurocognitive disorder range from 17% to 43% depending on specific surgical specialty.⁸

Pathophysiology and Risk Factors

Systemic inflammatory response to surgery and anaesthesia is believed to be the key pathophysiological mechanism in perioperative neurocognitive disorders.⁹⁻¹¹ Patient-related risk factors are essentially indicative of a vulnerable brain, which may be a result of compromised cognitive reserve, neurotoxic insults, and impaired cerebral perfusion (Table 1). The most consistent risk factors are old age and preoperative cognitive impairment.

On the other hand, procedure-related risk factors (Table 2) are reflection of the strength of inflammatory response. They include magnitude or complexity of the procedure, duration, and specific surgical specialty.¹²⁻¹⁴ Major cardiac, thoracic, and vascular procedures are associated with increased risk. Preexisting neuroinflammation or neurodegeneration either unmarks neurocognitive dysfunction or primes the brain to react more strongly to a systemic inflammatory and stress response.

Anaesthesia-related risk factors and medications (Table 2) associated with perioperative neurocognitive disorders are discussed in greater details in the subsequent section Perioperative Care. In recent years, several intraoperative electroencephalographic characteristics during general anaesthesia have been suggested to be markers of vulnerable brains—examples include diminished power of frontal alpha waves and the propensity of the brain to enter into burst suppression which may reflect reduced cerebral connectivity and decreased mitochondrial function or reserve, respectively.¹⁵

It is worth noting that this is a field of active research, with plenty of new theories and controversies. For instance, it has been postulated that the gut microbiome, being an essential part of the gut-brain axis, may also play a role in neuroinflammation and hence the development of neurocognitive disorders.¹⁶

Prognosis and Management

Postoperative delirium is associated with worse outcomes, such as prolonged hospitalisation, decline in functional status, and subsequent cognitive impairment.¹⁷

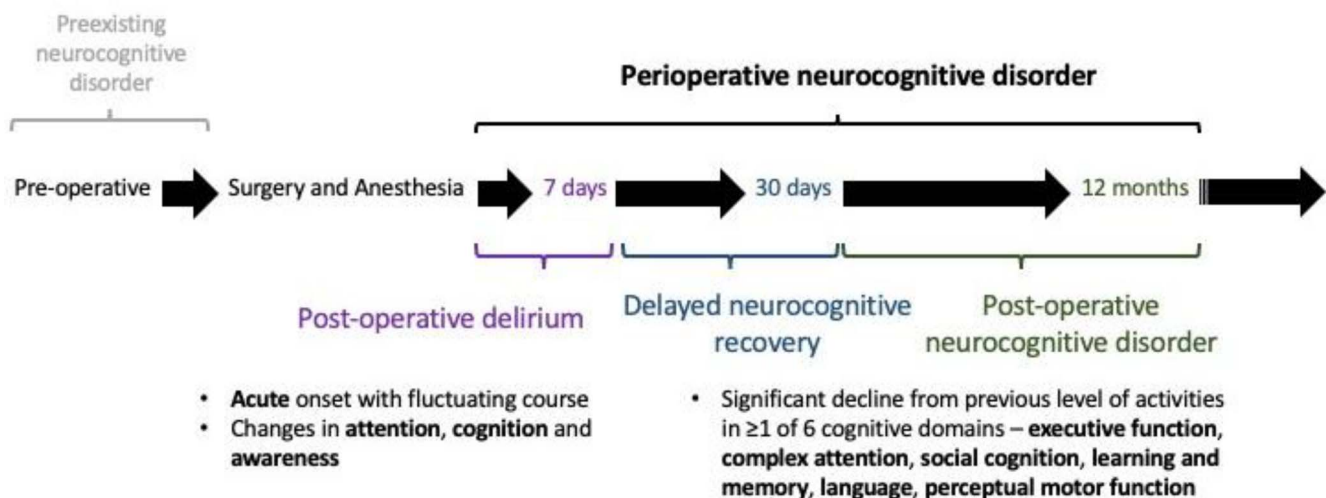


Figure 1. Definitions of perioperative neurocognitive disorder.⁵

Compromised Cognitive Reserve	Neurotoxic Insults	Impaired Cerebral Perfusion
<ul style="list-style-type: none"> • Old age >65 years • Cognitive impairment • Low educational level • Depression • Sleep disruption 	<ul style="list-style-type: none"> • Diabetes mellitus • Chronic alcoholism • Psychotropic drug use • Polypharmacy 	<ul style="list-style-type: none"> • Prior transient ischemic attack, stroke • Severe vascular disease

Table 1. Patient-Related Risk Factors for Perioperative Neurocognitive Disorders^{11,26}

Reversible triggers, including pain, respiratory failure, electrolyte disturbances, hypothermia, or hypoglycaemia, should be identified and treated accordingly. A complete neurological assessment is warranted in patients not responding to initial management. Early Neurology or Neurosurgery input should be considered in the presence of lateralising signs or features of raised intracranial pressure suggestive of neurological complications. After ruling out reversible causes, nonpharmacological measures should be the first line of management, with antipsychotics being limited to only refractory delirium that poses risk of harm to patient or staff.¹

A small proportion of patients with delayed neurocognitive recovery and postoperative neurocognitive disorder demonstrate persistent decline in subsequent cognitive testing.¹⁸ As with nonoperative cases of neurocognitive disorders, no effective treatment is currently available. General management is similar to that of nonoperative causes, and patients should be referred to the Geriatric/Neurology team for long-term follow-up after discharge.⁵

PERIOPERATIVE CARE

Preoperative

The goals of the preoperative visit are to identify risk factors, stratify risk, initiate risk-reduction strategies, and disclose risks to patients or their family members. Risk assessment is performed to identify high-risk patients, who may subsequently require characterisation of preexisting cognitive level and modification of anaesthetic technique to minimise risks. Currently, no validated risk stratification tool for perioperative neurocognitive disorders¹⁹ analogous to the Revised Cardiac Risk Index for major adverse cardiac events exists.

While a full set of cognitive tests is impossible for all patients in the clinical setting, a validated screening tool may instead be used to select patients for detailed assessments by neurogeriatricians. The Fifth International Perioperative Neurotoxicity Working Group recommended that baseline cognition should be objectively evaluated with a brief screening tool during preoperative evaluation in all patients over the age of 65 and any patient with risk factors for preexisting cognitive impairment.¹³ The Mini-Cog test is amongst the most cited screening tool that is quick to perform, with a reasonable test sensitivity.²⁰ It consists of a 3-item registration, followed by a clock-drawing test, and finally a 3-item recall. Other commonly cited cognitive screening tools are the Montreal Cognitive Assessment²¹ and the Minimal Mental State Examination.²²

One of the most important risk reduction strategies is the optimisation of medical comorbidities, particularly control of vascular risk factors such as hypertension and diabetes mellitus. In addition, while polypharmacy is often unavoidable in the older adults, they should be screened for any potential interactions. Prescription of medicines for the geriatric population should also be in accordance with the American Geriatrics Society Beers Criteria for potentially inappropriate medication use in older adults.²³ Since optimisation of medical conditions often takes time, it can be ineffective and impractical if commencing only in the immediate preoperative period. Therefore, perioperative brain health involves not only the anaesthesiologists, surgeons, and neurogeriatricians but also the primary care physicians, who can aid in optimising patients before they present for surgery and anaesthesia.

In addition, all patients over age of 65 and their family members should be informed of the risks of perioperative neurocognitive disorder preoperatively.^{24,25} This permits a reasonable level of expectation for the postoperative course of cognitive recovery, with pre-emptive actions to refrain from making major personal decisions in the immediate postoperative period. This also facilitates patients and their family members to actively participate in risk-reduction strategies, which include smoking cessation,

Procedure	Anaesthesia	Medication
<ul style="list-style-type: none"> • Procedural duration • Procedural complexity • Surgical approach • Cardiopulmonary bypass 	<ul style="list-style-type: none"> • Intraoperative hypotension • Excessive depth of anaesthesia • Hypoxemia • Hypothermia • Hypo/hyperglycaemia 	<ul style="list-style-type: none"> • Benzodiazepines • Gabapentinoids • Opioids • Anticholinergic agents

Table 2. Procedure, Anaesthesia and Medication-Related Risk Factors for Perioperative Neurocognitive Disorders^{11,26}

maintaining physical activity, bringing hearing aids and glasses for postoperative use, and having family or friends for visit after the procedure.⁴

Intraoperative

The overall intraoperative goals are to maintain cerebral perfusion and minimise neurotoxic insults. Specific issues include physiological parameters, anaesthetic agents, anaesthetic techniques, and monitoring. Hypotension should be avoided, as it decreases cerebral blood flow, although specific blood pressure targets are individualised.²⁶ In cases where significant hemodynamic changes are anticipated, arterial blood pressure and ventilation should be meticulously monitored and controlled. Normothermia and normoglycemia help to minimise stress.

Intravenous agents that have been implicated in the development of perioperative neurocognitive disorder include benzodiazepines, gabapentinoids, opioids, and anticholinergic agents. They should be used with caution and only when indicated in high-risk patients. While evidence is not well established for the use of dexmedetomidine in reducing risk of perioperative neurocognitive disorders, it may be used in high-risk patients with the aim of decreasing emergence delirium.¹⁰

Evidence is inconclusive in terms of the specific anaesthetic technique, anaesthetic depth, and depth of anaesthesia monitoring for reducing risks of perioperative neurocognitive disorders. Recommendations in these areas are therefore made based on best-practice guidelines.^{17,27}

Compared with general anaesthesia, regional anaesthesia—whether with deep, light, or no sedation—has not been consistently shown to decrease the incidence of perioperative neurocognitive disorders.^{13,28,29} That being said, appropriately administered regional techniques, in general, improve pain control and reduce opioid requirements. In addition, although total intravenous anaesthesia is less likely to produce emergence delirium especially in the paediatric group,³⁰ evidence again is inconclusive with regards to its use compared with volatile anaesthesia in decreasing risks of perioperative neurocognitive disorders in adults.³¹⁻³³ Thus, the decision of providing general or regional anaesthesia, total intravenous or volatile anaesthesia should not be made solely based on concerns for perioperative brain health.

On the other hand, excessive depth of anaesthesia is associated with an increased risk of perioperative neurocognitive disorder.³⁴⁻³⁶ Electroencephalography (EEG) signatures indicative of reduced neuronal activity include power shift towards lower frequencies, power reduction across all frequencies, and ultimately burst suppression.¹⁵ Evidence of benefits of depth of anaesthesia monitoring in mitigating its risks, however, has not been consistently demonstrated.³⁷⁻⁴⁰ Nonetheless, it remains prudent to avoid excessive depth that could cause hypotension, compromising cerebral perfusion. The Fifth International Perioperative Neurotoxicity Working Group recommended that anaesthesiologists should monitor age-adjusted end-tidal minimal alveolar gas fraction and perform EEG-based anaesthetic management in older adults.¹³ They provide additional information regarding the depth of anaesthesia in addition to clinical assessment findings such as heart rate and blood pressure.

Postoperative

The key postoperative goals are to optimise analgesia and facilitate reorientation.^{4,24} Paracetamol and nonsteroidal anti-inflammatory drugs should be considered as part of the analgesic regimen. Although ketamine produces psychomimetic effects that may manifest as emergence delirium, it has analgesic and opioid-sparing properties that may be advantageous for patients with poor postoperative pain control. Patients' medications should be carefully reviewed at discharge, especially looking out for potential interactions and opioid dosing.

Multicomponent nonpharmacological interventions targeting patients at risk of postoperative delirium have been advocated. To facilitate reorientation, early mobilisation should be encouraged by removing unnecessary lines, drains, and restraints. Sensory input should be maintained by returning hearing aids and glasses to patients as soon as practicable, and any disruption to the sleep-wake cycle should be minimised. Family members or friends are encouraged to visit, whereas familiar objects such as photographs or music may also be helpful.^{4,24} Input from the geriatrician, rehabilitation specialists, and social worker helps to identify medicopsychosocial issues and individualise cognitive training, risk prevention, and management bundles.

Delirium screening should be performed in the Postanaesthesia Care Unit to allow early intervention that include optimising analgesia and managing reversible causes.²⁴ They should also be followed up in the postoperative period for improvement or resolution of symptoms. The Confusion Assessment Method (CAM) is a validated screening tool for diagnosing delirium. It has been developed into a brief version termed the 3-Minute Diagnostic CAM (3D-CAM).⁴¹ The 3D-CAM is a questionnaire that identifies features of delirium according to the DSM-5 criteria. It is considered positive when the patient demonstrates features of both acute onset with fluctuating course and inattention, plus either impaired cognitive function or altered level of consciousness. An alternative screening tool for delirium is the 4A's Test (4AT), which scores based on acuity, attention, abbreviated mental test, and arousal. A summary of strategies targeting perioperative brain health is illustrated in Figure 2.

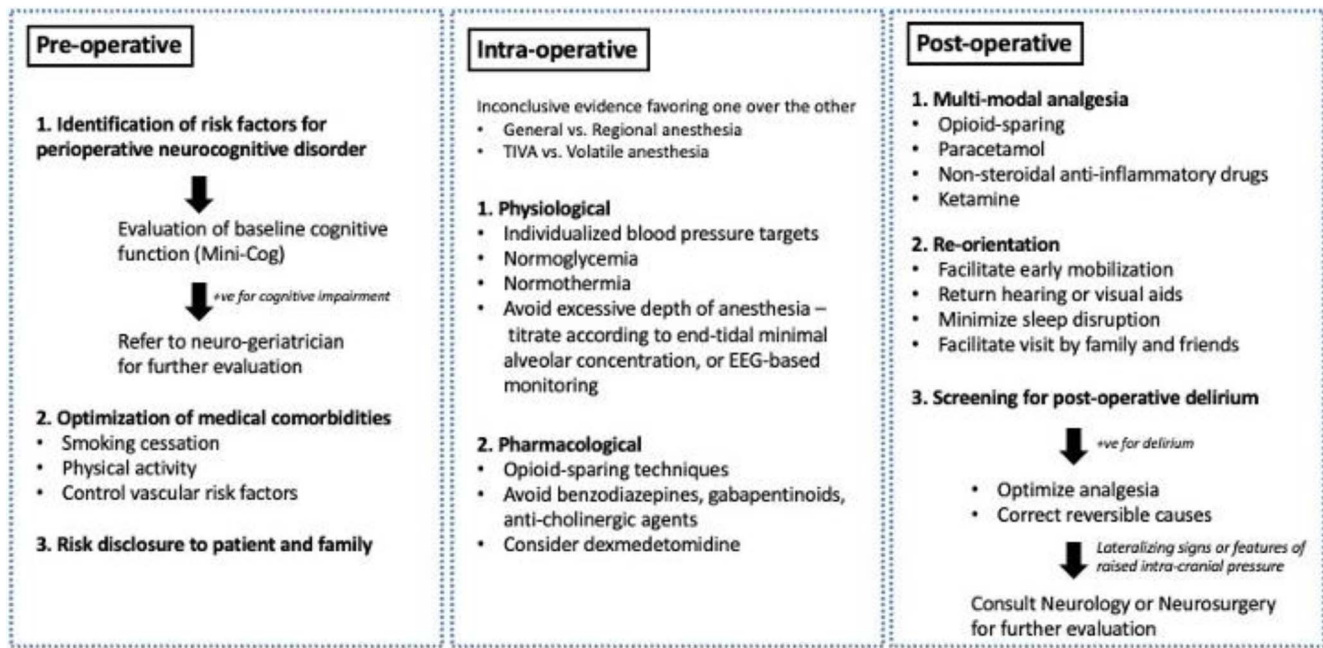


Figure 2. Summary of perioperative strategies targeting brain health.²³

SUMMARY

Perioperative brain health requires joint effort from patients, their families, anaesthesiologist, surgeon, neurogeriatrician, primary care physician, and allied health members. Perioperative neurocognitive disorders are prevalent, with significant consequences on patient outcomes. Although some precipitating risk factors are nonmodifiable such as the age of the patient and the extent of surgery, many other factors are within the control of anaesthesiologists. Emerging perioperative care bundles help identify high-risk patients who would benefit from multidisciplinary risk-reduction strategies and facilitate timely management of perioperative neurocognitive disorders. Bearing in mind that perioperative neurocognitive disorders have a multifactorial genesis, with each patient having a unique risk profile, interventions should be individualised, as it is unlikely that any single intervention is sufficient for all.

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