2025 American Society of Anesthesiologists Practice Advisory for Perioperative Care of Older Adults Scheduled for Inpatient Surgery

Frederick Sieber, M.D., Daniel I. McIsaac, M.D., M.P.H., Stacie Deiner, M.D., Tangwan Azefor, M.D., Miles Berger, M.D., Ph.D., Christopher Hughes, M.D., M.S., Jacqueline M. Leung, M.D., M.P.H., John Maldon, B.A., Julie R. McSwain, M.D., M.P.H., Mark D. Neuman, M.D., M.Sc., Marcia M. Russell, M.D., Victoria Tang, M.D., Elizabeth Whitlock, M.D., M.S., Robert Whittington, M.D., Anne M. Marbella, M.S., Madhulika Agarkar, M.P.H., Stephanie Ramirez, M.A., Alexandre Dyer, M.P.H., Jaime Friel Blanck, M.L.I.S., M.P.A., Stacey Uhl, M.S., Mark D. Grant, M.D., Ph.D., Karen B. Domino, M.D., M.P.H.

Anesthesiology 2025; 142:22–51

Practice advisories are systematically developed recommendations that assist anesthesiologists and patients in making decisions about health care. These recommendations may be adopted, modified, or rejected according to clinical needs and constraints and are not intended to replace local institutional policies. In addition, practice advisories developed by the American Society of Anesthesiologists (ASA; Schaumburg, Illinois) are not intended as standards, absolute requirements, or guidelines, and their use cannot guarantee any specific outcome. Practice advisories are subject to revision as warranted by the evolution of medical knowledge, technology, and practice. They provide basic recommendations supported by a synthesis and analysis of the current literature, expert and practitioner opinion, public comment, and clinical feasibility data.

Purpose

This advisory provides evidence-based recommendations regarding the management of older adults undergoing inpatient surgery. Recommendations concerning care of ambulatory surgical patients were not made as the scientific evidence only focused on inpatient surgery.

The focus of this advisory includes aspects of preoperative, intraoperative, and postoperative care of specific relevance to older adults, *i.e.*, 65 yr or older. The advisory

This article is featured in "This Month in Anesthesiology," page A1. Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTML text of this article on the Journal's Web site (www.anesthesiology.org).

Submitted for publication April 30, 2024. Accepted for publication July 5, 2024.

Frederick Sieber, M.D.: Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Hospital, Baltimore, Maryland.

Daniel I. McIsaac, M.D., M.P.H.: Department of Anesthesiology and Pain Medicine, University of Ottawa, Ottawa, Canada.

Stacie Deiner, M.D.: Department of Anesthesiology, Geisel School of Medicine and Dartmouth Health, Hanover, New Hampshire.

Tangwan Azefor, M.D.: Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Hospital, Baltimore, Maryland.

Miles Berger, M.D., Ph.D.: Department of Anesthesiology, Duke University Medical Center, Durham, North Carolina.

Christopher Hughes, M.D., M.S.: Department of Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee.

Jacqueline M. Leung, M.D., M.P.H.: Department of Anesthesia and Perioperative Care, University of California-San Francisco, San Francisco, California.

John Maldon, B.A.: Washington Medical Commission, Seattle, Washington.

Julie R. McSwain, M.D., M.P.H.: Department of Anesthesia and Perioperative Medicine, Medical University of South Carolina, Charleston, South Carolina.

Mark D. Neuman, M.D., M.Sc.: Department of Anesthesiology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania.

Marcia M. Russell, M.D.: Department of Surgery, David Geffen School of Medicine, University of California-Los Angeles, Los Angeles, California; Veterans Affairs Greater Los Angeles Health Care System, Los Angeles, California.

Victoria Tang, M.D.: Division of Geriatric Medicine, Department of Medicine, University of California-San Francisco, San Francisco, California.

Elizabeth Whitlock, M.D., M.S.: Department of Anesthesia and Perioperative Care, University of California-San Francisco, San Francisco, California.

Robert Whittington, M.D.: Department of Anesthesiology and Perioperative Medicine, David Geffen School of Medicine, University of California-Los Angeles, Los Angeles, California.

Anne M. Marbella, M.S.: American Society of Anesthesiologists, Schaumburg, Illinois.

Madhulika Agarkar, M.P.H.: American Society of Anesthesiologists, Schaumburg, Illinois.

Stephanie Ramirez, M.A.: American Society of Anesthesiologists, Schaumburg, Illinois.

Alexandre Dyer, M.P.H.: American Society of Anesthesiologists, Schaumburg, Illinois.

Jaime Friel Blanck, M.L.I.S., M.P.A.: Welch Medical Library, Johns Hopkins University, Baltimore, Maryland.

Stacey Uhl, M.S.: American Society of Anesthesiologists, Schaumburg, Illinois.

Mark D. Grant, M.D., Ph.D.: Division of Epidemiology and Biostatistics, University of Chicago, Chicago, Illinois.

Karen B. Domino, M.D., M.P.H.: Committee on Practice Parameters, American Society of Anesthesiologists, Schaumburg, Illinois; Department of Anesthesiology & Pain Medicine, University of Washington, Seattle, Washington.

 Anesthesiology 2025; 142:22–51. DOI: 10.1097/ALN.0000000000005172

addresses approaches to minimizing complications of anesthesia common among older patients.

Background

Improving the quality of perioperative care for older adults is a major priority for healthcare providers, policy makers, and the public. In the next 30 years, the population of U.S. adults aged 65 yr and older will double (from 46 to 98 million).[1] The U.S. population 85 yr and older will triple (from 6 to 20 million).[1] Even though adults older than 65 yr comprise only 15% of the U.S. population, they undergo more than 30% of all inpatient[2] and outpatient surgeries.[3] This demographic shift means that anesthesiologists will increasingly be asked to care for older surgical patients, who are at much greater risk of adverse postoperative outcomes than younger patients.

Preserving independence is a vital goal for older adults undergoing surgery. However, age-related physiologic changes, comorbidities, cognitive decline, frailty, and the surgical stress response all contribute to postoperative complications, prolonged hospital stays, and resulting decline in functional abilities and cognitive recovery.[4] Unfortunately, loss of independence is common in older adults after surgery, with the incidence increasing with age. Nineteen percent of patients aged 80 to 89 yr and 26% of patients 90 yr or older exhibited functional decline that persisted for 30 days after a surgical procedure.[5] While the postsurgical decline may be temporary, many older adults do not recover from this loss in function. Thirty-five percent of older adults with a new disability after surgery have no recovery 6 months later.[6] These findings highlight the vulnerability of older patients who are undergoing surgery. The results also pinpoint the need for targeted perioperative interventions to preserve the independence of older adults.

Neurocognitive Disorders

With more older patients presenting for surgery, anesthesiologists will routinely be required to care for patients with preoperative neurocognitive disorders. A preoperative neurocognitive disorder increases the risk of delayed neurocognitive recovery after surgery. Previously diagnosed neurocognitive disorders were present in 18% of older patients scheduled for elective noncardiac surgery.[7] Additionally, 37% of patients without known neurocognitive deficits were found to have significant cognitive impairment on preoperative testing.[7]

Preoperative neurocognitive disorders are associated with a greater likelihood of developing postoperative delirium.[8,9] Postoperative delirium is associated with adverse in-hospital and patient-reported outcomes.[8,9] Patients who experience postoperative delirium have more impaired functional recovery in the month after surgery than their counterparts without delirium.[10] Delirium is associated with long-term cognitive decline.[11] Cognitive decline after surgery is also associated with loss of ability to perform independent activities of daily living.[10] These findings highlight the importance of recognizing and addressing preoperative neurocognitive disorders in older patients, as emphasized by the ASA Perioperative Brain Health Initiative.[12]

Frailty

Frailty is a multidimensional loss of reserve due to accumulation of age- and disease-related deficits.[13] Because older adults with frailty live with multidimensional deficits, they are vulnerable to even minor stressors. Faced with the major physical, physiologic, and psychosocial stressors of invasive procedures and surgery, people with frailty represent one of the highest risk strata of the perioperative population in terms of their risks of major morbidity, delirium, cognitive decline, impaired functional recovery, and mortality. Specifically, frailty is associated with a two- to fivefold greater risk of complications, mortality, nonhome discharge, and development of a new disability.[14] Preoperative frailty is also one of the strongest predictors of postoperative delirium, increasing risk more than fourfold.[15,16]

The overall prevalence of frailty in older patients living in the community averages 10.7%, but varies considerably depending on the operationalization of frailty status.[17] The prevalence of frailty increases with age.[17,18] Frailty rates are higher in African American[18] and female patients.[17,18] Patients with less education, lower income, and poorer health also have a higher prevalence of frailty.[18] Twenty-five percent to 40% of older surgical patients live with a meaningful degree of frailty before surgery,[14] a higher prevalence than among older patients living in the community.[18] Thus, anesthesiologists will encounter frailty among surgical patients at a much greater rate than in age-matched older adults not having surgery.

Frailty can be identified using one of several instruments, including the Risk Analysis Index, Clinical Frailty Scale, Fried Phenotype, Frailty Index, or Edmonton Frail Scale. Preoperative identification of frailty status may allow optimization of one or more of the deficits present in physical, cognitive, nutritional, and/or mental health domains before surgery.[14,19]

Possible Methods to Improve Postoperative Outcomes

A variety of approaches might improve surgical outcomes in older adults. These approaches include enhanced preoperative assessment, optimal choice of primary anesthetic technique, and pharmacologic regimens specifically tailored to the needs of older patients. Enhanced preoperative assessment of older adults may include a focus on frailty, mood and anxiety issues, malnutrition risk, baseline function, polypharmacy, and preoperative cognition status.[20] Intraoperatively, management of the older patient entails its own set of considerations. The role of anesthetic technique in determining postoperative outcomes remains debated. Recent multicenter trials have failed to prove superiority of either neuraxial or general anesthesia, at least in patients with hip fractures.[21] Similarly, whether maintenance of general anesthesia with inhaled anesthesia or total intravenous anesthesia enhances recovery is not known.[22]

Other key questions in perioperative pharmacology for the older patient include considerations of medications with potential delirium prophylaxis and medications with central nervous system effects.[23] While a trend toward elimination of perioperative administration of these drugs is emerging, questions remain as to the management of patients with chronic use, and the safety of drug discontinuation immediately before surgery. Questions remain as to whether use of certain drugs, such as α_2 agonists, may reduce the incidence and/or severity of delirium in older patients having anesthesia and surgery.

While acknowledging the potential importance of anesthesia depth monitoring and postoperative pain management in preventing complications like delirium in older adults, these topics were not addressed in this advisory due to the limited and conflicting nature of the available evidence. Evidence from both meta-analyses[24,25] and recent randomized clinical trials conducted in East Asia[26] and Spain[27] suggested that processed electroencephalogram (EEG) monitoring may reduce the incidence of postoperative delirium and hospital stay. On the other hand, large randomized clinical trials conducted in North America (Electroencephalography Guidance of Anesthesia to Alleviate Geriatric Syndromes [ENGAGES][28,29] and SHaping Anesthesia techniques to Reduce Post-operative delirium [SHARP][30]) failed to demonstrate a clear benefit of EEG-guided anesthetic depth reduction on postoperative delirium in older adults undergoing major surgery. Additionally, no reduction in 1-yr mortality was observed.[31] There is an ongoing debate regarding the specific link between deep anesthesia and delirium, suggesting that baseline patient vulnerabilities might be more influential.[32–35] While adequate postoperative pain control is widely recognized as crucial,[36] there is a scarcity of high-quality research (randomized clinical trials) to definitively determine its impact on delirium in older adults.

Both the ASA Brain Health Initiative[12] and a recent brain health statement[37] offer recommendations based on expert and practitioner experience for putting a brain health program into action, specifically focusing on perioperative care for older adults. However, unlike these initiatives, this practice advisory seeks to address specific clinical management questions about anesthesia for older adults and develop recommendations for practice that are based on a systematic review and meta-analysis of relevant literature that includes using a known approach to grading the quality of evidence and strength of recommendations.

Recommendations

Recommendation	Strength of Recommendation	Strength of Evidence
1. Consider expanded preoperative evaluation in older adults scheduled for inpatient procedures to reduce the risk of postoperative delirium. If patients are identified with cognitive impairment and/or frailty, changes in patient care can be initiated. These changes include, but are not limited to, involvement of a multidisciplinary care team and geriatrician or geriatric nurse visits, and patient and family education on postoperative delirium risk.	Conditional	Low
2. We recommend choosing either neuraxial or general anesthesia for older adults when either is clinically appropriate, based on shared decision-making. The evidence suggests no superiority with either technique in reducing postoperative delirium.	Strong	Moderate
3. Either total intravenous or inhaled anesthesia is acceptable for general anesthesia in the older population. The evidence is inconclusive with respect to the comparative risk of postoperative delirium.	Conditional	Low
4. Among older patients scheduled for inpatient procedures, it is reasonable to consider dexmedetomidine to lower risk of postoperative delirium while also considering its effects on bradycardia and/or hypotension.	Conditional	Moderate

Best Practice Statement

Consider the risks and benefits of medications with potential central nervous system effects in older adults, as these drugs may increase the risk of postoperative delirium.

Materials and Methods

The advisory task force included physicians (anesthesiologists with expertise in caring for older adults, a geriatrician, and a geriatric surgeon), a patient representative, and epidemiology-trained methodologists. ASA requires all task force members to disclose all relationships that might pose a conflict of interest. None of the disclosed relationships posed a conflict. The task force was responsible for developing key questions; defining the patient populations, interventions, comparators, and outcomes for each key question; and determining the importance of each outcome in relation to the decision-making process (Supplemental Digital Content 1, Protocol, https://links.lww.com/ALN/D638). A scale of 1 to 9 (1 to 3, limited importance; 4 to 6, important; and 7 to 9, critical)[38] was used to survey the task force. The evidence synthesis focused on outcomes rated as critical and important.

The systematic review supporting the development of the recommendations in this advisory was guided by the following key questions:

- Key Question 1: Among older patients undergoing inpatient surgery and anesthesia, does expanded preoperative

evaluation that includes frailty, cognitive impairment, physical function, or psychosocial screening lead to improved postoperative outcomes?
- Key Question 2: Among older patients undergoing surgery, does neuraxial anesthesia as the primary anesthetic technique improve postoperative outcomes compared with general anesthesia?
- Key Question 3: Among older patients undergoing surgery with general anesthesia, does intravenous anesthesia for maintenance improve postoperative outcomes compared with inhaled volatile anesthesia?
- Key Question 4: Among older patients undergoing surgery and anesthesia, does dexmedetomidine administered during the perioperative period decrease the risk of postoperative delirium or other adverse cognitive outcomes?
- Key Question 5: Among older patients undergoing surgery and anesthesia, do medications with potential central nervous system effects (*i.e.*, benzodiazepines, antipsychotics, anticholinergics, ketamine, corticosteroids, gabapentin, or nonsteroidal anti-inflammatory drugs [NSAIDs]) administered during the perioperative period increase the risk of postoperative delirium or other adverse outcomes?

In the next section, we define the populations, interventions, comparators, and outcomes for each key question.

Populations, Interventions, Comparators, and Outcomes

- Population: The target population included older adults scheduled for or undergoing surgery with general or neuraxial anesthesia. This population can be defined by age (65 yr or older), as the review concerns clinically important age-dependent loss of physiologic or cognitive reserves. However, limiting study inclusion to only those enrolling participants 65 yr or older would have significantly narrowed the evidence base. Accordingly, we defined age-based inclusion criteria as (1) enrolled only patients 65 yr or older, (2) enrolled patients with a mean age 65 yr or older, (3) reported subgroup analysis for patients 65 yr or older, or (4) enrolled patients with a mean age 60 to 65 yr with either the upper bound of range 80 yr or older or twice the standard deviation greater than or equal to 80 yr.
- Interventions and comparators
    - Key Question 1: Preoperative evaluations including frailty, cognitive, functional, psychosocial, nutritional assessments, involvement of a multidisciplinary hospital team, and review of current medications and comorbidities *versus* standard preoperative evaluation
    - Key Question 2: Neuraxial *versus* general anesthesia
    - Key Question 3: Total intravenous *versus* inhaled anesthesia
    - Key Question 4: Dexmedetomidine, melatonin, or melatonin receptor agonists (*e.g.*, ramelteon) for delirium prophylaxis *versus* none
    - Key Question 5: Medications with potential central nervous system effects (*i.e.*, benzodiazepines, antipsychotics, anticholinergics, corticosteroids, H_2-receptor agonists, NSAIDs, ketamine, and gabapentin) *versus* none
- Outcomes: Critical outcomes included postoperative delirium, neurocognitive disorder less than 30 days, and neurocognitive disorder 30 days or more to 1 yr. Assessment tools for postoperative delirium included but were not limited to the Confusion Assessment Method, Confusion Assessment Method–Intensive Care Unit, Delirium Rating Scale, Diagnostic and Statistical Manual of Mental Disorders, and Intensive Care Delirium Screening Checklist. Assessment tools for neurocognitive disorder included but were not limited to the Mini-Mental State Examination, Montreal Cognitive Assessment, and Digit Span Test. Other outcomes rated as important included discharge location (institution *vs.* independent living), complications, physical function, patient and/or caregiver satisfaction, length of stay, and mortality.

Literature Search

Comprehensive searches were conducted per key question by a medical librarian for literature published from January 2000 through June 2023 and updated in October 2023 using the following databases: PubMed, Embase, Scopus, and Cochrane. The search start date was chosen to preserve applicability of results (the restriction is unlikely to meaningfully reduce search sensitivity).[39] In addition, task force members provided relevant references; citations in systematic reviews and meta-analyses were hand-searched; and trial registries were queried. The literature search strategy and Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) are available in the Supplemental Digital Content (Supplemental Digital Content 2, Search Strategy, https://links.lww.com/ALN/D639; and Supplemental Digital Content 3, PRISMA Flow Chart, https://links.lww.com/ALN/D640). The methodologies used for this advisory for study screening, data extraction, and data management are

Table 1. GRADE Strength of Evidence Definitions

GRADE	Interpretation
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

GRADE, Grading of Recommendations, Assessment, Development, and Evaluation.

similar to the methodology implemented in previous ASA guidelines[40,41] and are described in the systematic review protocol (Supplemental Digital Content 1, Protocol, https://links.lww.com/ALN/D638; and Supplemental Digital Content 4, Methodology, https://links.lww.com/ALN/D641). Methodology specific to this advisory or requiring additional emphasis is presented below.

Risk of Bias Assessment

Risk of bias for individual studies was evaluated using tools relevant for the study design: for randomized clinical trials, the Cochrane risk of bias tool, version 2, and for nonrandomized studies, ROBINS-I (Risk of Bias in Non-randomised Studies–or Interventions)[42,43] (Supplemental Digital Content 5, Risk of Bias, https://links.lww.com/ALN/D642).

Evidence Synthesis

The body of evidence was first described according to overall study characteristics and treatment arms. Results were then summarized in tabular form by outcome. When relevant, decision-informative, and practicable, pairwise, and network meta-analyses were performed. Analyses were conducted in R.[44] Details concerning the meta-analyses can be found in Supplemental Digital Content 4, Methodology (https://links.lww.com/ALN/D641; *e.g.*, choice of effect measure, pooling method, between-study variance estimators, examination of small study effects, prediction intervals, and other considerations).

Strength of Evidence

Methodologists rated the overall strength of evidence by comparators and outcome using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) system of rating evidence from high to very low (table 1). Evidence from randomized clinical trials starts at high strength of evidence, and evidence from nonrandomized studies starts at low. The strength was downgraded based on summary study–level risk of bias, inconsistency, indirectness, imprecision, and other considerations including small study effect due to suspected publication bias (Supplemental Digital Content 4, Methodology, https://links.lww.com/ALN/D641).[45]

Strength of Recommendations

For each key question, results of the evidence synthesis for important benefits and harms were summarized. Randomized clinical trials were prioritized for analysis when assessing outcomes and developing the recommendations. Nonrandomized studies, including before–after/time series, cohort, and case–control designs,[46] were only analyzed when insufficient numbers of randomized clinical trials were available to evaluate harms and for supportive confirmatory evidence. After reviewing the evidence summary and relevant details, the task force developed recommendations and rated the corresponding strength of the recommendations consistent with the body of evidence (table 2).

Expanded Preoperative Evaluation *versus* Standard Evaluation

Key Question

Among older patients undergoing inpatient surgery and anesthesia, does expanded preoperative evaluation that includes frailty, cognitive impairment, physical function, or psychosocial screening lead to improved postoperative outcomes?

Recommendation

Consider expanded preoperative evaluation in older adults scheduled for inpatient procedures to reduce the risk of postoperative delirium. If patients are identified with cognitive impairment and/or frailty, changes in patient care can be initiated. These changes include, but are not limited to, involvement of a multidisciplinary care team and geriatrician or geriatric nurse visits, and patient and family education on postoperative delirium risk.

- Strength of evidence: Low
- Strength of recommendation: Conditional

Summary of Evidence for Critical and Important Outcomes

Pooled results from six randomized trials suggest lower risk of postoperative delirium for patients receiving expanded preoperative evaluation (risk ratio, 0.77; 95% CI, 0.60 to 0.99; table 3).[47–52] Evidence from nonrandomized studies supports this effect (Supplemental Digital Content 6, Supporting Evidence, https://links.lww.com/ALN/D643).[53–60] The strength of the evidence for delirium was rated low due to limitations in study level risk of bias and potential publication bias due to small study effects (Supplemental Digital Content 6, Supporting Evidence, https://links.lww.com/ALN/D643). Evidence for other critical outcomes was limited. The findings of one nonrandomized study suggest no difference in neurocognitive disorders less than 30 days between patients receiving expanded *versus* standard preoperative evaluation (table 3).[54] No studies were identified for neurocognitive disorders from 30 days or more to 1 yr. Evidence for other outcomes is presented in table 3 and discussed in the appendix and Supplemental Digital Content 6, Supporting Evidence (https://links.lww.com/ALN/D643).

Comment

A review of the evidence suggests that older patients undergoing inpatient surgeries who received one or more preoperative

Table 2. Strength of Recommendations Definitions

Strength of Recommendation	Level of Evidence	Interpretation
Strong	High to moderate	Task force believes that all or almost all clinicians would choose (or not) the specific action or approach.
Conditional	Low to very low	Task force believes that most, but not all, would choose (or not choose) the action or approach.
Best practice statements	Ungraded	Best practice statements are statements for which there is sparse direct evidence or limitations in the available evidence that does not make them amenable to the GRADE process. However, they may be valuable for anesthesiologists to consider in the management of patient care.

GRADE, Grading of Recommendations, Assessment, Development, and Evaluation.

Table 3. Summary and Strength of Evidence for Critical and Important Outcomes in Studies Evaluating Expanded Preoperative Evaluation Compared to Standard Care

			Expanded	Standard		Effect		
Outcome	Randomized Clinical Trials	Nonrandomized Studies	n (Total)	n (Total)	Strength of Evidence	Measure	Estimate (95% CI)	I^2
Delirium	6		189 (662)	253 (703)	Low	Risk ratio	0.77 (0.60 to 0.99)	26%
Neurocognitive disorder < 30 days		1	13 (96)	16 (84)	Very low	Risk ratio	0.71 (0.36 to 1.39)	
Neurocognitive disorder ≥ 30 days to 1 yr	0	0						
Physical function	5		(563)	(576)	Very low	Standardized mean difference	0.09 (–0.16 to 0.31)	71%
Complications*	4	9			Very low		See Supplement 6†	
Patient satisfaction		1	32 (32)	29 (30)	Very low	Risk difference‡	3.3 (–5.3 to 12.0)§	
Length of stay (days)	8		(968)	(1001)	Very low	Mean difference	0.0 (–1.7 to 1.7)	94%
Discharged to institution	4		252 (419)	271 (424)	Low	Risk ratio	0.98 (0.76 to 1.27)	80%
Mortality (in-hospital and 30-day)	4		19 (498)	19 (526)	Very low	Risk ratio	1.02 (0.30 to 3.53)	60%

*Cardiovascular, pulmonary, and acute kidney injury. †https://links.lww.com/ALN/D643. ‡Per 100. §High *vs.* lower satisfaction.

evaluations for frailty, cognitive impairment, physical function, nutrition, and psychosocial issues may experience lower rates of delirium. Although the studies are heterogeneous in the combinations of components used in the preoperative evaluations for older patients, what was consistent among the studies was the gathering of information in a systematic manner. This approach provided the care team with knowledge about the patients' comorbidities and health vulnerabilities before surgery. Comprehensive geriatric assessment[48–52] evaluated comorbidities, nutritional status, physical activity, and cognitive function, and uncovered improvement opportunities such as comanagement, fall prevention, and medication management. The ASA task force's recommendations are consistent with recommendations from a systematic review of 13 other clinical practice guidelines for care of older adults living with frailty.[61]

Changes in Patient Care Resulting from Expanded Preoperative Assessment

Interventions for patients identified as cognitively impaired, psychologically vulnerable, nutritionally compromised, and/or frail differed among the studies. Interventions described in the randomized and nonrandomized studies included but were not limited to multidisciplinary team involvement in 26 of 31 (84%) of the studies, de-prescribing in 13 of 31 (42%) studies, nutritional supplementation in 9 of 31 (29%) studies, and geriatric visits in 11 of 31 studies (35%). Four of 31 (13%) studies reported an active delirium screen. Multidisciplinary care may include but is not limited to hospitalists, geriatric nurse champions, psychiatry, pharmacy, physical/occupational therapy, nutritionists, chaplaincy, and volunteer services. Optimized care of chronic medical conditions occurred in the inpatient[50,52] and outpatient settings, as well as during the prehospital phase.[55] Treatment plans for at-risk patients involved geriatric care throughout hospitalization, with some implementing daily visits,[48,50] and others occurring at prescribed stages of the study.

Research Gaps

There is a need for well-designed randomized clinical trials assessing the effects of preoperative frailty screening, cognitive evaluation, and nutritional assessments on postoperative outcomes in older patients. There is also a need for studies evaluating the interventions implemented after identification of an at-risk patient.

Neuraxial *versus* General Anesthesia

Key Question

Among older patients undergoing surgery, does neuraxial anesthesia as the primary anesthetic technique improve postoperative outcomes compared with general anesthesia?

Recommendation

We recommend choosing either neuraxial or general anesthesia for older adults when either is clinically appropriate, based on shared decision-making. The evidence suggests no superiority with either technique in reducing postoperative delirium.

- Strength of recommendation: Strong
- Strength of evidence: Moderate

Summary of Evidence for Critical and Important Outcomes

The evidence synthesis found neither neuraxial nor general anesthesia accompanied by a lower risk for delirium (table 4). This finding was similar in the subgroup of patients undergoing hip fracture repair (risk ratio, 1.05; 95% CI, 0.76 to 1.43),[21,62–66] and non–hip fracture procedures (risk ratio, 0.74; 95% CI, 0.35 to 1.60).[67–70] The strength of evidence for delirium was rated moderate due to concerns related to imprecision of the effect estimate (*i.e.*, CI compatible with either neuraxial or general anesthesia being favored). Evidence concerning neurocognitive disorders less than 30 days and 30 days or greater to 1 yr was limited but also did not favor either primary anesthetic approach.[70–73] Evidence for important and limited outcomes is presented in table 4 and further discussed in the appendix and Supplemental Digital Content 6, Supporting Evidence (https://links.lww.com/ALN/D643).

Comment

These results, obtained from randomized clinical trials of mostly patients with hip fractures, support the conclusion that the choice of neuraxial or general anesthesia is unlikely to affect the risk of delirium. Accordingly, anesthesiologists should consider individual patient preferences and characteristics when choosing an optimal primary anesthetic technique. Regarding complications on other organ systems, neuraxial anesthesia may reduce risk of acute kidney injury/failure[21,64,67,74] and pneumonia.[21,62–64,67,74,75] However, the strength of the evidence was low to very low in these studies, and confirmatory trials are necessary. In contrast to settings in which a single choice has overriding benefits *versus* others, the choice between neuraxial and general anesthesia for hip fracture is likely to involve tradeoffs for most patients. As a result, this is likely to be a "preference-sensitive" decision in many cases and a suitable target for shared decision-making.[76]

Research Gaps

When comparing neuraxial *versus* general anesthesia, there was a lack of randomized clinical trials that included patient-centered outcomes such as physical function and patient satisfaction. As these outcomes are important for decision-making, future studies should consider assessing these measures.

Total Intravenous Anesthesia *versus* Inhaled Volatile Anesthesia

Key Question

Among older patients undergoing surgery with general anesthesia, does intravenous anesthesia for maintenance improve postoperative outcomes compared with inhaled volatile anesthesia?

Recommendations

Either total intravenous or inhaled anesthesia is acceptable for general anesthesia in the older population. The evidence is inconclusive with respect to the comparative risk of postoperative delirium.

- Strength of recommendation: Conditional
- Strength of evidence: Low

Summary of Evidence for Critical and Important Outcomes

The pooled estimate from eight randomized clinical trials did not favor total intravenous or inhaled anesthesia with respect to risk of postoperative delirium.[77–84] The overall strength of evidence rating for delirium was rated low due to limitations in study level risk of bias and imprecision of the effect estimate (*i.e.*, wide CI). And while the pooled estimate from five randomized clinical trials suggests lower risk of neurocognitive disorder up to 30 days postprocedure for patients receiving total intravenous anesthesia, the evidence was limited by variability in how (*e.g.*, differences in scales and thresholds) and when (*e.g.*, day of ascertainment) this outcome was measured.[85–89] A single randomized clinical trial[90] and three nonrandomized studies[91–93] assessed the effects of total intravenous *versus* inhaled agents on neurocognitive disorder at 30 days or more to 1 yr and did not detect a difference (table 5). Evidence for important and limited outcomes is discussed in the appendix and

Table 4. Summary and Strength of Evidence for Critical and Important Outcomes in Studies Evaluating Neuraxial Compared to General Anesthesia

		Neuraxial	General		Effect		
Outcome	Randomized Clinical Trials	n (Total)	n (Total)	Strength of Evidence	Measure	Estimate (95% CI)	I^2
Delirium	10	215 (1,840)	213 (1,908)	Moderate	Risk ratio	1.06 (0.84 to 1.33)	21%
Neurocognitive disorder < 30 days	4	78 (336)	88 (355)	Low	Risk ratio	0.91 (0.56 to 1.48)	52%
Neurocognitive disorder ≥ 30 days to 1 yr	1	23 (176)	25 (188)	Very low	Risk ratio	0.98 (0.58 to 1.67)	
Physical function	3	(355)	(371)	Very low	Standardized mean difference	0.01 (–0.39 to 0.42)*	85%
Complications†	13			Low/very low		See Supplement 6‡	
Patient satisfaction	10	913 (1,055)	839 (991)	Low	Risk ratio	1.02 (0.98 to 1.05)§	46%
Length of stay (days)	13	(2,355)	(2,373)	Low	Mean difference	–0.4 (–1.1 to 0.3)	97%
Discharged to institution	1	576 (777)	586 (777)	Very low	Risk ratio	0.98 (0.93 to 1.04)	
Mortality (in-hospital and 30-day)	6	19 (1,789)	31 (1,859)	Low	Risk ratio	0.66 (0.28 to 1.50)	9%

*Using Neuman 2021 primary result of inability to walk 60 feet without human assistance in a sensitivity analysis including 1,644 patients yielded a pooled standardized mean difference of –0.07 (95% CI, –0.25 to 0.12).[21] †Cardiovascular, pulmonary, and acute kidney injury. ‡https://links.lww.com/ALN/D643. §Comparing higher/highest category or categories compared to lower ones.

Supplemental Digital Content 6, Supporting Evidence (https://links.lww.com/ALN/D643).

Comment

The complexity of surgical procedures across diverse studies complicates direct outcome comparisons between total intravenous and inhaled anesthesia for both delirium and delayed neurocognitive recovery. Consequently, drawing definitive conclusions about the specific impact of surgery type on these outcomes proves challenging. Pooled estimates of randomized clinical trials did not demonstrate differences in delirium rates between total intravenous and inhaled anesthesia. And while low strength of evidence suggests that total intravenous anesthesia is associated with a decrease in neurocognitive disorder up to 30 days postprocedure, the findings are not consistent at later time points. There were limited randomized clinical trials comparing complications between total intravenous anesthesia and inhalational anesthesia. Most evidence suggests no difference in complications studied except for low-grade evidence favoring decreased pulmonary embolism[77,94–97] and respiratory failure[77,90,96,97] associated with total intravenous anesthesia. Further, data suggest that patients undergoing ophthalmologic or gastrointestinal/abdominal surgery and receiving total intravenous anesthesia tend to report higher satisfaction levels compared to those receiving inhaled anesthesia (appendix). Notably, these findings are specific to certain surgical procedures and patient populations.

Research Gaps

Additional well-designed randomized clinical trials in older adults comparing total intravenous anesthesia to inhaled agents across various procedures are needed, as inconsistencies are present in the current evidence base. Trials building on the recently published feasibility pilot trial Trajectories of Recovery after Intravenous Propofol *versus* Inhaled VolatilE anesthesia,[98] funded by the Patient-Centered Outcomes Research Institute (Washington, D.C.), are needed.

Pharmacologic Delirium Prevention

Key Question

Among older patients undergoing surgery and anesthesia, does dexmedetomidine administered during the perioperative period decrease the risk of postoperative delirium or other adverse cognitive outcomes?

Recommendation

Among older patients scheduled for inpatient procedures, it is reasonable to consider dexmedetomidine to lower risk of postoperative delirium while also considering its effects on bradycardia and/or hypotension.

- Strength of recommendation: Conditional
- Strength of evidence: Moderate

Summary of Evidence for Critical and Important Outcomes

Pooled results of 31 randomized clinical trials suggested that patients receiving dexmedetomidine may experience lower postoperative delirium compared with patients receiving placebo or no intervention (risk ratio, 0.58; 95% CI, 0.49 to 0.67). The overall strength of the evidence was rated

Table 5. Summary and Strength of Evidence for Critical and Important Outcomes in Studies Evaluating Total Intravenous Anesthesia Compared to General Anesthesia with Inhaled Anesthesia Volatiles

			Total Intravenous Anesthesia	Inhalation		Effect		
Outcome	Randomized Clinical Trials	Nonrandomized Studies	n (Total)	n (Total)	Strength of Evidence	Measure	Estimate (95% CI)	I^2
Delirium	8		143 (1,001)	158 (995)	Low	Risk ratio	0.94 (0.62 to 1.43)	46%
Neurocognitive disorder < 30 days	5		125 (704)	175 (703)	Moderate	Risk ratio	0.72 (0.54 to 0.96)	22%
Neurocognitive disorder ≥ 30 days to 1 yr	1		4 (96)	6 (97)	Very low	Risk ratio	0.67 (0.20 to 2.31)	
Physical function	0	0						
Complications*	10	9			Very low		See Supplement 6†	
Patient satisfaction	3		90 (109)	82 (141)	Low	Risk ratio	1.39 (1.19 to 1.63)‡	0%
Length of stay (days)	6		(1,343)	(1,341)	Very low	Mean difference	0.0 (–1.5 to 1.4)	75%
Discharged to institution		1	8 (9)	26 (20)	Very low	Risk ratio	1.46 (0.69 to 3.41)	
Mortality (in-hospital and 30-day)	4		11 (377)	8 (375)	Very low	Risk ratio	1.17 (0.47 to 2.89)	0%

*Cardiovascular, pulmonary, and acute kidney injury. †https://links.lww.com/ALN/D643. ‡Comparing higher/highest category or categories with lower ones.

moderate due primarily to limitations in study level risk of bias (table 6).[99–129] Similarly, pooled results of nine randomized clinical trials suggested lower incidence of neurocognitive disorder less than 30 days postprocedure among patients receiving dexmedetomidine,[119,129–136] and results of two small randomized clinical trials showed a reduction in neurocognitive disorder at 30 days or more to 1 yr (table 6).[100,137]

These findings, however, should be interpreted with consideration of an increased risk of bradycardia and hypotension associated with dexmedetomidine. A pooled analysis of 17 randomized clinical trials showed an increased risk of bradycardia in patients receiving dexmedetomidine,[102,107,109,114,115,119,122,123,128,129,133,138–143] and a pooled analysis of 20 randomized trials showed an increased risk of hypotension.[99,102,103,107,109,111,114,115,118,119,121,124,125,128,129,133,139–141,143,144] Evidence for other outcomes is presented in table 6 and further discussed in the appendix and Supplemental Digital Content 6, Supporting Evidence (https://links.lww.com/ALN/D643).

Comment

The body of evidence supports the role of dexmedetomidine in delirium prophylaxis—weighing the increased risks of hypotension and bradycardia. However, additional aspects of the evidence require consideration: varying effects by country, baseline risk, optimal dose and timing, potential publication bias, variation according to surgery, and optimal nonpharmacologic care to prevent delirium. First, stronger and more homogeneous effects were reported from trials conducted in China (figure 1). How completely those trial results generalize to all target populations is unclear. Next, the relative effect appeared to diminish with decreasing baseline risk; when the risk of delirium is low, the tradeoff between avoiding delirium *versus* hypotension and bradycardia will accordingly be less favorable. The timing of administration (*i.e.*, preoperatively, intraoperatively, or postoperatively) did not clearly modify results. We did not examine dose, but wide variations across trials were not apparent (Supplemental Digital Content 6, Supporting Evidence, https://links.lww.com/ALN/D643). Small-study effects were apparent with potential publication bias—the pooled result may overstate the true effect. However, we judged the severity of publication bias required to negate the results unlikely. Although the effect magnitudes were generally consistent across types of surgeries, the degree of heterogeneity varied considerably. For example, there was little variability in orthopedic and thoracic surgery trials but wide variation across cardiac trials and those including multiple procedures (Supplemental Digital Content 6, Supporting Evidence, https://links.lww.com/ALN/D643). Finally, the extent to which similar effects would have been observed in settings of optimal nonpharmacologic care diminishing baseline risk should be considered. In summary, although there is substantial evidence concerning dexmedetomidine for reducing the risk of delirium, the decision calculus is not entirely straightforward.

Research Gaps

Further randomized clinical trials need to be performed to determine what patient risk characteristics, type of surgery, doses/timing of administration, level of anesthesia, and use

Table 6. Summary and Strength of Evidence for Critical and Important Outcomes in Studies Evaluating Dexmedetomidine Compared to Placebo

Outcome	Randomized Clinical Trials	Dexmedetomidine n (Total)	Placebo n (Total)	Strength of Evidence	Effect: Measure	Effect: Estimate (95% CI)	Effect: I^2
Delirium—overall	31	457 (4,035)	666 (3,739)	Moderate	Risk ratio	0.58 (0.49 to 0.67)	46%
Neurocognitive disorder < 30 days	9	68 (666)	83 (392)	Moderate	Risk ratio	0.54 (0.39 to 0.73)	0%
Neurocognitive disorder ≥ 30 days to 1 yr	2	5 (50)	22 (50)	Very low	Risk ratio	0.24 (0.11 to 0.55)	0%
Physical function	1	(30)	(31)	Very low	Standardized mean difference	0.39 (–1.57 to 2.34)	
Bradycardia	17	236 (2,031)	129 (1,755)	High	Risk ratio	1.52 (1.22 to 1.88)	0%
Hypotension	20	611 (2,797)	409 (2,539)	High	Risk ratio	1.37 (1.11 to 1.69)	49%
Complications*	27					See Supplement 6†	
Length of stay (days)	20	(3,051)	(3,075)	Low	Mean difference	–0.8 (–1.3 to –0.2)	95%
Mortality (in-hospital and 30-day)	12	19 (2,345)	39 (2,424)	Low	Risk ratio	0.58 (0.32 to 1.04)	0%

*Cardiovascular, pulmonary, and acute kidney injury. †https://links.lww.com/ALN/D643.

of other medications are optimal to further our understanding of the use dexmedetomidine for reducing postoperative delirium.

Perioperative Use of Medications with Potential Central Nervous System Effects

Key Question

Among older patients undergoing surgery and anesthesia, do medications with potential central nervous system effects (*i.e.*, benzodiazepines, antipsychotics, anticholinergics, ketamine, corticosteroids, gabapentin, or NSAIDs) administered during the perioperative period increase the risk of postoperative delirium or other adverse outcomes?

Best Practice Statement

Consider the risks and benefits of medications with potential central nervous system effects in older adults, as these drugs may increase the risk of postoperative delirium.

- Strength of evidence: Not applicable

Summary of Evidence

Studies evaluating postoperative delirium when benzodiazepines, antipsychotics, anticholinergics, ketamine, corticosteroids, gabapentin, or NSAIDs are administered differed in drug administration timing and dosage. Postoperative delirium was measured using different scales and at different times during the postoperative period. Due to the heterogeneity of the studies, pooled analyses of postoperative delirium incidence could only be conducted for studies assessing ketamine. Below, we provide a brief narrative synthesis of select evidence for each drug. Evidence for important and limited outcomes is discussed in the appendix and Supplemental Digital Content 6, Supporting Evidence (https://links.lww.com/ALN/D643).

Benzodiazepines. Four randomized clinical trials[101,145–147] and four nonrandomized studies[148–151] did not detect a difference in delirium incidence comparing short-acting benzodiazepines with placebo or no drug. However, two large retrospective database studies reported lower incidence of delirium with short-acting benzodiazepines but a higher incidence with long-acting benzodiazepines.[152,153]

Antipsychotics. Five randomized clinical trials reported lower delirium incidence with antipsychotics *versus* placebo or no drug.[154–158] However, three randomized trials were inconclusive concerning delirium incidence.[159–161]

Ketamine. Pooled analysis of four randomized clinical trials comparing ketamine with placebo did not detect a difference in delirium.[160,162–164] Details on the full body of evidence are reported in the appendix.

Other Drugs.

- Two studies examined the use of anticholinergics. One small randomized clinical trial evaluated an anticholinergic not available in the United States,[165] and one retrospective study did not detect a difference in delirium incidence comparing any anticholinergic with placebo.[166]
- Four randomized clinical trials[167–170] were inconclusive concerning delirium incidence with corticosteroids *versus* placebo or no drug, while two randomized clinical trials[171,172] reported lower delirium incidence with corticosteroids *versus* no drug.

Subgroup	Studies	Dexmedetomidine Events/Total	Placebo/None Events/Total	I²	Risk Ratio (95% CI)
Country					
China	21	276/2714	465/2490	3%	0.54 (0.46–0.62)
Other	10	181/1321	201/1249	63%	0.68 (0.46–1.00)
Timing					
Postoperative only	5	87/962	142/979	26%	0.62 (0.41–0.94)
Post- ± pre- to intra-operative	8	184/1682	222/1710	66%	0.76 (0.52–1.11)
Pre- to intra- ± post-operative	26	370/3073	524/2760	50%	0.56 (0.47–0.67)
Pre- to intra-operative no postoperative	23	273/2353	444/2029	1%	0.52 (0.45–0.60)
Procedure Category					
Orthopedic	8	67/795	150/792	0%	0.45 (0.35–0.59)
Cardiac	7	126/962	137/975	62%	0.71 (0.42–1.21)
Gastrointestinal/Abdominal	3	48/491	65/373	62%	0.53 (0.24–1.18)
Thoracic	5	58/375	109/373	0%	0.53 (0.44–0.63)
Various (mixed)	6	121/1202	161/910	33%	0.56 (0.42–0.74)
Oral/Maxillofacial	1	5/60	8/60		0.62 (0.22–1.80)
Otolaryngology	1	32/150	36/149		0.88 (0.58–1.34)
Risk of Bias					
Low	18	245/2440	362/2247	57%	0.55 (0.44–0.69)
Some concerns	8	81/615	144/616	18%	0.52 (0.36–0.74)
High	5	131/980	160/876	38%	0.70 (0.47–1.02)
Overall	31	457/4035	666/3739	46%	0.58 (0.49–0.67)

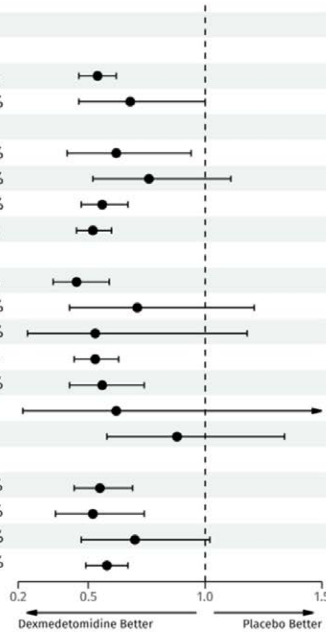

Fig. 1. Subgroup analysis of delirium risk in studies evaluating dexmedetomidine compared with placebo.

- Two large retrospective database studies reported lower incidence of delirium with NSAIDs compared to no drug.[152,153]
- One randomized clinical trial did not detect a difference in incidence of delirium between gabapentin and placebo[173]; however, one large retrospective study found an increase in delirium incidence.[174]

Comment

Studies assessing the effect of these drugs on incidence of delirium demonstrated heterogeneity in both dosing and timing of medication administration, and the evidence was inconclusive for postoperative delirium.

Based on current evidence, we cannot recommend or advise against administering these medications. We do recommend weighing the risks and benefits of giving these medications based on the patient's condition and chronic medications, comorbidities such as pre-existing neurocognitive disorders, and the planned procedure. Currently published randomized clinical trials are heterogenous, involving different medications and comparators given in different doses and at different times in the perioperative period. Thus, opportunities exist for more well-designed randomized clinical trials to strengthen the evidence for either administering or withholding common medications used in daily practice of anesthesia. When weighing the risk–benefit profile, one should also consider the issue of polypharmacy, a known risk factor for delirium, as well as any potential drug–drug interactions with medications that the patient may be taking chronically beyond the perioperative period. This best practice statement aligns with the American Geriatrics Society (New York, New York) 2023 Beer's Criteria of Potentially Inappropriate Medications.[175]

Research Gaps

There is opportunity for more well-designed randomized clinical trials to strengthen evidence for either including or withholding drugs with potential central nervous system effects to older adults in the perioperative period. For instance, the soon to be published B-FREE trial (Benzodiazepine-Free for Cardiac Anesthesia for Reduction of Postoperative Delirium in ICU), a multicenter, randomized cluster crossover trial evaluating restrictive *versus* liberal use of benzodiazepines among patients undergoing cardiovascular surgery (mean age, 65 yr), found no difference between restrictive *versus* liberal use on the incidence of delirium within 72 h of surgery (14.0% *vs.* 14.9%, respectively).[176]

Prehabilitation

Prehabilitation is an important issue for older adults; however, this topic was not included as a key question in the systematic review for this advisory due to the lack of studies focusing on older adults.

Comment

Prehabilitation is the process of enhancing capacity and reserve before an acute stressor (*e.g.*, surgery) to improve tolerance of the upcoming injury.[177,178] To date, prehabilitation before surgery has included physical exercise, nutritional supplementation, and/or cognitive training interventions. In adult patients undergoing specific major surgical procedures, there is moderate-certainty evidence that prehabilitation improves functional recovery and low-certainty evidence that prehabilitation improves other outcomes such as complications and length of stay.[177,179] However, minimal data are currently available specific to older adults undergoing surgery, especially vulnerable populations living with frailty or sarcopenia.[180,181] This lack of data specific to older people, combined with low certainty evidence for most well-studied outcomes, limits our ability to make specific recommendations about prehabilitation for older adults requiring anesthesia and surgery.[178,180] Additionally, major limitations in the evidence base across all adult patients include lack of an adequate understanding of what prehabilitation components (*e.g.*, physical exercise *vs*. nutrition *vs*. cognitive training[182]) are most effective for improving outcomes for older patients. In addition, little is known about what intervention intensity and duration are required to enhance preoperative reserve in a manner that translates into improved postoperative outcomes. Thus, whether and how prehabilitation programs should be optimally designed and delivered to meet the needs of vulnerable older patients must be addressed, including what structure and support programs are required to achieve safety, adequate adherence, and efficacy.

Research Gaps

- The efficacy of physical exercise and/or nutritional supplementation prehabilitation in improving outcomes specifically for older adults requiring anesthesia and surgery remains to be determined. Randomized clinical trials that target older patients, and in particular vulnerable populations living with frailty or sarcopenia, are required and should address outcomes that are prioritized by older patients, such as maintenance of independence (including returning to preoperative living situation), and physical and cognitive recovery.[177,181] The PREPARE trial, a multicenter trial powered to detect meaningful differences in patient-reported disability and complication rates specifically in older surgical patients with frailty, should provide important insights in the near future.
- Key questions related to optimal intervention design for older patients must be addressed. Further research is required to identify optimal components of an effective prehabilitation program, the minimal required duration of participation, appropriate intervention intensity, ideal program location (*e.g.*, home *vs*. facility-based, use of technology), and the best supervisory approaches (*e.g.*, concurrent *vs*. nonconcurrent coaching).[180]
- For older patients, and especially those with frailty and sarcopenia, baseline medical complexity and disease-related symptom burden are recognized barriers to participation in prehabilitation.[183] Strategies to enhance adherence to support prehabilitation efficacy for this vulnerable population are needed before recommending routine use of prehabilitation.
- There is a need for additional studies designed to evaluate the efficacy of different cognitive prehabilitation interventions (*e.g.*, product interface, target pathways, timing, intensity). While early evidence is promising for reduction of delirium, primary results remain inconclusive. Future research powered for more realistic effect sizes is required to determine if cognitive prehabilitation is an efficacious intervention for older adults preparing for anesthesia and surgery.[182]

Conclusions

This practice advisory makes clinical recommendations on perioperative anesthesia care in older adults to minimize adverse cognitive outcomes. For older adults scheduled for inpatient procedures, expanded preoperative evaluation that includes cognitive and frailty screening should be considered to reduce the risk of postoperative delirium. Care for patients found with cognitive or frailty impairments should include multidisciplinary teams and geriatric specialists when possible. However, this recommendation is conditional because the strength of the evidence for delirium prevention was rated low. Either neuraxial or general anesthesia, and total intravenous or inhalation agents, are acceptable for older patients. Consideration of the risks and benefits of drugs with potential central nervous system effects in older adults is suggested. Dexmedetomidine may be helpful to reduce the risk of delirium in older surgical patients, but it can be associated with bradycardia and hypotension, and there is uncertainty around the effects of dexmedetomidine for patients at different levels of baseline risk for delirium, different surgeries, timing of administration and dosage, and use with other medications.

Appendix

Expanded Preoperative Evaluation

Study and Patient Characteristics

The body of evidence included 31 studies (33 publications) of patients scheduled for inpatient surgeries (9 randomized clinical trials[47–52,184–188] and 22 nonrandomized studies[53–60,189–202]). Supplemental Digital Content 6, Supporting Evidence (https://links.lww.com/ALN/D643), provides additional study and patient characteristic details.

Six of the nine randomized clinical trials (67%) involved orthopedic surgery, including hip fracture repair or total hip arthroplasty, and the remaining were cardiac, gastrointestinal, and multiple surgeries. Nonrandomized studies included 27% orthopedic and 23% abdominal or gastrointestinal, and the remaining included various surgeries.

The most common vulnerability measured preoperatively was impaired cognition. Studies providing evidence for this recommendation used the following validated cognitive tools: Mini-Mental State Examination, Montreal Cognitive Assessment, Trail Making Test, and Digit Symbol Test. Validated frailty screening tools used in the studies include Clinical Frailty Scale, Edmonton Frail Scale, and the Fatigue, Resistance, Ambulation, Illnesses, and Loss of weight questionnaire (FRAIL). Tools to measure psychosocial status included the Geriatric Depression Scale, Short Form (SF)-36 Mental Health, and State-Trait Operation Anxiety Inventory. Studies that measured physical function used various tools, including the Groningen Activity Restriction Scale, Short Physical Performance Battery, and SF-36 Physical Functioning.

Findings for Other Outcomes

The task force identified the following as important or limited outcomes: physical function, complications, patient satisfaction, length of stay, discharge to institution, and mortality (in-hospital and 30-day). Pooled analyses of randomized clinical trials did not detect a difference between extended *versus* standard preoperative evaluation in physical function,[51,52,184,186,188] length of stay,[47–52,186,188] discharge to institution,[47,48,185,186] or in-hospital or 30-day mortality.[47,50,51,185,188] However, evidence from nonrandomized studies suggested a decrease in length of in-hospital stay,[53,54,56–60,189,190,192,194–196,198,201] 30-day mortality,[55–60,189–195,200,201] and institutional discharge.[53,58,59,190,195,198] Evidence from one nonrandomized study suggested no difference in patient satisfaction among patients receiving expanded *versus* standard preoperative evaluation.[197]

Complications

Evidence was inconclusive concerning any differences in complications—cardiac arrest,[49,195] myocardial infarction,[50,53,55,58,195] pneumonia,[49,50,53,55–58,192,195] respiratory failure,[195] pulmonary embolism,[53,55,56,195] and acute kidney injury[47,51,55,59,192,195]—between patients receiving expanded preoperative evaluation and standard care.

Neuraxial *versus* General Anesthesia

Study and Patient Characteristics

The body of evidence included 37 randomized clinical trials (39 publications) comparing neuraxial to general anesthesia.[21,62–75,203–226] General anesthesia maintenance included either total intravenous or inhaled agents. Neuraxial anesthesia included spinal, epidural, and combined spinal epidural anesthesia. Demographic race data was reported in only two (5%) randomized clinical trials. Baseline cognitive assessment data for Mini-Mental State Examination was reported in 10 (27%) randomized clinical trials. Most of the randomized clinical trials (54%) involved orthopedic surgery, including hip fracture repair, total hip arthroplasty, and total knee arthroplasty. Supplemental Digital Content 6, Supporting Evidence (https://links.lww.com/ALN/D643), provides additional study and patient characteristic details.

Findings for Other Outcomes

The evidence concerning other important outcomes was limited due to a lack of reporting across randomized clinical trials. Randomized clinical trials assessed the following important/limited outcomes: physical function, patient satisfaction, length of stay, institutional discharge, 30-day mortality, and complications. Physical function was measured using various scales across three randomized clinical trials, and a difference was not detected between neuraxial and general anesthesia in a pooled analysis.[21,218,222] Although conclusions regarding patient satisfaction,[204,205,208,212–215,217,220,225] length of hospital stay,[21,63–68,70,75,205,209,219,225] and institutional discharge[21] were limited by the very low strength of evidence, pooled results did not suggest an effect of the choice of primary anesthetic technique. Mortality rates, reported as a secondary outcome in most studies, were low among the trials, and the pooled estimate was inconclusive with wide CI.[21,63–65,67,70] Finally, the results suggested that pneumonia and renal complications might be less frequent after neuraxial anesthesia, but events were uncommon, and the strength of evidence was low. Definitions of renal complications varied, and the inconsistent outcome definitions more broadly across complications generally hinder conclusions.[227]

Complications

There was a lack of convincing evidence supporting regional anesthesia to general anesthesia across complications (no strength of evidence greater than low). Pooled results from randomized clinical trials were inconclusive for lower risk of myocardial infarction[21,63,64,67,74] and cardiac arrest[21] due to limitations in study-level risk of bias, inconsistency of effects, and imprecision. Stroke was reported in three randomized clinical trials, and no difference was found between the two types of anesthetic techniques.[21,63,67] Pooled analysis concerning renal complications seems to favor neuraxial anesthesia but was influenced by data from one large randomized clinical trial.[21,64,67,74] Evidence shows lower relative but not absolute risk for pneumonia with neuraxial anesthesia, but few events were observed.[21,62–64,67,74,75] Inconclusive evidence was found for pulmonary embolism and limited by study risk of bias and imprecision for low event rates.[21,64,67,70,74,209]

Total Intravenous Anesthesia *versus* Inhalation Anesthesia

Study and Patient Characteristics

The body of evidence included 51 studies (34 randomized clinical trials,[77–90,94,228–246] 1 nonrandomized study,[247] 13 retrospective cohort studies,[92,95–97,248–256] and 3 prospective cohort studies[91,93,257]) evaluating two methods of maintenance anesthesia: total intravenous and inhaled volatile anesthesia.

Inhaled volatile agents used for maintenance reported among the randomized clinical trials and the nonrandomized studies included sevoflurane, isoflurane, and desflurane. Intravenous agents included propofol, fentanyl, remifentanil, and sufentanil. Procedures included were gastrointestinal or abdominal (23.5%), mixed (23.5%), cardiac (11.8%), orthopedic (9.8%), thoracic (9.8%), ophthalmologic (3.9%), otolaryngological (3.9%), spine (3.9%), urologic (2.0%), head and neck (2.0%), and vascular (2.0%). Demographic race data were reported in only two (6%) randomized clinical trials and in none of the nonrandomized studies. Baseline cognitive assessment data for Mini-Mental State Examination were reported in 19 (56%) randomized clinical trials and in 3 (17.6%) nonrandomized studies. Supplemental Digital Content 6, Supporting Evidence (https://links.lww.com/ALN/D643), provides additional study and patient characteristic details.

Findings for Other Outcomes

Evidence for important and limited outcomes was generally limited. The pooled analyses from randomized clinical trials reporting on length of stay[77,78,86,89,94,236] and mortality[78,90,94,246] indicated no difference between total intravenous and inhaled anesthesia agents. However, the pooled results from three randomized clinical trials suggested higher patient satisfaction with total intravenous anesthesia.[82,231,237] These findings were, however, limited by trial risk of bias and small sample size. The evidence for cardiac, pulmonary, and renal complications was inconclusive. No randomized clinical trials were identified that reported on physical function, and only one nonrandomized study reported on discharge to institution, in which the findings suggested no difference between total intravenous and inhaled agents.

Complications

There was a lack of convincing evidence supporting total intravenous across important complication outcomes. Although a pooled analysis combining randomized clinical trials and nonrandomized studies suggested lower incidence of myocardial infarction in patients administered total intravenous anesthesia, confounding bias was present in all nonrandomized studies.[90,95–97,250,251] Pooled analysis combining randomized clinical trials and nonrandomized studies also suggests lower respiratory failure with total intravenous compared to inhaled anesthesia.[77,90,96,97] However, the finding is limited by trial risk of bias. No difference was detected in cardiac arrest,[77,95] bradycardia,[82,89,237,243,247] hypotension,[77,243,247,248] stroke,[77,96] acute kidney injury,[77,97,248,250,254,255] pneumonia,[86,90,94,96,250] or pulmonary edema/congestion.[95,97] Pooled analysis suggests increased risk of pulmonary embolism with total intravenous anesthesia; however, results were influenced by one large nonrandomized study.[77,94–97]

Pharmacologic Delirium Prevention

Dexmedetomidine

Study and Patient Characteristics. The body of evidence included 57 randomized clinical trials[99–143,258–268] and 6 nonrandomized studies[113,149,269–272] comparing the effects of dexmedetomidine with placebo or no intervention on patient outcomes. An additional eight studies were not included in the analyses because they compared dexmedetomidine to other drugs.

Demographic race data was reported in 56 (79%) randomized clinical trials and in 14 (93%) nonrandomized studies. There was heterogeneity in the dosing and timing of dexmedetomidine administration. Trials administered dexmedetomidine preoperatively, at induction, intraoperatively, postoperatively, or in combinations of times (for example, induction and intraoperatively, or intraoperatively and postoperatively). Loading doses ranged from 0.2 to 4.0 mcg/kg, and maintenance doses ranged from 0.1 to 1.5 mcg $\cdot$ kg^{-1} $\cdot$ h^{-1}. Supplemental Digital Content 6, Supporting Evidence (https://links.lww.com/ALN/D643), provides additional study and patient characteristic details.

Findings for Other Outcomes. Evidence was lacking supporting shorter length of stay[99,100,102,105,109–111,113–115,117,118,120–123,126,139,261] or mortality[99,109,110,114,115,117,118,120,121,123,136,269] for dexmedetomidine compared to placebo.

Complications. There was a lack of convincing evidence supporting dexmedetomidine compared with placebo or no intervention across complications. Pooled results from randomized clinical trials were inconclusive for risk of myocardial infarction,[99,114,121] cardiac arrest,[269] stroke,[99,109,114,118,120,121] and renal complications.[100,109,117,120,121] Evidence for pneumonia,[99,120,123] pulmonary congestion,[99] pulmonary embolism,[99] and respiratory failure[99] was inconclusive.

Melatonin or Ramelteon

Studies were included in the systematic review, and analyses were conducted looking at the effects of melatonin or ramelteon compared with placebo or no intervention on patient outcomes; however, no recommendations were made.

Study and Patient Characteristics. The analyses included 20 studies (15 randomized clinical trials,[145,273–286] 2 nonrandomized studies,[287,288] 2 before–after design,[289,290] and 1 retrospective[291]) comparing melatonin/ramelteon to placebo.

Types of surgery included were 30% orthopedic (6 of 20), 30% cardiac (6 of 20), 10% gastrointestinal/abdominal (2 of 20), 10% thoracic (2 of 20), and 20% other (4 of 20). Three studies administered melatonin/ramelteon only preoperatively, 10 studies administered the drug both preoperatively and postoperatively, and 2 studies administered the drug only postoperatively. Supplemental Digital Content 6, Supporting Evidence (https://links.lww.com/ALN/D643), provides additional study and patient characteristic details.

Summary of Evidence. Although a pooled analysis of 13 randomized clinical trials suggests there may be a lower risk of delirium in patients receiving melatonin/ramelteon,[145,273–275,277–281,283–286] it was limited by potential bias in 2 of the ramelteon studies and high variance across studies.[284,286]

There was a lack of evidence supporting melatonin/ramelteon across most important outcomes. A single randomized clinical trial evaluated neurocognitive disorder at 30 days or more to 1 yr and suggests there may be a lower risk in patients receiving melatonin/ramelteon compared with patients receiving placebo or no intervention[273]; no evidence concerning neurocognitive disorder of less than 30 days was identified. Evidence was inconclusive for complications,[289,290] length of stay,[273,276,278,280,285] and mortality.[273,280,285]

There was a lack of convincing evidence supporting melatonin or ramelteon compared with placebo or no intervention in pneumonia (risk ratio, 0.82; 95% CI, 0.21 to 3.18; very low strength of evidence).[289,290]

Comment. Interpretation of the evidence for use of melatonin/ramelteon was limited due to different dosages and duration of intervention across randomized clinical trials. In addition, formulations of melatonin were inconsistent. As a result, optimal dosage, formulation, and duration of treatment remain unanswered. A further limitation to making firm recommendations concerning use of melatonin/ramelteon concerns the heterogeneity of patient populations and clinical settings studied.

Perioperative Use of Medications with Potential Central Nervous System Effects. The taskforce considered the impact of medications with potential central nervous system effects (*i.e.*, benzodiazepines, antipsychotics, anticholinergics, ketamine, corticosteroids, gabapentin, or NSAIDs) on risk of delirium. Below, we summarize key characteristics of the studies included as evidence for these medications and present additional information about the findings from studies that are not presented in the main body of guideline document.

Benzodiazepines

Studies evaluating short-acting benzodiazepines included 27 studies (15 randomized clinical trials[101,134,141,145–147,292–300] and 12 nonrandomized studies[148–153,301–306]). There was heterogeneity in the dosing and timing of administration.

Ketamine

Studies evaluating ketamine included 20 studies (13 randomized clinical trials,[137,160,162–164,307–314] 3 prospective cohorts,[149,315,316] and 4 retrospective studies[152,153,317,318]). Types of surgical procedures included 40% orthopedic (8 of 20), 15% cardiac (3 of 20), 15% gastrointestinal/abdominal (3 of 20), 10% various (2 of 20), 10% ophthalmologic (2 of 20), and 1 each of thoracic and spinal.

There was heterogeneity in the dosing and timing of ketamine administration. Trials administered ketamine preoperatively, at induction, intraoperatively, postoperatively, or in combinations of times (for example, induction and intraoperatively, or intraoperatively and postoperatively). Doses ranged from 0.25 mg/kg to 1.0 mg/kg (Supplemental Digital Content 6, Supporting Evidence (https://links.lww.com/ALN/D643).

Antipsychotics

The body of evidence included eight randomized clinical trials[154–161] and two nonrandomized studies.[304,319] Medications included haloperidol, risperidone, and olanzapine, or any antipsychotic. There was heterogeneity in the dosing and timing of administration.

Anticholinergics

The body of evidence included one randomized clinical trial comparing the effects of preoperative administration of penehyclidine with placebo.[165] One retrospective study evaluated any anticholinergics *versus* none.[166]

Corticosteroids

The body of evidence included 12 randomized clinical trials[167–172,320–325] and 6 nonrandomized studies.[152,153,317,326–328] Medications included dexamethasone, methylprednisolone, or any corticosteroid.

Nonsteroidal Anti-inflammatory Drugs

The body of evidence included three randomized clinical trials[329–331] and three nonrandomized studies[152,153,332] comparing the effects of NSAIDs with placebo or none. Medications used included celecoxib preoperatively, ketoprofen, and flurbiprofen both pre- and intraoperatively.

Acknowledgments

The authors acknowledge the following for editorial support: Conor Kelley, M.S., consulting editor, Hektoen Institute of Medicine, Chicago, Illinois; Rohan Rajagopalan, M.P.H., research assistant, Chicago, Illinois; and Esther Ajai, M.F.A., research assistant, Seattle, Washington.

Research Support

Methodology support was provided by the American Society of Anesthesiologists (Schaumburg, Illinois). Other task force members volunteered their expertise and time.

Competing Interests

Dr. Berger discloses legal consultancy services; material support (an EEG monitor loan) from Massimo Inc; grant support from the National Institute on Aging (Bethesda, Maryland), the American Geriatrics Society (New York, New York), the Alzheimer's Drug Discovery Foundation, the International Anesthesia Research Society, and the Foundation for Anesthesia Education and Research, and has taken part in a peer-to-peer EEG education session organized by Masimo (for which his honorarium was donated at his request directly to the Foundation for Anesthesia Education and Research). Dr. Deiner discloses legal consultancy services and is Vice President of the American Board of Anesthesiology. The views expressed in the manuscript are her own and do not necessarily reflect the view of the board. Dr. Hughes discloses consultancy with Sedana Medical and an institutional research grant from Dr. Franz Kohler Chemie GMBH. Dr. McIsaac discloses institutional research grants from the Physician Services Incorporated Foundation, Council for Medical Specialty Societies, Canadian Institutes of Health Research, Ottawa Hospital Academic Medical Organization, Sunnybrook Alternative Funding Plan, University of Ottawa Department of Anesthesiology, Canadian Blood Services Intramural, CHEST Foundation Research Grant, and Heart and Stroke Foundation of Canada. Dr. McSwain discloses an institutional grant from the Council for Medical Specialty Societies. Dr. Neuman discloses an institutional grant from PCORI, the National Institute on Aging, the National Institute of Arthritis and Musculoskeletal and Skin Diseases (Bethesda, Maryland), the Donoghue Medical Research Foundation, and the National Institute on Drug Abuse (Bethesda, Maryland). Dr. Russell discloses consultancy for Healthgrades and an institutional research grant from the John A. Hartford Foundation. Dr. Tang discloses business ownership of Vicky Tang Coaching and an institutional grant from the National Institute on Aging. Dr. Whitlock reports an institutional research grant from the National Institute on Aging. She is a grant reviewer and associate editor and receives honoraria from the International Anesthesia Research Society. Dr. Whittington discloses that he is the geriatrics anesthesia section editor for the journal *Anesthesia & Analgesia*. Dr. Domino discloses an institutional research grant from Edwards Life Science Corporation. The other authors declare no competing interests.

Correspondence

Address correspondence to Dr. Domino: Department of Anesthesiology & Pain Medicine, Box 356540, University of Washington, Seattle, Washington 98195. kdomino@uw.edu

Supplemental Digital Content

Supplemental Digital Content 1, Protocol, https://links.lww.com/ALN/D638

Supplemental Digital Content 2, Search Strategy, https://links.lww.com/ALN/D639

Supplemental Digital Content 3, PRISMA Flow Chart, https://links.lww.com/ALN/D640

Supplemental Digital Content 4, Methodology, https://links.lww.com/ALN/D641

Supplemental Digital Content 5, Risk of Bias, https://links.lww.com/ALN/D642

Supplemental Digital Content 6, Supporting Evidence, https://links.lww.com/ALN/D643

References

1. Mather MJ, L A, Pollard KM: Aging in the United States. Population Bull 2015; 70:1–20
2. Hall MJ, DeFrances CJ, Williams SN, Golosinskiy A, Schwartzman A: National hospital discharge survey: 2007 summary. Natl Health Stat Rep 2010; 26:1–20, 24
3. Cullen KA, Hall MJ, Golosinskiy A: Ambulatory surgery in the United States, 2006. Natl Health Stat Rep 2009; 68:1–25
4. Turrentine FE, Wang H, Simpson VB, Jones RS: Surgical risk factors, morbidity, and mortality in elderly patients. J Am Coll Surg 2006; 203:865–77
5. Zhang LM, Hornor MA, Robinson T, Rosenthal RA, Ko CY, Russell MM: Evaluation of postoperative functional health status decline among older adults. JAMA Surg 2020; 155:950–8
6. Becher RD, Murphy TE, Gahbauer EA, Leo-Summers L, Stabenau HF, Gill TM: Factors associated with functional recovery among older survivors of major surgery. Ann Surg 2020; 272:92–8
7. Kapoor P, Chen L, Saripella A, et al.: Prevalence of preoperative cognitive impairment in older surgical patients: A systematic review and meta-analysis. J Clin Anesth 2022; 76:110574
8. Saczynski JS, Marcantonio ER, Quach L, et al.: Cognitive trajectories after postoperative delirium. N Engl J Med 2012; 367:30–9
9. Witlox J, Slor CJ, Jansen RW, et al.: The neuropsychological sequelae of delirium in elderly patients with hip fracture three months after hospital discharge. Int Psychogeriatr 2013; 25:1521–31
10. Hshieh TT, Saczynski J, Gou RY, et al.; SAGES Study Group: Trajectory of functional recovery after postoperative delirium in elective surgery. Ann Surg 2017; 265:647–53
11. Goldberg TE, Chen C, Wang Y, et al.: Association of delirium with long-term cognitive decline: A meta-analysis. JAMA Neurol 2020; 77:1373–81
12. American Society of Anesthesiologists: Perioperative Brain Health Initiative. Available at: https://www.asahq.org/brainhealthinitiative. Accessed April 22, 2024.
13. Searle SD, Mitnitski A, Gahbauer EA, Gill TM, Rockwood K: A standard procedure for creating a frailty index. BMC Geriatr 2008; 8:24

14. Aucoin SD, Hao M, Sohi R, et al.: Accuracy and feasibility of clinically applied frailty instruments before surgery: A systematic review and meta-analysis. Anesthesiology 2020; 133:78–95
15. Gracie TJ, Caufield-Noll C, Wang NY, Sieber FE: The association of preoperative frailty and postoperative delirium: A meta-analysis. Anesth Analg 2021; 133:314–23
16. Deiner SG, Marcantonio ER, Trivedi S, et al.: Comparison of the frailty index and frailty phenotype and their associations with postoperative delirium incidence and severity. J Am Geriatr Soc 2024; 72:1781–92
17. Collard RM, Boter H, Schoevers RA, Oude Voshaar RC: Prevalence of frailty in community-dwelling older persons: A systematic review. J Am Geriatr Soc 2012; 60:1487–92
18. Fried LP, Tangen CM, Walston J, et al.; Cardiovascular Health Study Collaborative Research Group: Frailty in older adults: Evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001; 56:M146–56
19. Rodríguez-Mañas L, Féart C, Mann G, et al.; FOD-CC Group (Appendix 1): Searching for an operational definition of frailty: A Delphi method based consensus statement. The Frailty Operative Definition-Consensus Conference Project. J Gerontol: Series A 2012; 68:62–7
20. Barnett SR: Preoperative assessment of older adults. Anesthesiol Clin 2019; 37:423–36
21. Neuman MD, Feng R, Carson JL, et al.; REGAIN Investigators: Spinal anesthesia or general anesthesia for hip surgery in older adults. N Engl J Med 2021; 385:2025–35
22. Herling SF, Dreijer B, Wrist Lam G, Thomsen T, Møller AM: Total intravenous anaesthesia versus inhalational anaesthesia for adults undergoing transabdominal robotic assisted laparoscopic surgery. Cochrane Database Syst Rev 2017; 4:Cd011387
23. American Geriatrics Society 2015 Beers Criteria Update Expert Panel: American Geriatrics Society 2015 updated Beers criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2015; 63:2227–46
24. Janssen TL, Alberts AR, Hooft L, Mattace-Raso F, Mosk CA, van der Laan L: Prevention of postoperative delirium in elderly patients planned for elective surgery: Systematic review and meta-analysis. Clin Interv Aging 2019; 14:1095–117
25. MacKenzie KK, Britt-Spells AM, Sands LP, Leung JM: Processed electroencephalogram monitoring and postoperative delirium: A systematic review and meta-analysis. Anesthesiology 2018; 129:417–27
26. Evered LA, Chan MTV, Han R, et al.: Anaesthetic depth and delirium after major surgery: A randomised clinical trial. Br J Anaesth 2021; 127:704–12
27. Perez-Otal B, Aragon-Benedi C, Pascual-Bellosta A, Ortega-Lucea S, Martínez-Ubieto J, Ramírez-Rodríguez JM; Research Group in Anaesthesia, Resuscitation, and Perioperative Medicine of Institute for Health Research Aragón (ISS Aragón): Neuromonitoring depth of anesthesia and its association with postoperative delirium. Sci Rep 2022; 12:12703
28. Wildes TS, Mickle AM, Ben Abdallah A, et al.; ENGAGES Research Group: Effect of electroencephalography-guided anesthetic administration on postoperative delirium among older adults undergoing major surgery: The ENGAGES randomized clinical trial. JAMA 2019; 321:473–83
29. Deschamps A, Ben Abdallah A, Jacobsohn E, et al.; Canadian Perioperative Anesthesia Clinical Trials Group: Electroencephalography-guided anesthesia and delirium in older adults after cardiac surgery: The ENGAGES-Canada randomized clinical trial. JAMA 2024; 332:112–23
30. Brown CH, Jones EL, Lin C, et al.: Shaping anesthetic techniques to reduce post-operative delirium (SHARP) study: A protocol for a prospective pragmatic randomized controlled trial to evaluate spinal anesthesia with targeted sedation compared with general anesthesia in older adults undergoing lumbar spine fusion surgery. BMC Anesthesiol 2019; 19:192
31. Fritz BA, King CR, Mickle AM, et al.; ENGAGES Research Group: Effect of electroencephalogram-guided anaesthesia administration on 1-yr mortality: Follow-up of a randomised clinical trial. Br J Anaesth 2021; 127:386–95
32. Abbott TEF, Pearse RM: Depth of anesthesia and postoperative delirium. JAMA 2019; 321:459–60
33. Hao D, Fritz BA, Saddawi-Konefka D, Palanca BJA: Pro-con debate: Electroencephalography-guided anesthesia for reducing postoperative delirium. Anesth Analg 2023; 137:976–82
34. Whitlock EL, Gross ER, King CR, Avidan MS: Anaesthetic depth and delirium: A challenging balancing act. Br J Anaesth 2021; 127:667–71
35. Pandharipande PP, Whitlock EL, Hughes CG: Baseline vulnerabilities may play a larger role than depth of anesthesia or sedation in postoperative delirium. Anesthesiology 2021; 135:940–2
36. Vaurio LE, Sands LP, Wang Y, Mullen EA, Leung JM: Postoperative delirium: The importance of pain and pain management. Anesth Analg 2006; 102:1267–73
37. Peden CJ, Miller TR, Deiner SG, Eckenhoff RG, Fleisher LA; Members of the Perioperative Brain Health Expert Panel: Improving perioperative brain health: An expert consensus review of key actions for the perioperative care team. Br J Anaesth 2021; 126:423–32

38. Guyatt GH, Oxman AD, Kunz R, et al.: GRADE guidelines: 2. Framing the question and deciding on important outcomes. J Clin Epidemiol 2011; 64:395–400
39. Xu C, Ju K, Lin L, et al.: Rapid evidence synthesis approach for limits on the search date: How rapid could it be? Res Synth Methods 2022; 13:68–76
40. Joshi GP, Abdelmalak BB, Weigel WA, et al.: 2023 American Society of Anesthesiologists practice guidelines for preoperative fasting: Carbohydrate-containing clear liquids with or without protein, chewing gum, and pediatric fasting duration—a modular update of the 2017 American Society of Anesthesiologists practice guidelines for preoperative fasting. Anesthesiology 2023; 138:132–51
41. Thilen SR, Weigel WA, Todd MM, et al.: 2023 American Society of Anesthesiologists practice guidelines for monitoring and antagonism of neuromuscular blockade: A report by the American Society of Anesthesiologists Task Force on Neuromuscular Blockade. Anesthesiology 2023; 138:13–41
42. Higgins JP, Altman DG, Gøtzsche PC, et al.; Cochrane Bias Methods Group: The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011; 343:d5928
43. Sterne JA, Hernán MA, Reeves BC, et al.: ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016; 355:i4919
44. R Core Team: R: A Language and Environment for Statistical Computing. Vienna, Austria, R Foundation for Statistical Computing, 2022
45. Schünemann HJ: Interpreting GRADE's levels of certainty or quality of the evidence: GRADE for statisticians, considering review information size or less emphasis on imprecision? J Clin Epidemiol 2016; 75:6–15
46. Reeves BC, Deeks JJ, Higgins JPT, Shea B, Tugwell P, Wells GA: Chapter 24: Including non-randomized studies on intervention effects. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.4 (updated August 2023). Cochrane, 2023
47. Hempenius L, Slaets JP, van Asselt D, de Bock GH, Wiggers T, van Leeuwen BL: Outcomes of a geriatric liaison intervention to prevent the development of postoperative delirium in frail elderly cancer patients: Report on a multicentre, randomized, controlled trial. PLoS One 2013; 8:e64834
48. Marcantonio ER, Flacker JM, Wright RJ, Resnick NM: Reducing delirium after hip fracture: A randomized trial. J Am Geriatr Soc 2001; 49:516–22
49. Partridge JS, Harari D, Martin FC, et al.: Randomized clinical trial of comprehensive geriatric assessment and optimization in vascular surgery. Br J Surg 2017; 104:679–87
50. Vidán M, Serra JA, Moreno C, Riquelme G, Ortiz J: Efficacy of a comprehensive geriatric intervention in older patients hospitalized for hip fracture: A randomized, controlled trial. J Am Geriatr Soc 2005; 53:1476–82
51. Watne LO, Torbergsen AC, Conroy S, et al.: The effect of a pre- and postoperative orthogeriatric service on cognitive function in patients with hip fracture: Randomized controlled trial (Oslo Orthogeriatric Trial). BMC Med 2014; 12:63
52. Zhu T, Yu J, Ma Y, Qin Y, Li N, Yang H: Effectiveness of perioperative comprehensive evaluation of hip fracture in the elderly. Comput Intell Neurosci 2022; 2022:4124354
53. Adogwa O, Elsamadicy AA, Vuong VD, et al.: Geriatric comanagement reduces perioperative complications and shortens duration of hospital stay after lumbar spine surgery: A prospective single-institution experience. J Neurosurg Spine 2017; 27:670–5
54. Bakker FC, Persoon A, Bredie SJH, et al.: The CareWell in Hospital program to improve the quality of care for frail elderly inpatients: Results of a before-after study with focus on surgical patients. Am J Surg 2014; 208:735–46
55. Bjorkelund KB, Hommel A, Thorngren KG, Gustafson L, Larsson S, Lundberg D: Reducing delirium in elderly patients with hip fracture: A multi-factorial intervention study. Acta Anaesthesiol Scand 2010; 54:678–88
56. Harari D, Hopper A, Dhesi J, Babic-Illman G, Lockwood L, Martin F: Proactive care of older people undergoing surgery ("POPS"): Designing, embedding, evaluating and funding a comprehensive geriatric assessment service for older elective surgical patients. Age Ageing 2007; 36:190–6
57. Indrakusuma R, Dunker MS, Peetoom JJ, Schreurs WH: Evaluation of preoperative geriatric assessment of elderly patients with colorectal carcinoma. A retrospective study. Eur J Surg Oncol 2015; 41:21–7
58. Lester PE, Ripley D, Grandelli R, Drew LA, Keegan M, Islam S: Interdisciplinary protocol for surgery in older persons: Development and implementation. J Am Med Dir Assoc 2022; 23:555–62
59. Paille M, Senage T, Roussel JC, et al.: Association of preoperative geriatric assessment with length of stay after combined cardiac surgery. Ann Thorac Surg 2021; 112:763–9
60. Tarazona-Santabalbina FJ, Llabata-Broseta J, Belenguer-Varea A, Álvarez-Martínez D, Cuesta-Peredo D, Avellana-Zaragoza JA: A daily multidisciplinary assessment of older adults undergoing elective colorectal cancer surgery is associated with reduced delirium and geriatric syndromes. J Geriatr Oncol 2019; 10:298–303
61. Engel JS, Tran J, Khalil N, et al.: A systematic review of perioperative clinical practice guidelines for care of older adults living with frailty. Br J Anaesth 2023; 130:262–71

62. Bielka K, Kuchyn I, Tokar I, Artemenko V, Kashchii U: Psoas compartment block efficacy and safety for perioperative analgesia in the elderly with proximal femur fractures: A randomized controlled study. BMC Anesthesiol 2021; 21:252
63. Li T, Li J, Yuan L, et al.; RAGA Study Investigators: Effect of regional vs general anesthesia on incidence of postoperative delirium in older patients undergoing hip fracture surgery: The RAGA randomized trial. JAMA 2022; 327:50–8
64. Parker MJ, Griffiths R: General versus regional anaesthesia for hip fractures. A pilot randomised controlled trial of 322 patients. Injury 2015; 46:1562–6
65. Shin S, Kim SH, Park KK, Kim SJ, Bae JC, Choi YS: Effects of anesthesia techniques on outcomes after hip fracture surgery in elderly patients: A prospective, randomized, controlled trial. J Clin Med 2020; 9:1605
66. Tzimas P, Samara E, Petrou A, Korompilias A, Chalkias A, Papadopoulos G: The influence of anesthetic techniques on postoperative cognitive function in elderly patients undergoing hip fracture surgery: General vs spinal anesthesia. Injury 2018; 49:2221–6
67. Brown CH, Edwards C, Lin C, et al.: Spinal anesthesia with targeted sedation based on Bispectral Index values compared with general anesthesia with masked Bispectral Index values to reduce delirium: The SHARP randomized controlled trial. Anesthesiology 2021; 135:992–1003
68. Jia Y, Jin G, Guo S, et al.: Fast-track surgery decreases the incidence of postoperative delirium and other complications in elderly patients with colorectal carcinoma. Langenbecks Arch Surg 2014; 399:77–84
69. Papaioannou A, Fraidakis O, Michaloudis D, Balalis C, Askitopoulou H: The impact of the type of anaesthesia on cognitive status and delirium during the first postoperative days in elderly patients. Eur J Anaesthesiol 2005; 22:492–9
70. Rasmussen LS, Johnson T, Kuipers HM, et al.; ISPOCD2 (International Study of Postoperative Cognitive Dysfunction) Investigators: Does anaesthesia cause postoperative cognitive dysfunction? A randomised study of regional versus general anaesthesia in 438 elderly patients. Acta Anaesthesiol Scand 2003; 47:260–6
71. Casati A, Aldegheri G, Vinciguerra E, Marsan A, Fraschini G, Torri G: Randomized comparison between sevoflurane anaesthesia and unilateral spinal anaesthesia in elderly patients undergoing orthopaedic surgery. Eur J Anaesthesiol 2003; 20:640–6
72. Silbert BS, Evered LA, Scott DA: Incidence of postoperative cognitive dysfunction after general or spinal anaesthesia for extracorporeal shock wave lithotripsy. Br J Anaesth 2014; 113:784–91
73. Wang Y, Zhang J, Zhang S: Influence of different anesthetic and analgesic methods on early cognitive function of elderly patients receiving non-cardiac surgery. Pak J Med Sci 2016; 32:369–72
74. Liang C, Wei J, Cai X, Lin W, Fan Y, Yang F: Efficacy and safety of 3 different anesthesia techniques used in total hip arthroplasty. Med Sci Monit 2017; 23:3752–9
75. Chu CPW, Yap JCCM, Chen PP, Hung HH: Postoperative outcome in Chinese patients having primary total knee arthroplasty under general anaesthesia/intravenous patient-controlled analgesia compared to spinal-epidural anaesthesia/analgesia. Hong Kong Med J 2006; 12:442–7
76. Wennberg JE, Fisher ES, Skinner JS: Geography and the debate over Medicare reform. Health Aff (Millwood) 2002:W96–114
77. Cao S-J, Zhang Y, Zhang Y-X, et al.; First Study of Perioperative Organ Protection (SPOP1) Investigators: Delirium in older patients given propofol or sevoflurane anaesthesia for major cancer surgery: A multicentre randomised trial. Br J Anaesth 2023; 131:253–65
78. Dai Z, Lin M, Li Y, et al.: Sevoflurane-remifentanil versus propofol-remifentanil anesthesia during noncardiac surgery for patients with coronary artery disease - A prospective study between 2016 and 2017 at a single center. Med Sci Monit 2021; 27:e929835
79. Farrer TJ, Monk TG, McDonagh DL, Martin G, Pieper CF, Koltai D: A prospective randomized study examining the impact of intravenous versus inhalational anesthesia on postoperative cognitive decline and delirium. Appl Neuropsychol Adult 2023; 1:1–7
80. Ishii K, Makita T, Yamashita H, et al.: Total intravenous anesthesia with propofol is associated with a lower rate of postoperative delirium in comparison with sevoflurane anesthesia in elderly patients. J Clin Anesth 2016; 33:428–31
81. Mei X, Zheng H-L, Li C, et al.: The effects of propofol and sevoflurane on postoperative delirium in older patients: A randomized clinical trial study. J Alzheimers Dis 2020; 76:1627–36
82. Nishikawa K, Kimura S, Shimodate Y, Igarashi M, Namiki A: A comparison of intravenous-based and epidural-based techniques for anesthesia and postoperative analgesia in elderly patients undergoing laparoscopic cholecystectomy. J Anesth 2007; 21:1–6
83. Nishikawa K, Nakayama M, Omote K, Namiki A: Recovery characteristics and post-operative delirium after long-duration laparoscope-assisted surgery in elderly patients: Propofol-based vs. sevoflurane-based anesthesia. Acta Anaesthesiol Scand 2004; 48:162–8
84. Tanaka P, Goodman S, Sommer BR, Maloney W, Huddleston J, Lemmens HJ: The effect of desflurane versus propofol anesthesia on postoperative delirium in elderly obese patients undergoing total knee replacement: A randomized, controlled, double-blinded clinical trial. J Clin Anesth 2017; 39:17–22

85. Egawa J, Inoue S, Nishiwada T, et al.: Effects of anesthetics on early postoperative cognitive outcome and intraoperative cerebral oxygen balance in patients undergoing lung surgery: A randomized clinical trial. Can J Anaesth 2016; 63:1161–9
86. Li Y, Chen D, Wang H, et al.: Intravenous versus volatile anesthetic effects on postoperative cognition in elderly patients undergoing laparoscopic abdominal surgery. Anesthesiology 2021; 134:381–94
87. Liang Y, Xin X, Wang H, et al.: A novel predictive strategy for the incidence of postoperative neurocognitive dysfunction in elderly patients with mild cognitive impairment. Front Aging Neurosci 2022; 14:985406
88. Tang N, Ou C, Liu Y, Zuo Y, Bai Y: Effect of inhalational anaesthetic on postoperative cognitive dysfunction following radical rectal resection in elderly patients with mild cognitive impairment. J Int Med Res 2014; 42:1252–61
89. Zhang Y, Shan GJ, Zhang YX, et al.; First Study of Perioperative Organ Protection (SPOP1) Investigators: Propofol compared with sevoflurane general anaesthesia is associated with decreased delayed neurocognitive recovery in older adults. Br J Anaesth 2018; 121:595–604
90. Lindholm EE, Aune E, Noren CB, et al.: The Anesthesia in Abdominal Aortic Surgery (ABSENT) study: A prospective, randomized, controlled trial comparing troponin T release with fentanyl-sevoflurane and propofol-remifentanil anesthesia in major vascular surgery. Anesthesiology 2013; 119:802–12
91. Deiner S, Luo X, Silverstein JH, Sano M: Can intraoperative processed EEG predict postoperative cognitive dysfunction in the elderly? Clin Ther 2015; 37:2700–5
92. Kadoi Y, Goto F: Sevoflurane anesthesia did not affect postoperative cognitive dysfunction in patients undergoing coronary artery bypass graft surgery. J Anesth 2007; 21:330–5
93. Konishi Y, Evered LA, Scott DA, Silbert BS: Postoperative cognitive dysfunction after sevoflurane or propofol general anaesthesia in combination with spinal anaesthesia for hip arthroplasty. Anaesth Intensive Care 2018; 46:596–600
94. Forsmo HM, Pfeffer F, Rasdal A, et al.: Compliance with enhanced recovery after surgery criteria and preoperative and postoperative counselling reduces length of hospital stay in colorectal surgery: Results of a randomized controlled trial. Colorectal Dis 2016; 18:603–11
95. Cho HB, Kim MG, Park SY, et al.: The influence of propofol-based total intravenous anesthesia on postoperative outcomes in end-stage renal disease patients: A retrospective observation study. PLoS One 2021; 16:e0254014
96. Hasselager RP, Hallas J, Gögenur I: Inhalation anaesthesia compared with total intravenous anaesthesia and postoperative complications in colorectal cancer surgery: An observational registry-based study†. Br J Anaesth 2022; 129:416–26
97. Yoshimura M, Shiramoto H, Morimoto Y, Koga M: Comparison of total intravenous with inhalational anesthesia in terms of postoperative delirium and complications in older patients: A nationwide population-based study. J Anesth 2022; 36:698–706
98. Tellor Pennington BR, Colquhoun DA, Neuman MD, et al.; THRIVE Research Group: Feasibility pilot trial for the Trajectories of Recovery after Intravenous Propofol versus Inhaled Volatile Anesthesia (THRIVE) pragmatic randomised controlled trial. BMJ Open 2023; 13:e070096
99. Deiner S, Luo X, Lin HM, et al.; and the Dexlirium Writing Group: Intraoperative infusion of dexmedetomidine for prevention of postoperative delirium and cognitive dysfunction in elderly patients undergoing major elective noncardiac surgery: A randomized clinical trial. JAMA Surg 2017; 152:e171505
100. Gao Y, Yu H, Wang W, Wang Y, Teng J, Li F: Effect of dexmedetomidine on the neuroglobin expression in elderly patients with minimally invasive coronary artery bypass graft surgery. Heart Surg Forum 2021; 24:E776–80
101. He F, Shen L, Zhong J: A study of dexmedetomidine in the prevention of postoperative delirium in elderly patients after vertebral osteotomy. Int J Clin Exper Med 2018; 11:4984–90
102. Hong H, Zhang DZ, Li M, et al.: Impact of dexmedetomidine supplemented analgesia on delirium in patients recovering from orthopedic surgery: A randomized controlled trial. BMC Anesthesiol 2021; 21:223
103. Hu J, Zhu M, Gao Z, et al.: Dexmedetomidine for prevention of postoperative delirium in older adults undergoing oesophagectomy with total intravenous anaesthesia: A double-blind, randomised clinical trial. Eur J Anaesthesiol 2021; 38:S9–S17
104. Hu G, Long A, Wang J, Wang X: Effects of oral atorvastatin on inflammatory markers and postoperative delirium in elderly patients with hip fracture surgery. Farmacia 2022; 70:944–53
105. Huyan T, Hu X, Peng H, Zhu Z, Li Q, Zhang W: Perioperative dexmedetomidine reduces delirium in elderly patients after lung cancer surgery. Psychiatr Danub 2019; 31:95–101
106. Lai Y, Chen Q, Xiang C, Li G, Wei K: Comparison of the effects of dexmedetomidine and lidocaine on stress response and postoperative delirium of older patients undergoing thoracoscopic surgery: A randomized controlled trial. Clin Interv Aging 2023; 18:1275–83

107. Lee C, Lee J, Lee G, Lee H, Koh E, Hwang J: Pregabalin and dexmedetomidine combined for pain after total knee arthroplasty or total hip arthroplasty performed under spinal anesthesia. Orthopedics 2018; 41:365–70
108. Lee C, Lee CH, Lee G, Lee M, Hwang J: The effect of the timing and dose of dexmedetomidine on postoperative delirium in elderly patients after laparoscopic major non-cardiac surgery: A double blind randomized controlled study. J Clin Anesth 2018; 47:27–32
109. Li X, Yang J, Nie XL, et al.: Impact of dexmedetomidine on the incidence of delirium in elderly patients after cardiac surgery: A randomized controlled trial. PLoS One 2017; 12:e0170757
110. Li CJ, Wang BJ, Mu DL, et al.: Randomized clinical trial of intraoperative dexmedetomidine to prevent delirium in the elderly undergoing major non-cardiac surgery. Br J Surg 2020; 107:e123–32
111. Liu T, Tuo J, Wei Q, et al.: Effect of perioperative dexmedetomidine infusion on postoperative delirium in elderly patients undergoing oral and maxillofacial surgery: A randomized controlled clinical trial. Int J Gen Med 2022; 15:6105–13
112. Liu Y, Ma L, Gao M, Guo W, Ma Y: Dexmedetomidine reduces postoperative delirium after joint replacement in elderly patients with mild cognitive impairment. Aging Clin Exp Res 2016; 28:729–36
113. Liu W, Wang Y, Chen K, et al.: Effect of intraoperative dexmedetomidine use on postoperative delirium in the elderly after laryngectomy: A randomized controlled clinical trial. Drug Des Devel Ther 2023; 17:2933–41
114. Lu Y, Fang PP, Yu YQ, et al.; POGF Study Collaborators: Effect of intraoperative dexmedetomidine on recovery of gastrointestinal function after abdominal surgery in older adults: A randomized controlled trial. JAMA Netw Open 2021; 4:e2128886
115. Lv Y, Gu L: Dexmedetomidine potential in attenuating postoperative delirium in elderly patients after total hip joint replacement. Rev Assoc Med Bras (1992) 2022; 68:1166–71
116. Kowalczyk M, Panasiuk-Kowalczyk A, Stadnik A, et al.: Dexmedetomidine increases MMP-12 and MBP concentrations after coronary artery bypass graft surgery with extracorporeal circulation anaesthesia without impacting cognitive function: A randomised control trial. Int J Environ Res Public Health 2022; 19:16512
117. Momeni M, Khalifa C, Lemaire G, et al.: Propofol plus low-dose dexmedetomidine infusion and postoperative delirium in older patients undergoing cardiac surgery. Br J Anaesth 2021; 126:665–73
118. Qu JZ, Mueller A, McKay TB, et al.; MINDDS Study Team: Nighttime dexmedetomidine for delirium prevention in non-mechanically ventilated patients after cardiac surgery (MINDDS): A single-centre, parallel-arm, randomised, placebo-controlled superiority trial. EClinicalMedicine 2023; 56:101796
119. Shi H, Du X, Wu F, Hu Y, Xv Z, Mi W: Dexmedetomidine improves early postoperative neurocognitive disorder in elderly male patients undergoing thoracoscopic lobectomy. Exp Ther Med 2020; 20:3868–77
120. Soh S, Shim JK, Song JW, Bae JC, Kwak YL: Effect of dexmedetomidine on acute kidney injury after aortic surgery: A single-centre, placebo-controlled, randomised controlled trial. Br J Anaesth 2020; 124:386–94
121. Turan A, Duncan A, Leung S, et al.; DECADE Study Group: Dexmedetomidine for reduction of atrial fibrillation and delirium after cardiac surgery (DECADE): A randomised placebo-controlled trial. Lancet 2020; 396:177–85
122. van Norden J, Spies CD, Borchers F, et al.: The effect of peri-operative dexmedetomidine on the incidence of postoperative delirium in cardiac and non-cardiac surgical patients: A randomised, double-blind placebo-controlled trial. Anaesthesia 2021; 76:1342–51
123. Xie K, Chen J, Tian L, et al.: Postoperative infusion of dexmedetomidine via intravenous patient-controlled analgesia for prevention of postoperative delirium in elderly patients undergoing surgery. Aging Clin Exp Res 2023; 35:2137–44
124. Xin X, Chen J, Hua W, Wang H: Intraoperative dexmedetomidine for prevention of postoperative delirium in elderly patients with mild cognitive impairment. Int J Geriatr Psychiatry 2021; 36:143–51
125. Xing C, Yan C: Effects of dexmedetomidine on the incidence of postoperative delirium and plasma s-100β protein levels following hip surgery in the elderly population. Int J Gerontol 2021; 15:207–11
126. Yan C, Ti-jun D: Effects of intraoperative dexmedetomidine infusion on postoperative delirium in elderly patients undergoing total hip arthroplasty. Int Surg 2021; 105:328–35
127. Yoo SH, Jue MJ, Kim YH, et al.: The effect of dexmedetomidine on the Mini-Cog score and high-mobility group box 1 levels in elderly patients with postoperative neurocognitive disorders undergoing orthopedic surgery. J Clin Med 2023; 12:6610
128. Zhang W, Wang T, Wang G, Yang M, Zhou Y, Yuan Y: Effects of dexmedetomidine on postoperative delirium and expression of IL-1beta, IL-6, and TNF-alpha in elderly patients after hip fracture operation. Front Pharmacol 2020; 11:678
129. Zhao W, Hu Y, Chen H, et al.: The effect and optimal dosage of dexmedetomidine plus sufentanil for postoperative analgesia in elderly patients with postoperative delirium and early postoperative cognitive dysfunction: A single-center, prospective, randomized,

double-blind, controlled trial. Front Neurosci 2020; 14:549516
130. Ding L, Zhang H, Mi W, et al.: Effects of dexmedetomidine on anesthesia recovery period and postoperative cognitive function of patients after robot-assisted laparoscopic radical cystectomy. Int J Clin Exp Med 2015; 8:11388–95
131. Gao Y, Zhu X, Huang L, Teng J, Li F: Effects of dexmedetomidine on cerebral oxygen saturation and postoperative cognitive function in elderly patients undergoing minimally invasive coronary artery bypass surgery. Clin Hemorheol Microcirc 2020; 74:383–9
132. Guo L, Liu Y, Wang M: Effect of perioperative dexmedetomidine anesthesia on prognosis of elderly patients with gastrointestinal tumor surgery. Comput Math Methods Med 2022; 2022:7889372
133. Li Z, Yao S, Cheng M, Chen J: Evaluation of the effect of dexmedetomidine on postoperative cognitive dysfunction through Aβ and cytokines analysis. Iran J Pharm Res 2021; 20:515–22
134. Mansouri N, Nasrollahi K, Shetabi H: Prevention of cognitive dysfunction after cataract surgery with intravenous administration of midazolam and dexmedetomidine in elderly patients undergoing cataract surgery. Adv Biomed Res 2019; 8:6
135. Mohamed S, Shaaban AR: The effect of dexmedetomidine on the incidence of postoperative cognitive dysfunction in elderly patients after prolonged abdominal surgery. Egypt J Anaesth 2014; 30:331–8
136. Zhou M, Lyu Y, Zhu Y, et al.: Effect of ulinastatin combined with dexmedetomidine on postoperative cognitive dysfunction in patients who underwent cardiac surgery. Front Neurol 2019; 10:1293
137. Oriby ME, Elrashidy AA, Elsharkawy A, Ahmed SA: Effects of ketamine or dexmedetomidine on postoperative cognitive dysfunction after cataract surgery: A randomized controlled trial. Indian J Anaesth 2023; 67:186–93
138. Chen H, Li F: Effect of dexmedetomidine with different anesthetic dosage on neurocognitive function in elderly patients after operation based on neural network model. World Neurosurg 2020; 138:688–95
139. Guo Y, Sun L, Zhang J, Li Q, Jiang H, Jiang W: Preventive effects of low-dose dexmedetomidine on postoperative cognitive function and recovery quality in elderly oral cancer patients. Int J Clin Exp Med 2015; 8:16183–90
140. Li JQ, Yuan H, Wang XQ, Yang M: Dexmedetomidine-induced anesthesia in elderly patients undergoing hip replacement surgery. World J Clin Cases 2023; 11:3756–64
141. Liao YQ, Min J, Wu ZX, Hu Z: Comparison of the effects of remimazolam and dexmedetomidine on early postoperative cognitive function in elderly patients with gastric cancer. Front Aging Neurosci 2023; 15:1123089
142. Wu LP, Kang WQ: Effect of dexmedetomidine for sedation and cognitive function in patients with preoperative anxiety undergoing carotid artery stenting. J Int Med Res 2020; 48:300060520938959
143. Zhao W, Zhang H, Li J: Effect of dexmedetomidine on postoperative cognitive dysfunction in elderly patients undergoing orthopaedic surgery: Study protocol for a randomized controlled trial. Trials 2023; 24:62
144. Xu T, Chen X, Li X, Wang M, Wang M: Effect of dexmedetomidine-assisted ultrasound-guided lower extremity nerve block on postoperative cognitive function in elderly patients undergoing hip surgery. Am J Transl Res 2022; 14:7977–84
145. Sultan SS: Assessment of role of perioperative melatonin in prevention and treatment of postoperative delirium after hip arthroplasty under spinal anesthesia in the elderly. Saudi J Anaesth 2010; 4:169–73
146. Kowark A, Keszei AP, Schneider G, et al.; I-PROMOTE Study Group: Preoperative midazolam and patient-centered outcomes of older patients: The I-PROMOTE randomized clinical trial. JAMA Surg 2024; 159:129–38
147. Yang JJ, Lei L, Qiu D, et al.: Effect of remimazolam on postoperative delirium in older adult patients undergoing orthopedic surgery: A prospective randomized controlled clinical trial. Drug Des Devel Ther 2023; 17:143–53
148. Aoki Y, Kurita T, Nakajima M, et al.: Association between remimazolam and postoperative delirium in older adults undergoing elective cardiovascular surgery: A prospective cohort study. J Anesth 2023; 37:13–22
149. Ke Y, Chew S, Seet E, et al.: Incidence and risk factors of delirium in post-anaesthesia care unit. Ann Acad Med Singap 2022; 51:87–95
150. Leigheb M, De Sire A, Zeppegno P, et al.: Delirium risk factors analysis post proximal femur fracture surgery in elderly. Acta Biomed 2022; 92:e2021569
151. Wang ML, Min J, Sands LP, Leung JM; The Perioperative Medicine Research Group: Midazolam premedication immediately before surgery is not associated with early postoperative delirium. Anesth Analg 2021; 133:765–71
152. Memtsoudis S, Cozowicz C, Zubizarreta N, et al.: Risk factors for postoperative delirium in patients undergoing lower extremity joint arthroplasty: A retrospective population-based cohort study. Reg Anesth Pain Med 2019; 44:934–43
153. Poeran J, Cozowicz C, Zubizarreta N, et al.: Modifiable factors associated with postoperative delirium after hip fracture repair: An age-stratified retrospective cohort study. Eur J Anaesthesiol 2020; 37:649–58

154. Fukata S, Kawabata Y, Fujishiro K, et al.: Haloperidol prophylaxis for preventing aggravation of postoperative delirium in elderly patients: A randomized, open-label prospective trial. Surg Today 2017; 47:815–26
155. Hakim SM, Othman AI, Naoum DO: Early treatment with risperidone for subsyndromal delirium after on-pump cardiac surgery in the elderly: A randomized trial. Anesthesiology 2012; 116:987–97
156. Larsen KA, Kelly SE, Stern TA, et al.: Administration of olanzapine to prevent postoperative delirium in elderly joint-replacement patients: A randomized, controlled trial. Psychosomatics 2010; 51:409–18
157. Prakanrattana U, Prapaitrakool S: Efficacy of risperidone for prevention of postoperative delirium in cardiac surgery. Anaesth Intensive Care 2007; 35:714–9
158. Wang W, Li HL, Wang DX, et al.: Prophylaxis decreases delirium incidence in elderly patients after noncardiac surgery: A randomized controlled trial. Crit Care Med 2012; 40:731–9
159. Fukata S, Kawabata Y, Fujisiro K, et al.: Haloperidol prophylaxis does not prevent postoperative delirium in elderly patients: A randomized, open-label prospective trial. Surg Today 2014; 44:2305–13
160. Hollinger A, Rust CA, Riegger H, et al.: Ketamine vs. haloperidol for prevention of cognitive dysfunction and postoperative delirium: A phase IV multicentre randomised placebo-controlled double-blind clinical trial. J Clin Anesth 2021; 68:110099
161. Kalisvaart KJ, de Jonghe JF, Bogaards MJ, et al.: Haloperidol prophylaxis for elderly hip-surgery patients at risk for delirium: A randomized placebo-controlled study. J Am Geriatr Soc 2005; 53:1658–66
162. Avidan MS, Maybrier HR, Abdallah AB, et al.; PODCAST Research Group: Intraoperative ketamine for prevention of postoperative delirium or pain after major surgery in older adults: An international, multicentre, double-blind, randomised clinical trial. Lancet 2017; 390:267–75
163. Hudetz JA, Patterson KM, Iqbal Z, et al.: Ketamine attenuates delirium after cardiac surgery with cardiopulmonary bypass. J Cardiothorac Vasc Anesth 2009; 23:651–7
164. Ma J, Wang F, Wang J, et al.: The effect of low-dose esketamine on postoperative neurocognitive dysfunction in elderly patients undergoing general anesthesia for gastrointestinal tumors: A randomized controlled trial. Drug Des Devel Ther 2023; 17:1945–57
165. Hongyu X, Qingting W, Xiaoling S, Liwu Z, Ailing Y, Xin L: Penehyclidine hydrochloride on postoperatively cognitive function. Med Hypotheses 2019; 129:109246
166. Slor CJ, de Jonghe JF, Vreeswijk R, et al.: Anesthesia and postoperative delirium in older adults undergoing hip surgery. J Am Geriatr Soc 2011; 59:1313–9
167. Mardani D, Bigdelian H: Prophylaxis of dexamethasone protects patients from further post-operative delirium after cardiac surgery: A randomized trial. J Res Med Sci 2013; 18:137–43
168. Sauer AM, Slooter AJ, Veldhuijzen DS, van Eijk MM, Devlin JW, van Dijk D: Intraoperative dexamethasone and delirium after cardiac surgery: A randomized clinical trial. Anesth Analg 2014; 119:1046–52
169. Whitlock RP, Devereaux PJ, Teoh KH, et al.; SIRS Investigators: Methylprednisolone in patients undergoing cardiopulmonary bypass (SIRS): A randomised, double-blind, placebo-controlled trial. Lancet 2015; 386:1243–53
170. Xiang XB, Chen H, Wu YL, Wang K, Yue X, Cheng XQ: The effect of preoperative methylprednisolone on postoperative delirium in older patients undergoing gastrointestinal surgery: A randomized, double-blind, placebo-controlled trial. J Gerontol A Biol Sci Med Sci 2022; 77:517–23
171. Dieleman JM, Nierich AP, Rosseel PM, et al.; Dexamethasone for Cardiac Surgery (DECS) Study Group: Intraoperative high-dose dexamethasone for cardiac surgery: A randomized controlled trial. JAMA 2012; 308:1761–7
172. Huang JW, Yang YF, Gao XS, Xu ZH: A single preoperative low-dose dexamethasone may reduce the incidence and severity of postoperative delirium in the geriatric intertrochanteric fracture patients with internal fixation surgery: An exploratory analysis of a randomized, placebo-controlled trial. J Orthop Surg Res 2023; 18:441
173. Leung JM, Sands LP, Chen N, et al.; Perioperative Medicine Research Group: Perioperative gabapentin does not reduce postoperative delirium in older surgical patients: A randomized clinical trial. Anesthesiology 2017; 127:633–44
174. Park CM, Inouye SK, Marcantonio ER, et al.: Perioperative gabapentin use and in-hospital adverse clinical events among older adults after major surgery. JAMA Intern Med 2022; 182:1117–27
175. By the 2023 American Geriatrics Society Beers Criteria Update Expert Panel: American Geriatrics Society 2023 updated AGS Beers Criteria(r) for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2023; 71:2052–81
176. Spence J, Belley-Cote E, Jacobsohn E, et al.; B-Free Investigators: Benzodiazepine-free cardiac anesthesia for reduction of postoperative delirium (B-Free): A protocol for a multi-centre randomized cluster crossover trial. CJC Open 2023; 5:691–9
177. McIsaac DI, Gill M, Boland L, et al.; Prehabilitation Knowledge Network: Prehabilitation in adult patients

undergoing surgery: An umbrella review of systematic reviews. Br J Anaesth 2022; 128:244–57
178. Scheede-Bergdahl C, Minnella EM, Carli F: Multi-modal prehabilitation: Addressing the why, when, what, how, who and where next? Anaesthesia 2019; 74:20–6
179. Gillis C, Buhler K, Bresee L, et al.: Effects of nutritional prehabilitation, with and without exercise, on outcomes of patients who undergo colorectal surgery: A systematic review and meta-analysis. Gastroenterology 2018; 155:391–410.e4
180. Lobo DN, Pavel S, Gomez D, Greenhaff PL: Prehabilitation: High-quality evidence is still required. Br J Anaesth 2023; 130:9–14
181. Milder DA, Pillinger NL, Kam PCA: The role of prehabilitation in frail surgical patients: A systematic review. Acta Anaesthesiol Scand 2018; 62:1356–66
182. Humeidan ML, Reyes JC, Mavarez-Martinez A, et al.: Effect of cognitive prehabilitation on the incidence of postoperative delirium among older adults undergoing major noncardiac surgery: The Neurobics randomized clinical trial. JAMA Surg 2021; 156:148–56
183. Berian JR, Rosenthal RA, Baker TL, et al.: Hospital standards to promote optimal surgical care of the older adult: A report from the coalition for quality in geriatric surgery. Ann Surg 2018; 267:280–90
184. Hempenius L, Slaets JP, van Asselt D, de Bock TH, Wiggers T, van Leeuwen BL: Long term outcomes of a geriatric liaison intervention in frail elderly cancer patients. PLoS One 2016; 11:e0143364
185. Ommundsen N, Wyller TB, Nesbakken A, et al.: Preoperative geriatric assessment and tailored interventions in frail older patients with colorectal cancer: A randomized controlled trial. Colorectal Dis 2018; 20:16–25
186. Prestmo A, Hagen G, Sletvold O, et al.: Comprehensive geriatric care for patients with hip fractures: A prospective, randomised, controlled trial. Lancet 2015; 385:1623–33
187. Shyu Y-IL, Liang J, Wu C-C, et al.: Interdisciplinary intervention for hip fracture in older Taiwanese: Benefits last for 1 year. J Gerontol A Biol Sci Med Sci 2008; 63:92–7
188. Shyu Y-IL, Liang J, Wu C-C, et al.: A pilot investigation of the short-term effects of an interdisciplinary intervention program on elderly patients with hip fracture in Taiwan. J Am Geriatr Soc 2005; 53:811–8
189. Braude P, Goodman A, Elias T, et al.: Evaluation and establishment of a ward-based geriatric liaison service for older urological surgical patients: Proactive Care of Older People Undergoing Surgery (POPS)-urology. BJU Int 2017; 120:123–9
190. Deschodt M, Braes TF, Broos P, et al.: Effect of an inpatient geriatric consultation team on functional outcome, mortality, institutionalization, and readmission rate in older adults with hip fracture: A controlled trial. J Am Geriatr Soc 2011; 59:1299–308
191. Ernst KF, Hall DE, Schmid KK, et al.: Surgical palliative care consultations over time in relationship to systemwide frailty screening. JAMA Surg 2014; 149:1121–6
192. Giannotti C, Massobrio A, Carmisciano L, et al.: Effect of geriatric comanagement in older patients undergoing surgery for gastrointestinal cancer: A retrospective, before-and-after study. J Am Med Dir Assoc 2022; 23:1868.e9–16
193. Hall DE, Arya S, Schmid KK, et al.: Association of a frailty screening initiative with postoperative survival at 30, 180, and 365 days. JAMA Surg 2017; 152:233–40
194. Jones TS, Jones EL, Richardson V, et al.: Preliminary data demonstrate the geriatric surgery verification program reduces postoperative length of stay. J Am Geriatr Soc 2021; 69:1993–9
195. McDonald SR, Heflin MT, Whitson HE, et al.: Association of integrated care coordination with postsurgical outcomes in high-risk older adults: The Perioperative Optimization of Senior Health (POSH) initiative. JAMA Surg 2018; 153:454–62
196. Olsson LE, Karlsson J, Berg U, Karrholm J, Hansson E: Person-centred care compared with standardized care for patients undergoing total hip arthroplasty--A quasi-experimental study. J Orthop Surg Res 2014; 9:95
197. Richter HE, Redden DT, Duxbury AS, Granieri EC, Halli AD, Goode PS: Pelvic floor surgery in the older woman: Enhanced compared with usual preoperative assessment. Obstet Gynecol 2005; 105:800–7
198. Romano LU, Rigoni M, Torri E, et al.: propensity score-matched analysis to assess the outcomes in pre- and post-fast-track hip and knee elective prosthesis patients. J Clin Med 2021; 10:1–13
199. Smoor RM, van Dongen EPA, Daeter EJ, et al.: The association between preoperative multidisciplinary team care and patient outcome in frail patients undergoing cardiac surgery. J Thorac Cardiovasc Surg 2023; 168:608–16
200. Souwer ETD, Bastiaannet E, de Bruijn S, et al.: Comprehensive multidisciplinary care program for elderly colorectal cancer patients: “From prehabilitation to independence.” Eur J Surg Oncol 2018; 44:1894–900
201. Staiger RD, Curley D, Attwood NV, Haile SR, Arulampalam T, Simpson JC: Surgical outcome improvement by shared decision-making: Value of a preoperative multidisciplinary target clinic for the elderly in colorectal surgery. Langenbecks Arch Surg 2023; 408:316
202. Vochteloo AJ, Moerman S, van der Burg BL, et al.: Delirium risk screening and haloperidol prophylaxis

program in hip fracture patients is a helpful tool in identifying high-risk patients, but does not reduce the incidence of delirium. BMC Geriatr 2011; 11:39
203. Alas A, Martin L, Devakumar H, et al.: Anesthetics' role in postoperative urinary retention after pelvic organ prolapse surgery with concomitant midurethral slings: A randomized clinical trial. Int Urogynecol J 2020; 31:205–13
204. Apan A, Cuvas Apan O, Kose EA: Segmental epidural anesthesia for percutaneous kyphoplasty: Comparison with general anesthesia. Turk J Med Sci 2016; 46:1801–7
205. Carron M, Freo U, Innocente F, et al.: Recovery profiles of general anesthesia and spinal anesthesia for chemotherapeutic perfusion with circulatory block (stop-flow perfusion). Anesth Analg 2007; 105:1500–3
206. Edipoglu IS, Celik F: The associations between cognitive dysfunction, stress biomarkers, and administered anesthesia type in total knee arthroplasties: Prospective, randomized trial. Pain Physician 2019; 22:495–507
207. Haghighi M, Sedighinejad A, Nabi BN, et al.: Is spinal anesthesia with low dose lidocaine better than sevoflorane anesthesia in patients undergoing hip fracture surgery. Arch Bone Jt Surg 2017; 5:226–30
208. Harsten A, Kehlet H, Ljung P, Toksvig-Larsen S: Total intravenous general anaesthesia vs. spinal anaesthesia for total hip arthroplasty: A randomised, controlled trial. Acta Anaesthesiol Scand 2015; 59:298–309
209. Harsten A, Kehlet H, Toksvig-Larsen S: Recovery after total intravenous general anaesthesia or spinal anaesthesia for total knee arthroplasty: A randomized trial. Br J Anaesth 2013; 111:391–9
210. Mandal S, Basu M, Kirtania J, et al.: Impact of general versus epidural anesthesia on early post-operative cognitive dysfunction following hip and knee surgery. J Emerg Trauma Shock 2011; 4:23–8
211. Mazul-Sunko B, Hromatko I, Tadinac M, et al.: Subclinical neurocognitive dysfunction after carotid endarterectomy-The impact of shunting. J Neurosurg Anesthesiol 2010; 22:195–201
212. Meuret P, Bouvet L, Villet B, Hafez M, Allaouchiche B, Boselli E: Hypobaric unilateral spinal anaesthesia versus general anaesthesia in elderly patients undergoing hip fracture surgical repair: A prospective randomised open trial. Turk J Anaesthesiol Reanim 2018; 46:121–30
213. Nesek-Adam V, Rasic Z, Schwarz D, et al.: The effect of spinal versus general anesthesia on postoperative pain and analgesic requirements in patients undergoing peripheral vascular surgery. Coll Antropol 2012; 36:1301–5
214. Neuman MD, Feng R, Ellenberg SS, et al.; REGAIN (Regional versus General Anesthesia for Promoting Independence after Hip Fracture) Investigators*: Pain, analgesic use, and patient satisfaction with spinal versus general anesthesia for hip fracture surgery: A randomized clinical trial. Ann Intern Med 2022; 175:952–60
215. Nishikawa K, Yoshida S, Shimodate Y, Igarashi M, Namiki A: A comparison of spinal anesthesia with small-dose lidocaine and general anesthesia with fentanyl and propofol for ambulatory prostate biopsy procedures in elderly patients. J Clin Anesth 2007; 19:25–9
216. O'Brien K, Feng R, Sieber F, et al.; REGAIN (Regional versus General Anesthesia for Promoting Independence after Hip Fracture) Investigators: Outcomes with spinal versus general anesthesia for patients with and without preoperative cognitive impairment: Secondary analysis of a randomized clinical trial. Alzheimers Dement 2023; 19:4008–19
217. Ornek D, Metin S, Deren S, et al.: The influence of various anesthesia techniques on postoperative recovery and discharge criteria among geriatric patients. Clinics (Sao Paulo) 2010; 65:941–6
218. Purwar B, Ismail KM, Turner N, et al.: General or spinal anaesthetic for vaginal surgery in pelvic floor disorders (GOSSIP): A feasibility randomised controlled trial. Int Urogynecol J 2015; 26:1171–8
219. Ren WX, Wu RR: Effect of general and sub-arachnoid anesthesia on the incidence of postoperative delirium and cognitive impairments in elderly Chinese patients. Trop J Pharma Res 2021; 20:433–9
220. Salonia A, Crescenti A, Suardi N, et al.: General versus spinal anesthesia in patients undergoing radical retropubic prostatectomy: Results of a prospective, randomized study. Urology 2004; 64:95–100
221. Salonia A, Suardi N, Crescenti A, Colombo R, Rigatti P, Montorsi F: General versus spinal anesthesia with different forms of sedation in patients undergoing radical retropubic prostatectomy: Results of a prospective, randomized study. Int J Urol 2006; 13:1185–90
222. Sciberras SC, Vella AP, Vella B, et al.: A randomized, controlled trial on the effect of anesthesia on chronic pain after total knee arthroplasty. Pain Manag 2022; 12:711–23
223. Wang Q, Lin F, Huang B, Pan LH: The effectiveness and safety of general and spinal anesthesia on systemic inflammatory response in patients with tumor-type total knee arthroplasty. Oncol Res Treat 2020; 43:428–34
224. Wongyingsinn M, Kohmongkoludom P, Trakarnsanga A, Horthongkham N: Postoperative clinical outcomes and inflammatory markers after inguinal hernia repair using local, spinal, or general anesthesia: A randomized controlled trial. PLoS One 2020; 15:e0242925

225. Xu CS, Qu XD, Qu ZJ, Wang G, Wang HJ: Effect of subarachnoid anesthesia combined with propofol target-controlled infusion on blood loss and transfusion for posterior total hip arthroplasty in elderly patients. Chin Med J (Engl) 2020; 133:650–6
226. Zhang X, Dong Q, Fang J: Impacts of general and spinal anaesthesia on short-term cognitive function and mental status in elderly patients undergoing orthopaedic surgery. J Coll Physicians Surg Pak 2019; 29:101–4
227. Boney O, Moonesinghe SR, Myles PS, Grocott MPW; StEP-COMPAC Group: Core Outcome Measures for Perioperative and Anaesthetic Care (COMPAC): A modified Delphi process to develop a core outcome set for trials in perioperative care and anaesthesia. Br J Anaesth 2022; 128:174–85
228. Cai Y, Hu H, Liu P, et al.: Association between the apolipoprotein e4 and postoperative cognitive dysfunction in elderly patients undergoing intravenous anesthesia and inhalation anesthesia. Anesthesiology 2012; 116:84–93
229. Celik JB, Topal A, Erol A, Guven S, Kara I: A comparison of recovery characteristics of sevoflurane and propofol remifentanil anesthesia in geriatric patients. Turk J Geriatr 2011; 14:208–13
230. Ding DF, Wang P, Jiang YX, Zhang XP, Shi W, Luo YW: Effects of apolipoprotein epsilon epsilon4 allele on early postoperative cognitive dysfunction after anesthesia. Anaesthesist 2021; 70:60–7
231. Epple J, Kubitz J, Schmidt H, et al.: Comparative analysis of costs of total intravenous anaesthesia with propofol and remifentanil vs. balanced anaesthesia with isoflurane and fentanyl. Eur J Anaesthesiol 2001; 18:20–8
232. Fazel MR, Kheirkhah P, Atoof F: Sevoflurane versus propofol anesthesia on early postoperative cognitive function in older adults: A randomized controlled trial. Middle East J Anesthesiol 2017; 24:237–41
233. Geng YJ, Wu QH, Zhang RQ: Effect of propofol, sevoflurane, and isoflurane on postoperative cognitive dysfunction following laparoscopic cholecystectomy in elderly patients: A randomized controlled trial. J Clin Anesth 2017; 38:165–71
234. Jellish WS, Sheikh T, Baker WH, Louie EK, Slogoff S: Hemodynamic stability, myocardial ischemia, and perioperative outcome after carotid surgery with remifentanil/propofol or isoflurane/fentanyl anesthesia. J Neurosurg Anesthesiol 2003; 15:176–84
235. Kalimeris K, Kouni S, Kostopanagiotou G, et al.: Cognitive function and oxidative stress after carotid endarterectomy: Comparison of propofol to sevoflurane anesthesia. J Cardiothorac Vasc Anesth 2013; 27:1246–52
236. Kang TH, Kim WJ, Lee JH: Efficacy of the erector spinae plane block with sedation for unilateral biportal endoscopic spine surgery and comparison with other anesthetic methods. Acta Neurochir 2023; 165:2651–63
237. Luntz SP, Janitz E, Motsch J, Bach A, Martin E, Böttiger BW: Cost-effectiveness and high patient satisfaction in the elderly: Sevoflurane versus propofol anaesthesia. Eur J Anaesthesiol 2004; 21:115–22
238. Özer E, Yilmaz R: Effect of different anesthetic techniques on mental outcome in elderly patients undergoing off-pump coronary artery bypass graft surgery. Turkiye Klinikleri J Cardiovasc Sci 2017; 29:17–22
239. Qiao H, Chen J, Huang Y, et al.: Early neurocognitive function with propofol or desflurane anesthesia after laser laryngeal surgery with low inspired oxygen. Laryngoscope 2023; 133:640–6
240. Qiao Y, Feng H, Zhao T, Yan H, Zhang H, Zhao X: Postoperative cognitive dysfunction after inhalational anesthesia in elderly patients undergoing major surgery: The influence of anesthetic technique, cerebral injury and systemic inflammation. BMC Anesthesiol 2015; 15:154
241. Qin Y, Ni J, Kang L, Zhong Z, Wang L, Yin S: Sevoflurane effect on cognitive function and the expression of oxidative stress response proteins in elderly patients undergoing radical surgery for lung cancer. J Coll Physicians Surg Pak 2019; 29:12–5
242. Rohan D, Buggy DJ, Crowley S, et al.: Increased incidence of postoperative cognitive dysfunction 24 hr after minor surgery in the elderly. Can J Anaesth 2005; 52:137–42
243. Tian HT, Duan XH, Yang YF, Wang Y, Bai QL, Zhang X: Effects of propofol or sevoflurane anesthesia on the perioperative inflammatory response, pulmonary function and cognitive function in patients receiving lung cancer resection. Eur Rev Med Pharmacol Sci 2021; 21:5515–22
244. Villalobos D, Reese M, Wright MC, et al.: Perioperative changes in neurocognitive and Alzheimer's disease-related cerebrospinal fluid biomarkers in older patients randomised to isoflurane or propofol for anaesthetic maintenance. Br J Anaesth 2023; 131:328–37
245. Yang L, Chen Z, Xiang D: Effects of intravenous anesthesia with sevoflurane combined with propofol on intraoperative hemodynamics, postoperative stress disorder and cognitive function in elderly patients undergoing laparoscopic surgery. Pak J Med Sci 2022; 38:1938–44
246. Zangrillo A, Testa V, Aldrovandi V, et al.: Volatile agents for cardiac protection in noncardiac surgery: A randomized controlled study. J Cardiothorac Vasc Anesth 2011; 25:902–7
247. Zhou Y, Xu T: Effect of propofol and sevoflurane on perioperative and postoperative outcomes in lung

cancer patients after thoracoscopic surgery. Trop J Pharma Res 2021; 20:873–9
248. Chang JE, Min SW, Kim H, et al.: Association between anesthetics and postoperative delirium in elderly patients undergoing spine surgery: Propofol versus sevoflurane. Global Spine J 2024; 14:478–84
249. Goins AE, Smeltz A, Ramm C, et al.: General anesthesia for transcatheter aortic valve replacement: Total intravenous anesthesia is associated with less delirium as compared to volatile agent technique. J Cardiothorac Vasc Anesth 2018; 32:1570–7
250. Huang YY, Hui CK, Lau NC, et al.: Total intravenous anesthesia for geriatric hip fracture with severe systemic disease. Eur J Trauma Emerg Surg 2023; 49:2139–45
251. Jakobsen CJ, Berg H, Hindsholm KB, Faddy N, Sloth E: The influence of propofol versus sevoflurane anesthesia on outcome in 10,535 cardiac surgical procedures. J Cardiothorac Vasc Anesth 2007; 21:664–71
252. Kishimoto M, Yamana H, Inoue S, et al.: Suspected periprosthetic joint infection after total knee arthroplasty under propofol versus sevoflurane anesthesia: A retrospective cohort study. Can J Anaesth 2018; 65:893–900
253. Koo BW, Sim JB, Shin HJ, et al.: Surgical site infection after colorectal surgery according to the main anesthetic agent: A retrospective comparison between volatile anesthetics and propofol. Korean J Anesthesiol 2016; 69:332–40
254. Oh TK, Kim J, Han S, Kim K, Jheon S, Ji E: Effect of sevoflurane-based or propofol-based anaesthesia on the incidence of postoperative acute kidney injury: A retrospective propensity score-matched analysis. Eur J Anaesthesiol 2019; 36:649–55
255. Park J, Lee SH, Lee JH, et al.: Volatile versus total intravenous anesthesia for 30-day mortality following non-cardiac surgery in patients with preoperative myocardial injury. PLoS One 2020; 15:e0238661
256. Shimizu K, Hirose M, Mikami S, et al.: Effect of anaesthesia maintained with sevoflurane and propofol on surgical site infection after elective open gastrointestinal surgery. J Hosp Infect 2010; 74:129–36
257. Deiner S, Lin HM, Bodansky D, Silverstein J, Sano M: Do stress markers and anesthetic technique predict delirium in the elderly? Dement Geriatr Cogn Disord 2014; 38:366–74
258. Chen J, Yan J, Han X: Dexmedetomidine may benefit cognitive function after laparoscopic cholecystectomy in elderly patients. Exp Ther Med 2013; 5:489–94
259. Du X, Song F, Zhang X, Ma S: Protective efficacy of combined use of parecoxib and dexmedetomidine on postoperative hyperalgesia and early cognitive dysfunction after laparoscopic cholecystectomy for elderly patients. Acta Cir Bras 2019; 34:e201900905
260. Gao C, Huang T, Wu K, et al.: Multimodal analgesia for accelerated rehabilitation after total knee arthroplasty: A randomized, double-blind, controlled trial on the effect of the co-application of local infiltration analgesia and femoral nerve block combined with dexmedetomidine. Brain Sci 2022; 12:1652
261. Ge YL, Li X, Gao J, et al.: Beneficial effects of intravenous dexmedetomidine on cognitive function and cerebral injury following a carotid endarterectomy. Exp Ther Med 2016; 11:1128–34
262. Li Y, He R, Chen S, Qu Y: Effect of dexmedetomidine on early postoperative cognitive dysfunction and peri-operative inflammation in elderly patients undergoing laparoscopic cholecystectomy. Exp Ther Med 2015; 10:1635–42
263. Liu T, Liu FC, Xia Y, et al.: Effect of dexmedetomidine on the Montreal Cognitive Assessment in older patients undergoing pulmonary surgery. J Int Med Res 2022; 50:3000605221123680
264. Tang Y, Liu J, Huang X, Ding H, Tan S, Zhu Y: Effect of dexmedetomidine-assisted intravenous inhalation combined anesthesia on cerebral oxygen metabolism and serum Th1/Th2 level in elderly colorectal cancer patients. Front Surg 2021; 8:832646
265. Wang F, Xie D, Xu H, Ye Q, Wu L, Gao XP: The effects of remifentanil-propofol combined with dexmedetomidine on cognitive dysfunction in elderly patients after ureteroscopic holmium laser lithotripsy: A double-blind randomized controlled trial. Trials 2022; 23:192
266. Wang W, Ma Y, Liu Y, Wang P, Liu Y: Effects of dexmedetomidine anesthesia on early postoperative cognitive dysfunction in elderly patients. ACS Chem Neurosci 2022; 13:2309–14
267. Zhang Z, Li W, Jia H: Postoperative effects of dexmedetomidine on serum inflammatory factors and cognitive malfunctioning in patients with general anesthesia. J Healthc Eng 2021; 2021:7161901
268. Zhu Y, Le G: The effect of dexmedetomidine combined with epidural anesthesia on post-operative cognitive dysfunction in elderly patients after orthopedic surgery. Am J Transl Res 2021; 13:12058–64
269. Cheng H, Li Z, Young N, et al.: The effect of dexmedetomidine on outcomes of cardiac surgery in elderly patients. J Cardiothorac Vasc Anesth 2016; 30:1502–8
270. Sun Y, Peng HP, Wu TT: Postoperative c-reactive protein predicts postoperative delirium in colorectal cancer following surgery. Clin Interv Aging 2023; 18:559–70
271. Xie S, Xie M: Effect of dexmedetomidine on postoperative delirium in elderly patients undergoing hip fracture surgery. Pak J Pharm Sci 2018; 31:2277–81
272. Yin L, Yuan H, Chen X, Liao M, Lu F: Mechanism of action of dexmedetomidine on hemodynamics, analgesic and sedative effects and postoperative delirium

in elderly patients undergoing hip fracture surgery. Int J Clin Exper Med 2020; 13:6703–9
273. de Jonghe A, van Munster BC, Goslings JC, et al.; Amsterdam Delirium Study Group: Effect of melatonin on incidence of delirium among patients with hip fracture: A multicentre, double-blind randomized controlled trial. CMAJ 2014; 186:E547–56
274. El-Naggar DI, Sharaf SI, Nasr El-Din DA, Mahran MG, Nawar DFA: A study of the prophylactic and curative effect of melatonin on postoperative delirium after coronary artery bypass grafting surgery in elderly patients. Egypt J Hosp Med 2018; 72:4919–26
275. Esmaeili A, Fanoodi A, Ebrahimi A, Zangoue M, Khojasteh-Kaffash S: The efficacy of melatonin and clonidine in preventing emergence delirium in the elderly undergoing orthopedic surgery, neurosurgery, and general surgery: A placebo-controlled randomized clinical trial. J Kermanshah Univ Med Sci 2022; 26:e128831
276. Fan Y, Yuan L, Ji M, Yang J, Gao D: The effect of melatonin on early postoperative cognitive decline in elderly patients undergoing hip arthroplasty: A randomized controlled trial. J Clin Anesth 2017; 39:77–81
277. Fazel MR, Mofidian S, Mahdian M, Akbari H, Razavizadeh MR: The effect of melatonin on prevention of postoperative delirium after lower limb fracture surgery in elderly patients: A randomized double blind clinical trial. Int J Burns Trauma 2022; 12:161–7
278. Ford AH, Flicker L, Kelly R, et al.: The Healthy Heart-Mind trial: Randomized controlled trial of melatonin for prevention of delirium. J Am Geriatr Soc 2020; 68:112–9
279. Gupta PK, Verma R, Kohli M, Shukla N, Kannaujia S: The effect of ramelteon on postoperative delirium in elderly patients: A randomised double-blind study. J Clin Diag Res 2019; 13:UC15–9
280. Jaiswal SJ, Vyas AD, Heisel AJ, et al.: Ramelteon for prevention of postoperative delirium: A randomized controlled trial in patients undergoing elective pulmonary thromboendarterectomy. Crit Care Med 2019; 47:1751–8
281. Javaherforoosh Zadeh F, Janatmakan F, Shafaeebejestan E, Jorairahmadi S: Effect of melatonin on delirium after on-pump coronary artery bypass graft surgery: A randomized controlled trial. Iran J Med Sci 2021; 46:120–7
282. Kinouchi M, Mihara T, Taguri M, Ogura M: The efficacy of ramelteon to prevent postoperative delirium after general anesthesia in the elderly: A double-blind, randomized, placebo-controlled trial. Am J Geriatr Psychiatry 2023; 31:1178–89
283. Mohamed SA, Rady A, Youssry M, Abdelaziz Mohamed MR, Gamal M: Performance of melatonin as prophylaxis in geriatric patients with multifactorial risk for postoperative delirium development: A randomized comparative study. Turk J Anaesthesiol Reanim 2022; 50:178–86
284. Oh ES, Leoutsakos JM, Rosenberg PB, et al.: Effects of ramelteon on the prevention of postoperative delirium in older patients undergoing orthopedic surgery: The RECOVER randomized controlled trial. Am J Geriatr Psychiatry 2021; 29:90–100
285. Shi Y: Effects of melatonin on postoperative delirium after PCI in elderly patients: A randomized, single-center, double-blind, placebo-controlled trial. Heart Surg Forum 2021; 24:E893–7
286. Tanifuji T, Otsuka I, Okazaki S, et al.: Preventive effects of preoperative ramelteon on postoperative delirium in Asian elderly population: A randomized, double-blind, placebo-controlled trial, and a systematic review and meta-analysis. Asian J Psychiatr 2022; 78:103282
287. Artemiou P, Bily B, Bilecova-Rabajdova M, et al.: Melatonin treatment in the prevention of postoperative delirium in cardiac surgery patients. Kardiochir Torakochirurgia Pol 2015; 12:126–33
288. Bily B, Sabol F, Török P, Artemiou P, Bilecova-Rabajdova M, Kolarcik P: Influence of prophylactic melatonin administration on the incidence of early postoperative delirium in cardiac surgery patients. Anesteziol Intenzivni Med 2015; 26:319–27
289. Hokuto D, Nomi T, Yoshikawa T, Matsuo Y, Kamitani N, Sho M: Preventative effects of ramelteon against postoperative delirium after elective liver resection. PLoS One 2020; 15:e0241673
290. Miyata R, Omasa M, Fujimoto R, Ishikawa H, Aoki M: Efficacy of ramelteon for delirium after lung cancer surgery. Interact Cardiovasc Thorac Surg 2017; 24:8–12
291. Ishibashi-Kanno N, Takaoka S, Nagai H, et al.: Postoperative delirium after reconstructive surgery for oral tumor: A retrospective clinical study. Int J Oral Maxillofac Surg 2020; 49:1143–8
292. Azeem TMA, Yosif NE, Alansary AM, Esmat IM, Mohamed AK: Dexmedetomidine vs morphine and midazolam in the prevention and treatment of delirium after adult cardiac surgery; A randomized, double-blinded clinical trial. Saudi J Anaesth 2018; 12:190–7
293. Deng Y, Qin Z, Wu Q, et al.: Efficacy and safety of remimazolam besylate versus dexmedetomidine for sedation in non-intubated older patients with agitated delirium after orthopedic surgery: A randomized controlled trial. Drug Des Devel Ther 2022; 16:2439–51
294. Kuang Q, Zhong N, Ye C, Zhu X, Wei F: Propofol versus remimazolam on cognitive function, hemodynamics, and oxygenation during one-lung ventilation

in older patients undergoing pulmonary lobectomy: A randomized controlled trial. J Cardiothorac Vasc Anesth 2023; 37:1996–2005

295. Li WX, Luo RY, Chen C, et al.: Effects of propofol, dexmedetomidine, and midazolam on postoperative cognitive dysfunction in elderly patients: A randomized controlled preliminary trial. Chin Med J (Engl) 2019; 132:437–45
296. Spence J, Belley-Cote E, Jacobsohn E, et al.: Restricted versus liberal intraoperative benzodiazepine use in cardiac anaesthesia for reducing delirium (B-Free Pilot): A pilot, multicentre, randomised, cluster crossover trial. Br J Anaesth 2020; 125:38–46
297. Sun Y, Zhang J, Feng S: Remimazolam supplemented to general anesthesia alleviates stress and cognitive impairment in elder patients after hip surgery. Psychiatry Investig 2023; 20:301–6
298. Tan Y, Ouyang W, Tang Y, Fang N, Fang C, Quan C: Effect of remimazolam tosilate on early cognitive function in elderly patients undergoing upper gastrointestinal endoscopy. J Gastroenterol Hepatol 2022; 37:576–83
299. Wang L, Zhang T, Huang L, Peng W: Comparison between dexmedetomidine and midazolam for sedation in patients with intubation after oral and maxillofacial surgery. Biomed Res Int 2020; 2020:7082597
300. Yu DN, Zhu Y, Ma J, Sun Q: Comparison of post-anesthesia delirium in elderly patients treated with dexmedetomidine and midazolam maleate after thoracic surgery. Biomed Res (India) 2017; 28:6852–5
301. Kaneko T, Takahashi S, Naka T, Hirooka Y, Inoue Y, Kaibara N: Postoperative delirium following gastrointestinal surgery in elderly patients. Surg Today 1997; 27:107–11
302. Koch S, Blankertz B, Windmann V, Spies C, Radtke FM, Röhr V: Desflurane is risk factor for postoperative delirium in older patients' independent from intraoperative burst suppression duration. Front Aging Neurosci 2023; 15:1067268
303. Liu J, Li J, Gao D, Wang J, Liu M, Yu D: High ASA Physical Status and low serum uric acid to creatinine ratio are independent risk factors for postoperative delirium among older adults undergoing urinary calculi surgery. Clin Interv Aging 2023; 18:81–92
304. Mueller A, Spies CD, Eckardt R, et al.; PERATECS-Group: Anticholinergic burden of long-term medication is an independent risk factor for the development of postoperative delirium: A clinical trial. J Clin Anesth 2020; 61:109632
305. Yoshimura M, Hidaka Y, Morimoto Y: Association between the use of midazolam during cardiac anesthesia and the incidence of postoperative delirium: A retrospective cohort study using a nationwide database. J Cardiothorac Vasc Anesth 2023; 37:2546–51
306. Zarour S, Weiss Y, Kiselevich Y, et al.: The association between midazolam premedication and postoperative delirium - A retrospective cohort study. J Clin Anesth 2023; 92:111113
307. Bornemann-Cimenti H, Wejbora M, Michaeli K, Edler A, Sandner-Kiesling A: The effects of minimal-dose versus low-dose s-ketamine on opioid consumption, hyperalgesia, and postoperative delirium: A triple-blinded, randomized, active- and placebo-controlled clinical trial. Minerva Anestesiol 2016; 82:1069–76
308. Han C, Ji H, Guo Y, et al.: Effect of subanesthetic dose of esketamine on perioperative neurocognitive disorders in elderly undergoing gastrointestinal surgery: A randomized controlled trial. Drug Des Devel Ther 2023; 17:863–73
309. Hudetz JA, Iqbal Z, Gandhi SD, et al.: Ketamine attenuates post-operative cognitive dysfunction after cardiac surgery. Acta Anaesthesiol Scand 2009; 53:864–72
310. Lee KH, Kim JY, Kim JW, Park JS, Lee KW, Jeon SY: Influence of ketamine on early postoperative cognitive function after orthopedic surgery in elderly patients. Anesth Pain Med 2015; 5:e28844
311. Rascon-Martinez DM, Fresan-Orellana A, Ocharan-Hernandez ME, Genis-Zarate JH, Castellanos-Olivares A: The effects of ketamine on cognitive function in elderly patients undergoing ophthalmic surgery: A pilot study. Anesth Analg 2016; 122:969–75
312. Remerand F, Le Tendre C, Baud A, et al.: The early and delayed analgesic effects of ketamine after total hip arthroplasty: A prospective, randomized, controlled, double-blind study. Anesth Analg 2009; 109:1963–71
313. Siripoonyothai S, Sindhvananda W: Comparison of postoperative delirium within 24 hours between ketamine and propofol infusion during cardiopulmonary bypass machine: A randomized controlled trial. Ann Card Anaesth 2021; 24:294–301
314. Tu W, Yuan H, Zhang S, et al.: Influence of anesthetic induction of propofol combined with esketamine on perioperative stress and inflammatory responses and postoperative cognition of elderly surgical patients. Am J Transl Res 2021; 13:1701–9
315. Barreto Chang OL, Kreuzer M, Morgen DF, Possin KL, Garcia PS: Ketamine associated intraoperative electroencephalographic signatures of elderly patients with and without preoperative cognitive impairment. Anesth Analg 2022; 135:683–92
316. Juliebo V, Bjoro K, Krogseth M, Skovlund E, Ranhoff AH, Wyller TB: Risk factors for preoperative and postoperative delirium in elderly patients with hip fracture. J Am Geriatr Soc 2009; 57:1354–61
317. Fuchita M, Khan SH, Perkins AJ, et al.: Perioperative risk factors for postoperative delirium in patients

undergoing esophagectomy. Ann Thorac Surg 2019; 108:190–5
318. Weinstein SM, Poultsides L, Baaklini LR, et al.: Postoperative delirium in total knee and hip arthroplasty patients: A study of perioperative modifiable risk factors. Br J Anaesth 2018; 120:999–1008
319. Duprey MS, Devlin JW, Griffith JL, et al.: Association between perioperative medication use and postoperative delirium and cognition in older adults undergoing elective noncardiac surgery. Anesth Analg 2022; 134:1154–63
320. Brøndum TL, Leerhøy B, Jensen KK: Effect of preoperative, high-dose glucocorticoid on early cognitive function after abdominal wall reconstruction – A randomized controlled trial. Int J Surg Open 2022; 48:100567
321. Glumac S, Kardum G, Sodic L, Supe-Domic D, Karanovic N: Effects of dexamethasone on early cognitive decline after cardiac surgery: A randomised controlled trial. Eur J Anaesthesiol 2017; 34:776–84
322. Ottens TH, Dieleman JM, Sauer AM, et al.; DExamethasone for Cardiac Surgery (DECS) Study Group: Effects of dexamethasone on cognitive decline after cardiac surgery: A randomized clinical trial. Anesthesiology 2014; 121:492–500
323. Royse CF, Saager L, Whitlock R, et al.: Impact of methylprednisolone on postoperative quality of recovery and delirium in the steroids in cardiac surgery trial: A randomized, double-blind, placebo-controlled substudy. Anesthesiology 2017; 126:223–33
324. Valentin LS, Pereira VF, Pietrobon RS, et al.: Effects of single low dose of dexamethasone before noncardiac and nonneurologic surgery and general anesthesia on postoperative cognitive dysfunction-A phase III double blind, randomized clinical trial. PLoS One 2016; 11:e0152308
325. Zeng Y, Wang Q, Hu J, Yang J: Adding dexamethasone to adductor canal block combined with iPACK block improve postoperative analgesia of total knee arthroplasty. Clin J Pain 2022; 38:575–81
326. Burfeind KG, Zarnegarnia Y, Tekkali P, O'Glasser AY, Quinn JF, Schenning KJ: Potentially inappropriate medication administration is associated with adverse postoperative outcomes in older surgical patients: A retrospective cohort study. Anesth Analg 2022; 135:1048–56
327. Choi H, Shin B, Yoo H, et al.: Early corticosteroid treatment for postoperative acute lung injury after lung cancer surgery. Ther Adv Respir Dis 2019; 13:1753466619840256
328. Ushida T, Yokoyama T, Kishida Y, et al.: Incidence and risk factors of postoperative delirium in cervical spine surgery. Spine (Phila Pa 1976) 2009; 34:2500–4
329. Zhou ZJ, Tang J, Li WH, Tao WD: Preoperative intravenous flurbiprofen reduces postoperative pain and inflammatory cytokines in elderly patients after hip arthroplasty. Exp Ther Med 2019; 17:354–8
330. Zhu Y, Yao R, Li Y, et al.: Protective effect of celecoxib on early postoperative cognitive dysfunction in geriatric patients. Front Neurol 2018; 9:633
331. Shen L, Chen JQ, Yang XL, et al.: Flurbiprofen used in one-lung ventilation improves intraoperative regional cerebral oxygen saturation and reduces the incidence of postoperative delirium. Front Psychiatry 2022; 13:889637
332. Mangusan RF, Hooper V, Denslow SA, Travis L: Outcomes associated with postoperative delirium after cardiac surgery. Am J Crit Care 2015; 24:156–63