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REVIEW

Preoperative Cognitive Optimization and Postoperative Cognitive Outcomes: A Narrative Review

Yumiko Ishizawa

Department of Anesthesia, Critical Care & Pain Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Correspondence: Yumiko Ishizawa, Department of Anesthesia, Critical Care & Pain Medicine, Massachusetts General Hospital, 55 Fruit Street Gray Jackson 444, Boston, MA, 02114, USA, Email yishizawa@mgh.harvard.edu

Background: Perioperative neurocognitive disorder (PND) is a growing concern and affects millions of older adult surgical patients each year in the United States. However, the effective prevention of PND has yet to be established. Recently, preoperative brain exercise has been suggested to decrease postoperative delirium incidence in older patients. This review aims to interpret existing preoperative cognitive optimization research, determine if the research supports preoperative cognitive optimization, and identify gaps in the knowledge of the older surgical population.

Methods: A literature search was performed in Pub Med (1995–2024) using the keywords (Older Surgical Patients, Presurgical Assessment, Cognitive Optimization, Neurocognitive Disorder, Postoperative Cognitive Impairment, Postoperative Delirium, Dementia, Frailty Syndrome, Prehabilitation, and Brain Plasticity). The type of literature included clinical trials, case series, cohort studies, and reviews. Among these articles, I included the one in which full text is available in Pub Med and is identified that specifically investigates cognitive function in older adults.

Results and Conclusion: Evidence of the effect of preoperative cognitive optimization on postoperative cognitive functions in older adult surgical patients is still limited. Postoperative delirium was reduced by preoperative cognitive training. A limited number of clinical studies suggest the beneficial effect of preoperative cognitive training, but others show no effects. Further studies are needed on the cognitive training dosage, duration, and platform type. Studies are also required in presurgical patients with preexisting cognitive impairment or dementia.

Keywords: perioperative neurocognitive disorder, postoperative cognitive impairment, postoperative delirium, cognitive frailty, cognitive optimization

Introduction

Cognitive dysfunction after anesthesia and surgery in older adult patients was first reported in 1955.[1] However, the reversibility of cognitive functions after anesthesia and surgery was not seriously questioned until a few decades ago. The first large clinical trial was published in 1998 and suggested that age is a significant risk factor for late cognitive dysfunction after anesthesia and surgery.[2] Postoperative cognitive dysfunction or perioperative neurocognitive disorder (PND) is now widely recognized as a disorder that affects patients undergoing surgery, especially in patients of advanced age, a growing population. PND is an overarching term that describes changes in behavior and cognition and includes cognitive impairment diagnosed in the preoperative period, postoperative delirium (POD), delayed neurocognitive recovery (cognitive decline diagnosed up to 30 days after the procedure), and postoperative (persisting) neurocognitive disorder (diagnosed up to 12 months after the procedure). PND is known to increase overall morbidity and mortality and is associated with an increasing risk of Alzheimer's Disease (AD) and related dementia (ADRD), devastating neurocognitive problems.[3,4]

According to the latest national statistics on outpatient[5,6] and inpatient surgery in the United States (US),[7] approximately 40 million older adult patients underwent surgery. Since studies suggested that up to 54% of these aged patients

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may develop a form of PND after anesthesia and surgery, 20 million or more patients may suffer from PND each year in the US.[8] The population of older adults is rapidly increasing in the US and worldwide. The population having surgery is aging faster than the general population.[9] Patients with PND experience a much higher incidence of new disabilities after surgery.[10] Moreover, a recent cohort study of Medicare patients aged 65 years or older suggested that a diagnosis of PND was associated with a significant increase in healthcare costs for one year following surgery.[11] Preexisting cognitive impairment and older age are identified as PND's most critical predisposing factors.[12,13] Anesthetic drugs and surgery are considered precipitating factors, but evidence is insufficient as a cause of PND or AD.[14,15] The effective prevention and treatment of PND have yet to be established.[16,17]

Optimizing predisposing factors of PND, such as preexisting cognitive impairment, is newly gaining attention. Preoperative optimization of heart failure, hypertension, and diabetes has been the mainstay in preoperative patient care. This narrative review primarily focuses on interpreting existing research on preoperative cognitive optimization, understanding whether the research supports that, and identifying gaps in the current knowledge in older surgical populations. A literature search was performed in Pub Med (1995–2024) using the keywords (Older Surgical Patients, Presurgical Assessment, Cognitive Optimization, Neurocognitive Disorders, Postoperative Cognitive Impairment, Postoperative Delirium, Dementia, Frailty Syndrome, Prehabilitation, and Brain Plasticity). The type of literature included clinical trials, case series, cohort studies, and reviews. Among these articles, I included the one in which full text was available in Pub Med and was identified that explicitly investigated cognitive function in older adults. In this review, I first discuss preoperative cognitive assessment as the foundation for cognitive training and then the studies on preoperative cognitive optimization. I also review cognitive training in non-surgical populations since the data are crucial for surgical populations, and their successful training programs can be incorporated into preoperative studies.

Preoperative Cognitive Assessment

Preoperative Cognitive Impairment and Dementia

Older adult patients are often undiagnosed with cognitive impairment or dementia until they develop POD or PND.[18] The prevalence of undiagnosed dementia in older surgical patients is largely unknown. Alzheimer's Disease International reported that over 55 million people lived with dementia worldwide in 2019 and that 75% of people with dementia are not diagnosed.[19] A prospective cohort study from South Africa reported undiagnosed cognitive impairment in 57% of older surgical patients (median age: 65 years old) using the Mini-Cog test.[20] The lower scores were associated with increased age, low level of education, unskilled occupation, low functional status, and frailty. Another cohort study showed cognitive deficits in 23.5% of the unselected elderly surgical patients 65 years and older on preoperative cognitive screening.[21] These deficits were associated with older age, decreased function, decreased BMI, and several common medical comorbidities. These studies suggest that anesthesiologists and surgeons are confronted with managing a large number of patients with undiagnosed cognitive impairment.

It is imperative to have standardized diagnostic tools that can be used in various preoperative settings to diagnose undiagnosed cognitive deficits or evaluate preexisting cognitive impairment, one of the major risk factors for PND.[3,16,22] The prevalence of presurgical cognitive impairment or dementia appears to vary in different patient groups. Still, a wide range of older presurgical patients (19–83%) seem to have preexisting cognitive impairment.[18] During the preoperative period, a thorough medical and social history is essential, including the patient's decision-making capacity, history of depression and other psychiatric illnesses, functional dependence, frailty, nutritional status, alcohol and drug use, and list of medications.[18] Thus, PND predisposing factors can be identified. Comprehensive geriatric assessment has been known as an approach involving multi-domain assessment, which can be a valuable tool to identify potentially modifiable risk factors in older surgical patients. Studies suggest that comprehensive geriatric assessment has a positive impact on postoperative outcomes.[23–25] Recent cohort studies from Japan indicated a significantly lower surgical complication rate, including surgical site infection and delirium, in elderly patients aged 75 years and older who underwent preoperative comprehensive geriatric assessment compared to the control group.[26,27] Current multidisciplinary guidelines emphasize cognitive assessment and recommend preoperative cognitive screening of older adults undergoing surgery.[8,18,22,28–30] So that medically treatable conditions contributing to cognitive impairment, including vitamin deficiencies, metabolic abnormalities, and medication effects, can be diagnosed and treated before surgery.

Some preoperative assessment programs have been provided remotely, especially since the COVID-19 pandemic. Yet, cognitive assessments that can be performed remotely by phone or video call are neither available nor tested for clinical use. Recent studies showed that cognitive deficits in brief cognitive testing in an emergency setting contributed to postoperative complications in older patients.[31] The Mini-Cog test on surgery day and that at the preoperative clinic visit (average 8.4 days before surgery) are highly agreed upon in older surgical patients.[32] These data are promising in a setting with insufficient presurgical time for assessment. Still, the choice of testing tools varies in different programs, and the criterion for optimization depends on the team and clinicians,[18] suggesting the need for standardized assessment across the institutions.

Frailty Syndrome and Cognitive Impairment

Frailty is a clinical syndrome, and its importance has been rapidly recognized in the perioperative population.[33] The frailty syndrome is measured as a sum of various indicators, including unintentional weight loss, fatigue, muscle weakness, low physical activity, low gait speed, poor balance, visual impairment, and cognitive impairment.[34,35] The prevalence of preoperative frailty (up to 50–60%) depends on multiple factors, including age, gender, financial exploitation, and the type of surgery, with a steep increase in older patients.[36–40] Preoperative frailty is known to be associated with poor postoperative morbidity and mortality.[41] Whether frailty is associated with PND has been actively investigated. Gracie et al performed a meta-analysis of nine qualified clinical studies. They reported evidence for an association of preoperative frailty and POD in elective surgical patients aged 65 years or older compared to the non-frail control patients.[36] Multiple recent studies have also suggested the association between frailty and POD.[42–46] It remains unclear whether any components of frailty syndrome drive the association with POD or whether preoperative cognitive impairment by a single entity is a major factor driving this association. Susano et al, in a prospective cohort study, suggested that preoperative frailty and cognitive impairment are independently associated with POD.[37]

The term cognitive frailty is used for a condition of cognitive impairment caused by physical ailments.[47] Cognitive frailty may be less prevalent in the general population but is suggested in higher incidence (up to 39%) and with worse outcomes in clinical patients.[47] A recent meta-analysis indicated that cognitive frailty was a better predictor for all-cause mortality and dementia than just frailty in the general older population.[48] Another meta-analysis demonstrated that cognitive frailty was associated with higher mortality and hospitalization.[49] These data together suggest that cognitive frailty is a predictor for adverse outcomes in the general older population and needs to be diagnosed in preoperative assessment.

Preoperative Cognitive Optimization

Cognitive optimization is a relatively new concept compared to preoperative optimization in other specific organ systems. Optimizing congestive heart failure, hypertension, diabetes, or kidney failure has been a core practice of perioperative medicine with positive outcomes.[50–52] Whether preoperative cognitive optimization improves postoperative cognitive outcomes in older adult surgical patients is an urgent question, considering the growing impact of PND socially and individually.[53,54] Humeidan et al demonstrated that preoperative brain exercise reduced delirium incidence in noncardiac and nonneurological surgical patients aged 60 years and older.[55] This randomized single-blinded clinical trial used a tablet-based cognitive exercise targeting memory, attention, processing speed, flexibility, and problem-solving functions for 1 hour at least 10 days before surgery. POD (up to postoperative day 7) was significantly decreased in the cognitive exercise group compared with the control participants (13.2% vs 23.0%, $p = 0.04$). Still, there were no differences between study groups in the delirium onset day, duration, or total delirium-positive days. There was no follow-up for long-term cognitive functions.

The effect of cognitive training on long-term cognitive functions, or PND, is suggested in smaller clinical studies using a randomized control group. Presurgical cognitive training (three 1-hour sessions) using the method of loci, a memory enhancement strategy, decreased postoperative cognitive dysfunction one week after gastrointestinal surgery in older adult patients compared to control patients (15.9% vs 36.1%, $p=0.007$).[56] Song et al reported that an 8-week home-based computerized cognitive training (focused on attention, processing speed, and working memory) improved post-operative verbal memory at 12 weeks in lung transplant recipients aged 55 years and older compared with the control group.[57] Recently, Ros-Nebot showed that a 10-day cognitive training program based on artificial intelligence reduced cognitive dysfunction and memory disturbance rates 30 days after surgery in noncardiac surgical patients aged between 55 and 75.[58] The training was given on a digital platform through directed play, working on multiple different cognitive processes, which were tailored to adapt to the cognitive profile of each user and their progression. In this study, improvement was also shown in the subjective memory. These clinical studies show promising results, but each study was performed in a specific group of patients, and the type of cognitive training, timing, dosage, and platform varied. Of note is that patients with preexisting cognitive impairment are excluded from these studies.

Nevertheless, a prospective randomized controlled trial demonstrated that computer-based cognitive training provided both *pre*operatively and *post*operatively did not change cognitive outcomes, including delirium incidence, in older patients undergoing coronary artery bypass grafting surgery.[59,60] In this trial, cognitive training focused on psychomotor speed, attention, memory, and executive function, the cognitive domains most affected by heart failures. Interestingly, Butz et al reported that early *post*operative cognitive training decreased the frequency of cognitive dysfunction in older heart surgery patients at discharge from rehabilitation and three months after the discharge.[61] This randomized controlled trial used paper-and-pencil-based cognitive training for 3 weeks starting 1 week after surgery. The same group reported the positive impact of postoperative cognitive training on health-related quality of life, including emotional well-being, social functioning, and mental components, 3 months after discharge.[62]

Additionally, several feasibility studies on preoperative cognitive training have been reported. Perioperative cognitive training via a mobile device was shown to be feasible in older adults undergoing cardiac surgery (60–90 years old).[63] On the other hand, preoperative short-term, home-based, unsupervised cognitive training using the computer-based cognitive battery is shown to be unfeasible for older patients undergoing noncardiac surgery.[64] The barriers to the training appear to include feeling overwhelmed, technical difficulties, and preoperative time constraints, suggesting that enrollment in the program over a short time frame may worsen anxiety and apprehension in the patients.[64] A randomized pilot study combining preoperative cognitive training and physical exercise prehabilitation suggested the feasibility of the combined training at home and the tendency to improve cognitive scores in the intervention group with no difference in physical scores.[65]

In comparison to cognitive optimization, *prehabilitation* needs to be clarified. Prehabilitation is a widespread concept intended to enhance general health or optimize comorbidities before major surgery.[66–68] Prehabilitation initially focused on improving physical function and nutritional status but shifted to a more multimodal approach, including mind-body prehabilitation and stress and anxiety reduction. Psychological factors are increasingly considered essential and often added to a prehabilitation program.[66] In older surgical patients, a meta-analysis demonstrated that trimodal prehabilitation improved postoperative functional status but did not reduce postoperative mortality or complications.[69] The PREHAB randomized clinical trial demonstrated that multimodal prehabilitation reduced severe and medical complications and improved walking capacity at four weeks postoperatively in older patients (median age: 69 years old) who underwent elective surgery for non-metastasized colorectal cancer compared with standard care.[70] However, these studies do not include cognitive prehabilitation or cognitive outcome measurements, requiring future investigation.

Cognitive Training in Older Non-Surgical Population

Since there are limited clinical studies on preoperative cognitive optimization, as discussed, it is essential to know whether cognitive training can improve cognitive functions in the general non-surgical population. Normal aging is associated with progressive functional losses in perception, cognition, and memory. However, brain plasticity is considered a lifelong capacity and has been shown in the aged brain,[71,72] suggesting that the aged brain can be optimized. A pioneering study by Mahncke et al demonstrated that brain plasticity-based intensive training (computer-based home aural language reception accuracy training for 60 min per day, five days per week, 8–10 weeks) improved trained auditory and language functions and nontrained memory tasks for three months in adults aged 60 years and older with normal age-related cognitive decline.[73] Active control (DVD-based lecture viewing on the same schedule) and no-contact control groups showed no significant change in the cognitive functions in this study. Advanced Cognitive Training for

Independent and Vital Elderly (ACTIVE) study demonstrated that three distinct cognitive training interventions (memory, reasoning, speed of processing) in ten 60–75-minute sessions effectively improved targeted cognitive abilities in adults aged 65 and older.[74] At the 10-year follow-up, cognitive training for reasoning and processing speed, but not for memory, indicated beneficial effects on the trained cognitive abilities, and the study participants reported less decline in daily functioning compared with the control group.[75] Meta-analysis of seven randomized controlled studies of cognitive intervention in older adults suggested long-lasting protective effects on cognition in healthy older adults for up to six years.[76]

Anguera et al examined the underlying neurophysiology of the effect of cognitive training using a custom-designed video game.[77] They demonstrated that older adults (60–85 years old) who completed the video game training in multitasking mode (signal detection and car control on the game) for 12 hours over four weeks showed improved multitasking performance for six months. The multitasking training group demonstrated improvements in untrained cognitive tasks, such as working memory and attention, suggesting a transfer of benefits to cognitive abilities most affected by aging. The study also showed multitasking training-induced increases in midline frontal theta power in the electroencephalography (EEG), positively correlated with sustained multitasking performance improvements and sustained attention, and the signature EEG change continued for six years.

Some studies investigate the effect of cognitive training in non-surgical adults with preexisting cognitive impairment. Hill et al used a meta-analysis and reported that computerized cognitive training improved cognitive functions in older adults with mild cognitive impairment; the effect size was more significant than that for older adults without mild cognitive impairment.[78,79] Another study suggests that traditional paper-based cognitive training (60-min 24 sessions over 12 weeks) improved cognitive functions in multiple domains in patients with early-stage Alzheimer's disease (mean age: 68.9 years old, diagnosis at 66.4 years old) compared to the control patients without training.[80] Overall, these studies in older non-surgical populations show the long-lasting effects of cognitive training using a variety of platforms. The duration and dosage of the training seem more extensive than that used in the preoperative studies.

Conclusion

Evidence of the effects of preoperative cognitive optimization in older adult surgical patients is limited. Preoperative brain exercise is shown to reduce the incidence of POD in older adult noncardiac and nonneurological surgical patients, as shown in a randomized single-blinded clinical trial.[55] The study used a tablet-based cognitive exercise targeting memory, attention, processing speed, flexibility, and problem-solving functions for at least 10 days before surgery. Three clinical studies using a randomized control group suggest the benefit of preoperative cognitive training (3 days to 8 weeks) for reducing postoperative cognitive impairment.[56–58] Contrarily, a prospective randomized controlled trial demonstrated that cognitive training provided both *pre*operatively and *post*operatively did not change cognitive outcomes in older patients undergoing coronary artery bypass grafting surgery.[59]

Still, many questions need to be answered to determine whether cognitive training programs are beneficial to reduce postoperative cognitive impairment. First, the studies discussed above have used multi-domain cognitive training for various durations (up to 8 weeks) on different platforms. Future studies are needed on the dosage- and duration-response and comparing the platform types of cognitive training. Secondly, patients with cognitive impairment, neurological disease, or psychiatric illness are mostly excluded from current preoperative studies. These vulnerable patients may most benefit from cognitive training. Future research is needed on whether preoperative cognitive training can improve postoperative outcomes in patients with preexisting cognitive impairment.

Lastly, long-lasting cognitive improvement after cognitive training in the non-surgical older population suggests brain plasticity in older adults and supports using cognitive training in the older surgical population. The studies in non-surgical populations appear to have used intense training over a long period (4–10 weeks),[73–75] suggesting that the extended training period may be necessary for preoperative patients. Furthermore, some studies investigated the effect of cognitive training in non-surgical adults with preexisting cognitive impairment, including early-stage Alzheimer's disease, and demonstrated improved cognitive functions,[78–80] encouraging the inclusion of the patients with preexisting cognitive impairment in preoperative cognitive training.

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