BJA

British Journal of Anaesthesia, 117 (S3): iii52–iii61 (2016)

doi: 10.1093/bja/aew361
Review Article

Perioperative cognitive protection

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Abstract

There is significant evidence that many older surgical patients experience at least a transient decrease in cognitive function. Although there is still equipoise regarding the degree, duration, and mechanism of cognitive dysfunction, there is a concurrent need to provide best-practice clinical evidence. The two major cognitive disorders seen after surgery are postoperative delirium and postoperative cognitive dysfunction. Delirium is a public health problem; millions of dollars are spent annually on delirium-related medical resource use and prolonged hospital stays. Postoperative cognitive dysfunction is a research construct that historically signifies decline in performance on a neuropsychiatric test or group of tests and begins days to weeks after surgery. This review focuses on the current state of information gathered by several interdisciplinary stakeholder groups. Although there is still a need for high-level evidence to guide clinical practice, there is an emerging literature that can guide practitioners.

Key words: cognition; delirium; perioperative period; surgery

There is significant evidence that many older surgical patients experience at least a transient decrease in cognitive function. Although there is still equipoise regarding the degree, duration, and mechanism of cognitive dysfunction, there is a need to provide best-practice clinical evidence. Under this paradigm, the ASA has recently developed a Brain Health Initiative, the goal of which is to create health policy and improve patient safety. In this review, we discuss pre-, intra-, and postoperative strategies to maintain cognitive abilities in older patients.

The two major cognitive disorders seen after surgery are postoperative delirium and postoperative cognitive dysfunction (POCD). Postoperative delirium is a clinical syndrome characterized by an acute attentional deficit that by definition waxes and wanes; motor symptoms are hyperactive or hypoactive. Generally, postoperative delirium occurs on or after postoperative day 1, and may or may not be related to emergence delirium. Delirium is a public health problem; millions of dollars are spent annually on delirium-related medical resource use and prolonged hospital stays.[1 2] Delirium is also associated with long-term cognitive decline and mortality.[3] Postoperative cognitive dysfunction is a research construct that historically signifies some amount of decline in performance on a neuropsychiatric test or group of tests, and begins days to weeks after surgery. Up to 60% of patients after cardiac surgery and 10% of patients after general major surgery exhibit cognitive deterioration months after surgery.[4] The International Perioperative Neurotoxicity Group, a special interest research group of anaesthetists, neuropsychologists, and neuroscientists, has convened a panel to work toward a consensus on what defines POCD and how it relates to the current Diagnostic and Statistical Manual of Mental Disorders terminology for neurocognitive disorders. Currently, most agree that POCD begins at least 7 days after surgery and up to 1 yr after surgery. It is unclear whether POCD is heralded by delirium or related to long-term cognitive dysfunction or dementia. There is observational evidence suggesting that patients with delirium are at

Editor's key points

- Postoperative delirium and postoperative cognitive dysfunction are commonly seen in the elderly, but the aetiology is unclear.
- A number of perioperative factors have been implicated, but high-level evidence for causation, prevention, or treatment is lacking.

higher risk for long-term cognitive decline after both cardiac and non-cardiac surgery.[5] Development of delirium might play an important role in the pathophysiology of longer-term cognitive decline, as shown in Fig. 1. However, the precise contribution and mechanism for this association need to be better defined. Nevertheless, these results raise the intriguing prospect that prevention of delirium might be a strategy for prevention of cognitive decline.

This review focuses on the current state of information gathered by several interdisciplinary stakeholder groups, including the American Geriatrics Delirium Guidelines Panel and the American College of Surgeons Coalition for Quality in Geriatric Surgery. The latter is in the process of developing standards for comprehensive care for geriatric surgical patients. Both have evaluated the literature for evidence and where evidence is not present have developed expert consensus. This article expands on what is known regarding cognition and delirium as summarized by Mashour and colleagues[6] to emphasize implications for clinical care. Although there is still a need for additional high-level evidence to guide clinical practice, there is an emerging literature that can guide practitioners.

Preoperative risk stratification

Recent studies suggest that preoperative patient-level factors are equally or more important than intraoperative anaesthetic management.[7 8] Several risk factors for postoperative delirium and cognitive decline consistently emerge in observational studies: increasing age, low baseline cognitive status, and low level of education.[9–12] These factors contribute to individual brain and cognitive reserve, which might provide protection from short- and long-term cognitive changes, including dementia.[13 14]

The American Geriatrics Society has partnered with the American College of Surgeons to develop an optimal preoperative assessment for geriatric patients that incorporates measures of cognition and risk factors for delirium.[15] However, this important information has not yet become a routine part of preoperative testing. Cognitive impairment is probably more common among patients presenting for surgery than generally assumed, with one study showing a 22% prevalence of amnestic mild cognitive impairment in patients presenting for elective hip replacement.[16 17] Although formal neurocognitive testing can be time consuming, even a brief assessment can add important information, with the goal of counselling patients on perioperative risk and implementing targeted strategies to prevent postoperative cognitive change.[18]

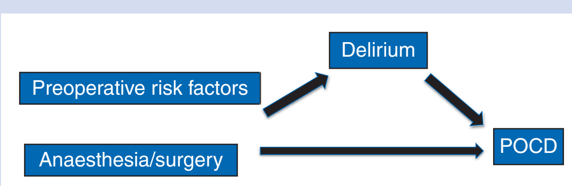

Fig 1 Relationship between delirium, postoperative cognitive dysfunction (POCD) and anesthesia/surgery

Beyond basic epidemiology, there are several validated risk models to predict delirium, as shown in Table 1. In cardiac surgery, Rudolph and colleagues[12] found that four risk factors (low Mini-Mental State Examination, history of stroke, low albumin, and depression) were highly predictive of postoperative delirium, and age also appeared to be important. In non-cardiac surgery, Marcantonio and colleagues[9] developed a risk model with the following independent predictors of delirium: age ≥70 yr, alcohol abuse, cognitive impairment, physical impairment, abnormal electrolytes, and type of surgery (aortic aneurysm and thoracic).

There are fewer validated risk models for postoperative cognitive decline, although several large cohort studies have examined risk factors. In the ISPOCD study of 1218 patients undergoing non-cardiac surgery, only age was an independent risk factor for cognitive dysfunction 3 months after surgery.[10] Likewise, in a study of 1064 patients undergoing major non-cardiac surgery, independent risk factors for cognitive decline at 3 months after surgery were increasing age, lower education, history of stroke, and cognitive dysfunction at hospital discharge.[11]

Several models have been developed specifically to predict global risk for postoperative complications in older adults, although these models are not specifically focused on risk for delirium and cognitive decline. The Comprehensive Geriatric Assessment is an established multidomain method for evaluating and optimizing older adults, and information on the Comprehensive Geriatric Assessment has been shown to correlate with postoperative complications, including delirium.[19–21] Frailty is a validated geriatric syndrome that characterizes the phenotype of extreme vulnerability.[22] Frailty before surgery has consistently been associated with increased postoperative complications, institutionalization, and mortality, in addition to postoperative delirium.[23–26]

As our understanding of the pathogenesis of cognitive decline after surgery improves, there is hope that more precise characterization of underlying risk will be possible. Potential markers of high-risk patients include intracerebral amyloid-β (Aβ) deposition, genotypes with an elevated risk of dementia, and high tau/Aβ ratio in the cerebrospinal fluid. Furthermore, several cohort studies of hospitalized patients have shown that critical illness is associated with long-term cognitive decline and structural changes on brain magnetic resonance imaging.[27–29] Patients with these characteristics are expected to be at high risk for cognitive decline after surgery, but further work needs to be done in order to provide better definition of risk profiles and develop strategies targeted to these patients.

Preoperative optimization

Optimizing patients before surgery is an attractive concept with intrinsic face value for both patients and clinicians, but the literature supporting preoperative optimization to improve cognitive outcomes is sparse. Nevertheless, it is the authors' opinion that multidisciplinary efforts to improve perioperative

Table 1 Validated risk models for prediction of postoperative delirium in cardiac and non-cardiac surgery patients. MMSE, Mini-Mental State Examination. [a]Defined as telephone interview for cognitive status<30. [b]Specific Activity Scale=IV. [c]Defined as sodium<130 or >150 mmol litre^{-1}, potassium <3.0 or >6.0 mmol litre^{-1}, and glucose <60 or >300 mg dl^{-1}

Authors	Patients and surgery	Risk factors	Results
Rudolph and colleagues[12]	Cardiac surgery (n=122 for derivation cohort, n=109 for validation cohort)	i. Previous stroke (1 point) ii. Geriatric Depression Scale >4 (1 point) iii. Abnormal albumin (1 point) iv. MMSE 24–27 (1 point) or MMSE<24 (2 points)	In the validation cohort, the cumulative incidence of delirium for each point level was as follows: 0 points, 18%; 1 point, 43%; 2 points, 60%; and ≥3 points, 87%
Marcantonio and colleagues[9]	General, orthopaedic, and gynaecology surgery (n=876 for derivation cohort, n=465 for validation cohort)	i. Age>70 yr ii. Alcohol abuse iii. Poor cognitive status[a] iv. Poor functional status[b] v. Markedly abnormal sodium, potassium, or glucose[c] vi. Non-cardiac thoracic surgery vii. Aortic aneurysm surgery	In the validation cohort, the cumulative incidence of delirium for each point level was as follows: 0 points, <1%; 1 point, 8%; 2 points, 19%; and ≥3 points, 45%

outcomes for older adults will have the added benefits of preserving brain health after surgery. Indeed, complications, critical illness, and prolonged hospitalization have been associated with both delirium and long-term cognitive decline, and thus general preoperative strategies to improve postoperative outcomes writ large in older adults are likely to be important.[1 27 28]

A fundamental concept in perioperative optimization of older adults is the importance of team-based approaches. In an important perspective, Glance and colleagues[30] discuss the value of multidisciplinary team-based care, including coordination of care processes, incorporation of diverse opinions, and increased teamwork among care providers. Importantly, team-based approaches have the opportunity to engage patients before surgery, and several studies support the effectiveness of perioperative geriatric consultation in both medical and surgical patients.[19 31] In a trial of hip fracture surgery patients, Marcantonio and colleagues[32] demonstrated that geriatrics consultation reduced the incidence of postoperative delirium from 50 to 32%. In this study, 61% of patients were seen before surgery, even though hip fracture is non-elective surgery. A subsequent meta-analysis of perioperative interventions to reduce delirium also found that a geriatrics consultation before surgery was one of only two perioperative interventions that were associated with a reduction in delirium.[33]

In the weeks leading up to elective surgery, there is evidence to support physical activity and inspiratory muscle training. In cardiac surgery, a Cochrane review of eight trials found that preoperative physical activity, inspiratory muscle training, or both reduced pneumonia and length of stay, whereas in elective non-cardiac surgery, a systematic review could draw no strong conclusions regarding the efficacy of exercise programmes.[34 35] Currently, there is a gap in knowledge about whether preoperative optimization protocols can improve cognitive outcomes. Two trials are currently enrolling patients to determine whether a preoperative physical exercise programme or a programme of cognitive exercises can reduce postoperative delirium.[36 37]

From the population-health perspective, physical activity and control of cardiovascular risk factors are important modifiable factors to preserve brain health and slow progression to dementia.[38] Given that the preoperative period is a time when patients are highly impressionable, strategies to promote long-term physical activity and control of cardiovascular risk factors can have important and outsized effects on long-term cognitive outcomes.

Intraoperative strategies

There is a great deal of interest in optimizing intraoperative management to promote postoperative brain recovery. In this section, we focus on evidence concerning anaesthetic approaches, management of cerebral perfusion pressure, anaesthetic drugs, and results of other important trials.

Anaesthetic approaches

There is evidence from the basic science realm supporting the hypothesis that anaesthetic drugs have neurological effects that extend beyond the intraoperative period. In rodent models, volatile anaesthetics have been shown to increase oligomerization of Aβ, contribute to decreased clearance of Aβ, and increase production and phosphorylation of tau; changes consistent but not pathognomonic of dementia progression.[39–41] For example, several studies in rodents have demonstrated that hypothermia induced by i.v. and inhalation anaesthetics (and not the direct effect of the drugs) can produce tau hyperphosphorylation.[42–44] In humans, several studies have shown changes in cerebrospinal fluid concentrations of Aβ, tau, and the ratio of Aβ:tau after surgery; however, the long-term cognitive effects of these changes are unclear.[45 46]

In the clinical realm, there are no consistent demonstrable differences between various anaesthetic agents with respect to prevention of delirium and cognitive decline.[47 48] Two recent studies found a slight improvement in early cognitive dysfunction (<7 days after surgery) in patients who received a volatile anaesthetic compared with propofol, but this difference did not remain at 3 months after surgery in the one study with longer follow-up.[49 50] These results are inconsistent with a separate study reporting opposite results, favouring propofol for early cognitive protection.[51]

In contrast, reduced depth of anaesthesia might be effective in reducing postoperative delirium, with a meta-analysis of perioperative interventions finding a significant benefit to this strategy (odds ratio 2.66; 95% confidence interval 1.27–5.56).[33] These findings were true in traumatic hip fracture patients undergoing spinal anaesthesia and in patients undergoing general anaesthesia.[52–55] A summary of these trials is presented in Table 2. In cardiac surgery, avoidance of burst suppression has been associated with a reduced risk of delirium in an observational study, and a current trial is underway to determine whether avoidance of burst suppression can reduce the incidence of delirium in patients undergoing major cardiac and non-cardiac surgery.[56 57] For longer-term cognitive protection, the results of trials examining the effects of reduced depth of anaesthesia have been more conflicting, with studies reporting improvement, no difference, and worsening in cognitive function in patients randomized to reduced depth of anaesthesia.[53 54 58] In an observational study, burst suppression appeared protective for POCD.[55]

As a corollary, it is tempting to speculate that avoidance of general anaesthesia might be beneficial for cognitive outcomes. However, multiple studies have examined cognitive outcomes after regional compared with general anaesthesia and have found no differences. In a large study of 438 older adults undergoing major non-cardiac surgery, regional anaesthesia was associated with a trend towards improvement in cognitive outcomes at 7 days after surgery ($P=0.06$), but no differences were seen at 3 months.[59] A meta-analysis likewise found no difference in the incidence of delirium for patients randomized to regional *vs* general anaesthesia, and a non-significant trend favouring regional anaesthesia for prevention of longer-term cognitive decline. However, these results need to be interpreted with caution because depth of anaesthesia was not monitored in many of these trials, with the real possibility that patients undergoing regional anaesthesia may have been sedated to a significant anaesthetic depth, as has been demonstrated.[60] A large pragmatic trial (NCT02507505) is currently enrolling patients undergoing surgical repair of a traumatic hip fracture to determine whether regional anaesthesia improves outcomes, including delirium, compared with general anaesthesia.

Cerebral perfusion

Maintenance of adequate cerebral perfusion is a crucially important goal in the perioperative period. However, defining an adequate mean arterial pressure (MAP) to achieve this goal is difficult, with a systematic review identifying 140 definitions of 'hypotension' in the literature.[61] In the absence of agreed-upon MAP goals, several studies have examined whether increasing MAP during surgery could improve postoperative neurological outcomes. In cardiac surgery, MAP goals of 80–90 mm Hg during cardiopulmonary bypass in one trial resulted in less delirium and decline in Mini-Mental Status Examination scores compared with MAP goals of 60–70 mm Hg.[62] However, in a similar study comparing MAP goals of 80 *vs* 50 mm Hg, less cardiac and neurological morbidity was observed in the high-MAP group, but there was no difference in cognitive outcomes at 6 months after surgery.[63]

As opposed to generic arterial pressure goals, many have proposed tailoring targets to individual patients based on real-time cerebral monitoring in the operating room. Near-infrared spectroscopy (NIRS) is routinely used during cardiac surgery at many institutions to monitor regional tissue oxygen saturation in the frontal cortex. Several observational studies have demonstrated associations between declines in regional tissue oxygen saturation from baseline and postoperative delirium and cognitive change, but the results have been inconsistent.[64–67] There have been no high-quality randomized studies examining interventions based on NIRS monitoring to improve postoperative cognitive outcomes. Limitations of NIRS-based monitoring include defining normal values for each patient, defining and implementing an intervention, and lack of additional trials showing benefit.

Individualizing arterial pressure targets during surgery may also be accomplished by real-time monitoring of cerebral autoregulation, although these methods are not routinely used in clinical practice.[68] To monitor cerebral autoregulation, changes in cerebral blood flow (using middle cerebral artery Doppler or NIRS-based methods) are correlated with changes in MAP, thus allowing determination below the lower limit of autoregulation and optimal cerebral perfusion pressure. Observational data in cardiac surgery support the hypothesis that blood pressure below the lower limit of autoregulation is associated with acute kidney injury and major morbidity and mortality.[69 70] Blood pressure above the upper limit of autoregulation (i.e. hyperperfusion) might be associated with postoperative delirium.[71] An ongoing trial (NCT00981474) is examining whether randomization to arterial pressure targets during cardiopulmonary bypass based on individual monitoring of cerebral autoregulation can reduce both postoperative delirium and cognitive decline.

Specific anaesthetic drugs

The effects of single anaesthetic drugs on postoperative delirium and cognitive decline have been investigated in many trials. The American Geriatric Society frequently releases a list of drugs that are not recommended for older adults (i.e. Beers criteria). Important drugs to avoid from this list that are common in the perioperative arena are shown in Table 3 and include pethidine, long-acting benzodiazepines, and drugs with anticholinergic properties.[72] It is important that benzodiazepines be used judiciously in patients at risk for delirium and cognitive decline.[73] There is clear evidence in the intensive care unit (ICU) that avoidance of benzodiazepines as sedative agents reduces the risk of delirium, although the evidence regarding a single low-dose short-acting benzodiazepine (i.e. premedication with midazolam) is less clear.[74] In several trials, dexmedetomidine started during surgery and continued into the ICU resulted in less postoperative delirium in major non-cardiac surgery and cardiac surgery patients.[75–77] Ketamine has also been the focus of intense interest, with at least one trial showing benefit in the reduction of delirium and cognitive decline.[78 79] There are several large ongoing trials assessing the neurological benefit of perioperative ketamine, including the PODCAST trial (NCT01690988).[80]

Other considerations

Given that inflammation has been hypothesized to play an important role in delirium, anti-inflammatory drugs may be

Table 2 Randomized trials examining the effect of depth of anaesthesia on postoperative delirium. BIS, bispectral index; CAM-ICU, Confusion Assessment Method for the intensive care unit; DSM, Diagnostic and Statistical Manual; ICU, intesive care unit; MMSE, Mini-Mental State Examination; POCD, postoperative cognitive dysfunction

Authors	Patients	Intervention	Comparison	Outcome	Results	Comment
Sieber and colleagues[52]	114 patients >65 yr old for hip fracture surgery under spinal anaesthesia	Light sedation (BIS >80) with spinal anaesthesia	Deep sedation (BIS ~50) with spinal anaesthesia	Delirium was defined by DSM-III criteria using the Confusion Assessment Method	The prevalence of delirium in the light sedation group (19%) was significantly lower than in the deep sedation group (40%; P=0.02)	Patients were extremely vulnerable, with a baseline dementia prevalence of 35%
Radtke and colleagues[54]	1155 patients >60 yr old with planned elective surgery under general anaesthesia for >60 min	BIS-guided anaesthesia	Usual care. BIS information recorded, but not available to the anaesthetist	Delirium was defined by DSM-IV criteria. Postoperative cognitive change was assessed by a test battery at baseline and 7 days and 3 months after surgery. POCD was defined using reliable change indices	Delirium was lower in the BIS-guided group (16.7%) compared with the usual care group (21.4%; P=0.036). BIS monitoring did not alter the incidence of POCD	BIS protocol was not well defined and was left up to the treating anaesthetist
Chan and colleagues[153]	921 older adults undergoing major non-cardiac surgery	BIS-guided depth of anaesthesia with target BIS 40–60	Usual care. BIS information recorded, but not available to the anaesthetist	Delirium was assessed using Confusion Assessment Method. Cognition was assessed using a neuropsychological battery at baseline, 1 week and 3 months after surgery. POCD was defined as at least two Z-scores >1.96	The incidence of delirium was lower in the BIS group (15.6%) *vs* usual care group (24.1%; P=0.01). Patients in the BIS group had a lower rate of POCD at 3 months (10.2%) *vs* usual care (14%.7%; P=0.025)	Chinese population, with adapted outcome measures
Whitlock and colleagues[107]	310 patients enrolled in a single-centre substudy of the BAG-RECALL trial	BIS-guided depth of anaesthesia (alarms if BIS <40 or > 60)	End-tidal anaesthetic concentration-guided depth of anaesthesia (alarms if MAC <0.7 or > 1.3)	CAM-ICU twice daily until postoperative day 10 or ICU discharge	The incidence of delirium was 18.8% in the BIS group and 28% in the end-tidal group	No baseline cognitive assessments. CAM-ICU may be insensitive in non-intubated patients

Table 3 Common medications in the perioperative period with potential neurological effects that are also on the 2012 Beers criteria list for potentially inappropriate medication use in older adults

Drug	Rationale
Diphenhydramine	Highly anticholinergic; may increase confusion
Hydroxyzine	Highly anticholinergic; may increase confusion
Scopolamine	Highly anticholinergic
Amitriptyline	Highly anticholinergic; sedating
Antipsychotics	Increased risk of stroke and mortality in persons with dementia
Benzodiazepines	Older adults have increased sensitivity and decreased metabolism. Risk of cognitive impairment, delirium, and falls
Metoclopramide	Extrapyramidal side-effects; risk may be increased in older adults
Pethidine	Not effective analgesic; may cause neurotoxicity
Pentazocine	May cause central nervous system adverse events, including confusion and hallucinations
Neuromuscular blocking drugs	Poorly tolerated by older adults, with anticholinergic adverse effects

beneficial. However, a large well-done trial in cardiac surgery found no difference in the incidence of delirium or cognitive decline among patients who received dexamethasone (1 mg kg^{-1}) compared with placebo.[81 82] Likewise, given that anticholinergic drugs have been implicated in delirium, a potential benefit of cholinesterase inhibitors has been examined, with the results showing no benefit in the intervention arm.[81–83] Remote ischaemic preconditioning has been shown to confer a potential benefit after ischaemic injury, although results have been conflicting after cardiac surgery.[84 85] A small pilot trial showed no benefit for remote ischaemic preconditioning in preventing delirium after cardiac surgery (The Effect of Remote Ischemic Preconditioning on Delirium after Cardiac Surgery Daria Lymar, MD; Dan Berkowitz, MD; Ashish Shah, MD; Laura Max, BA; Emily Ledford, BA; Karin Neufeld, MD MPH; Charles Hogue, MD; Charles Brown, MD MHS Departments of Anesthesiology & Critical Care Medicine and Psychiatry; The Johns Hopkins University School of Medicine, Baltimore, MD, 21287. Department of Surgery. Vanderbilt University Medical Center. Nashville TN 37232). Antipsychotic drugs have been given prophylactically to prevent delirium, with mixed results.[33] However, guidelines from the critical care literature do not recommend the use of prophylactic antipsychotic drugs to prevent delirium.[86]

For pharmacological perioperative prevention of POCD, a qualitative review found no clear benefit to any single drug, but found conflicting evidence for administration of ketamine, lidocaine, and magnesium sulfate.[87] For each of these interventions, however, the number of trials was small (two to four), so it is difficult to draw firm conclusions. A potential deleterious effect of cardiopulmonary bypass has been examined by comparing on-pump *vs* off-pump cardiac surgery. Although early studies were promising, the large OCTOPUS randomized trial showed no difference in cognitive outcomes at 3 months or 5 yr after surgery between patients randomized to on-pump *vs* off-pump surgery.[88 89] There is also no clear difference in cognitive outcome between hypothermic compared with normothermic approaches during cardiopulmonary bypass; however, it appears that hyperthermia and, in particular, fast rates of warming are deleterious to the brain.[90]

Postoperative prevention of delirium

More than half of the recommendations from the American Geriatrics Society Delirium Guidelines Panel deal with the postoperative period.[91] The strongest recommendations include the following: postoperative multicomponent non-pharmacological interventions by an interdisciplinary team, medical reconciliation, pain management, and avoidance of high-risk medications and new use of anticholinergic medications. Weaker recommendations include the following: beginning a multicomponent non-pharmacological programme once a patient is diagnosed with delirium, use of regional anaesthesia for postoperative pain control, and the use of antipsychotic drugs to treat severely agitated patients with delirium. Multicomponent non-pharmacological therapy includes the following: mobilization and exercise, cognitive stimulation, support of circadian rhythms with sleep protocols and hygiene, vision and hearing aids, and education for nurses.[92 93] The most successful multicomponent non-pharmacological programme is the Hospital Elder Life Program.[94] This programme focuses on maintaining orientation to surroundings, nutrition, sleep, and mobilization. There are more than 200 HELP sites in 32 states and 11 countries, and it has been associated with up to 30% reduction in postoperative delirium.[95] Hospitals can join the Program and obtain training and support to implement the Program at their institution. Although HELP has been very successful in prevention of delirium, there is insufficient evidence at this time for the creation of specialized ‘delirium units’ to care for patients who have developed delirium.

Specialized geriatric medical evaluation has been found to decrease the incidence of delirium.[32] Although this may be difficult to accomplish using geriatric inpatient consultation, the effort may be more feasible if extended to training of geriatric nurse practitioners. Many of the interventions suggested are often basic medical care (e.g. maintenance of electrolytes, removal of the urinary catheter at the earliest possible time) and can be identified and accomplished by education of those who will regularly work with these patients after surgery. One could argue that the only potential harm to geriatric medical education is cost. However, studies suggest that geriatric focused education and a component of delirium intervention is cost effective.[96]

Pain management for the older adult should focus on non-opioid strategies because opioid use itself is associated with gastrointestinal complications, respiratory depression, and impaired cognition. Strategies to optimize pain control in the elderly include use of gabapentin, acetaminophen, and non-steroidal anti-inflammatory drugs. It should be recognized that non-opioids also have side-effects and so selection should be made with regard to co-morbidities, and drugs can be used in combination to minimize dosage and side-effects of a single agent. Regional anaesthesia is another strategy to optimize postoperative pain control while minimizing opioids. However, there is very minimal literature comparing delirium between patients with and without regional anaesthesia either as an adjunct or a primary technique. The recommendation from the Delirium Guidelines was based on neuraxial anaesthesia because there are no high-quality studies that test the benefit of nerve catheters to prevent delirium (femoral, upper extremity etc.).[97]

Avoidance of cognitive complications resulting from medications includes avoidance of polypharmacy, the novel use of anticholinergic medications in the perioperative period, and benzodiazepines for sedation in the ICU to treat agitation. In the elderly, polypharmacy can occur when providers neglect to terminate orders for medications (antihypertensive, antibiotic, sleep, or pain medication) after a patient no longer requires them. Certain drugs used in combination can cause side-effects either through their interaction or use over time. Antipsychotics are generally avoided and indicated after surgery only when the patient is judged to be at risk of harming themselves or others. When used, antipsychotics should be used at the lowest possible dosage for the shortest period possible. Of note, there is currently no evidence that the prophylactic use of antipsychotics in the perioperative period prevents delirium. In the event of hypoactive delirium, there is no role for antipsychotics to treat or prevent delirium.[98] Benzodiazepines should not be used to treat hyper- or hypo-active delirium and are paradoxically associated with a longer duration of delirium. Several high-quality studies have found that dexmedetomidine is superior to benzodiazepines to reduce the prevalence, duration, or both of delirium in mechanically ventilated medical and surgical ICU patients.[74 99]

Postoperative cognitive dysfunction

Postoperative prevention of longer-term cognitive decline is a somewhat murky subject because the syndrome has not been defined in a consistent way and the cause is still poorly understood.[4] Further complicating matters, as discussed earlier, cognitive dysfunction that is evident after surgery can in fact be pre-existing, but not fully recognized before surgery. On the contrary, cognitive function can even improve in the postoperative period as overall medical health improves after surgery. As such, recovery of cognition can be either a cause or an effect of postoperative health status.

It is likely that POCD is not global cognitive dysfunction, but rather a domain-based decline in either executive function (judgment, processing speed) or memory.[100] This is an important distinction, because executive function is related to fall risk and the ability to make medical and social appointments and follow instructions.[101 102] Additionally, prevention of cognitive dysfunction might be related to what type of dysfunction the patient has experienced. For example, executive function has been found to respond to cognitive or physical conditioning exercises in community-dwelling elderly.[102–104] Whether exercise-based prehabilitation could help surgical patients, and if so, what dose or form, has not been established.

Currently, there is no evidence for drug-based therapy for postoperative cognition. Early studies using stimulants such as modafinil in the immediate postoperative period reduced patient tiredness but had no effect on psychomotor function.[105 106]

Conclusions

Prevention of perioperative cognitive complications is an important public health issue. Although the underlying aetiology of delirium and POCD is not entirely clear, at least for the former there are some evidence-based strategies to improve patient outcomes. For postoperative delirium, preoperative risk stratification, referral for enhanced services such as geriatric consultation, availability of multidisciplinary programmes such as the HELP, optimization of depth of anaesthesia, opioid-sparing pain management, and avoidance of polypharmacy and Beers list medications might decrease the incidence of delirium. Postoperative cognitive function is likely to be bolstered by general medical health measures, although this is unclear. Many important studies in the field of delirium and POCD are underway, and it is likely that our understanding of best practices for brain health will improve. As our population of elderly surgical patients has grown, researchers and clinicians continue to work toward maintaining cognitive health and functional recovery. National Institute of Aging AG17-015, American Federation of Aging.

Authors' contributions

Design, planning and writing: S.D. and C.B.

Funding

S.D. and C.B. are funded by The International Anesthesia Research Society, the Research Career Development Core in the Johns Hopkins Pepper Older Americans Independence Center–NIA P30AG021334, and Johns Hopkins Clinical Scientist Award

Declaration of interest

None declared.

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Handling editor: H. C. Hemmings