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Perioperative Brain Health and Postoperative Delirium Prevention:

Recommendations from the APSF Brain Health Patient Safety Priority Advisory Group

by Ryan Field, MD; Lisa Bethea, MD; Arney Abcejo, MD; and Jeffrey Huang, MD

As we celebrate the 40th anniversary of the APSF, it is important to reflect on the growth and evolution of our specialty—specifically around the patient safety outcomes that matter most to our patients. Postoperative delirium (POD) is the most common adverse event following surgery in older adults, with an incidence as high as 65%. It is associated with prolonged hospital stay, increased morbidity and mortality, and significant distress for both patients and their families.[1,2] Recognizing the critical importance of brain health, the APSF has identified it as a Patient Safety Priority. Optimizing brain health through targeted perioperative interventions is of utmost importance. In 2023, the *APSF Newsletter* published an article titled "Perioperative Brain Health: A Patient Safety Priority All Anesthesia Professionals Must Address,"[3] which, along with the American Society of Anesthesiologists (ASA) Brain Health Initiative, has served as a foundational guide for developing brain health implementation protocols. Many hospitals have successfully created and implemented their own protocols, achieving positive outcomes.

Several evidence-based interventions have been shown to potentially reduce the risk of postoperative delirium. These include preoperative cognitive screening, early mobilization, maintaining orientation, promoting sleep hygiene, ensuring the timely return of personal items (such as glasses, hearing aids, and dentures) after surgery, intraoperative dexmedetomidine use, and providing delirium education for health care professionals.[4] However, the role of intraoperative anesthetic management remains a topic of ongoing debate and controversy. Numerous new studies have emerged, some with conflicting results that may create uncertainty among anesthesia professionals regarding best practices. Consequently, the APSF Perioperative Brain Health Patient Safety Priority Advisory Group (PSPAG) believes it is essential to present these new findings to anesthesia professionals, along with updated recommendations, to facilitate effective implementation and ultimately improve patient safety and outcomes.

INTRAOPERATIVE HYPOTENSION (IOH)

Intraoperative hypotension, defined by episodes of low blood pressure during anesthesia, has been proposed as a modifiable risk factor for postoperative delirium particularly in elderly or high-risk patients.[5] The brain normally maintains constant blood flow despite fluctuating systemic pressures (cerebral autoregulation), but this capacity is blunted in the elderly and those with vascular disease.[5] During intraoperative hypotension, cerebral perfusion pressure falls, especially if mean arterial pressure (MAP) drops below the lower autoregulatory limits (~50–60 mmHg).[5,6] Experimental and clinical evidence suggest that sustained cerebral hypoperfusion can trigger neuronal dysfunction, blood brain barrier breakdown, and neuroinflammation, all of which are implicated in delirium pathophysiology.[5,6] Thus, hypotension can lead to reduced cerebral blood flow and oxygen delivery, potentially causing brain tissue injury and contributing to the development of postoperative delirium.[5]

Several retrospective studies[5,7] suggest an association between intraoperative hypoten-

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Table 1: Studies on the Relationship Between Intraoperative Hypotension and Postoperative Delirium.

Study Type	Authors / Source	Population	Key Findings	Conclusion
Retrospective Study	Wang et al.[5] (2025)	Elderly laryngectomy patients	Sustained ≥30% MAP drop for ≥30 min → OR ≈ 1.74 (95% CI 1.04–2.91); surgery duration amplified risk	IOH + prolonged surgery synergistically increases POD risk
Large Retrospective Cohort	Wachtendorf et al.[7] (2022)	316,717 patients (mean age >70)	MAP<55 mmHg: OR ≈ 1.22 (short) to 1.57 (prolonged); +6% POD risk per 10 min MAP<55	Duration- and dose-dependent effect; absolute MAP<55 is key risk factor
Meta-analysis (RCTs)	Feng et al.[8] (2019)	5 RCTs comparing high vs low MAP	No significant POD difference; RR ≈ 3.30 (CI 0.80–13.54), *P*=0.10	RCTs show non-significant trend toward harm; small sample sizes, few POD cases
Prospective Cohort	Hirsch et al.[9] (2015)	594 patients >65, major noncardiac	No POD association with MAP<50 or 20–40% drops; BP variability was predictive	BP instability, not absolute level, linked to POD
Retrospective Study	Yang et al.[10] (2025)	1,002 elderly hip fracture patients	MAP Coefficient of Variation >10% → OR ≈ 1.45 for POD	BP variability independently predicts POD
Retrospective Cohort	Zarour et al.[11] (2024)	2,352 elective elderly patients	No POD association with MAP <65 AUC after adjustment	Contradictory finding; may reflect differing IOH definitions or patient factors
Randomized controlled trial	Marcucci et al.[12] (2025)	2,603 patients with mean age, 70 years undergoing noncardiac surgery	Intraoperative MAP>80 vs MAP >60, no difference in Montreal Cognitive Assessment (MoCA) 1 year after surgery	No difference in neurocognitive outcomes between the hypotension-avoidance and hypertension-avoidance strategies

IOH: intraoperative hypotension; POD: postoperative delirium; RCT: randomized controlled trial; CI: confidence interval; MAP: mean arterial pressure; BP: blood pressure; AUC: area under curve.

Maintaining Optimal Intraoperative Blood Pressure May Maintain Perioperative Brain Health

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sion and postoperative delirium, but in general evidence is mixed (Table 1). A prospective randomized trial,[9,12] a systematic review and meta-analysis,[8] and other retrospective studies[10,11] found no association between intraoperative hypotension and postoperative delirium. Overall, the evidence more strongly suggests that intraoperative hypotension may not be a primary cause of postoperative delirium.

Variability in definitions (absolute vs relative hypotension) and patient populations make universal conclusions difficult. Given that intraoperative hypotension is modifiable, it remains a reasonable prevention target; guidelines now advocate vigilant blood pressure monitoring and management in older surgical patients.[7] The ASA Practice Advisory for Perioperative Care of Older Adults Scheduled for Inpatient Surgery suggests individualized hemodynamic goals and rapid correction of hypotension.[13] Future high-quality trials are needed to determine whether strict BP control or autoregulation-guided management reduces postoperative delirium.

Therefore, the APSF Brain Health PSPAG agrees that maintaining optimal intraoperative blood pressure, with proactive and individualized management strategies to minimize the occurrence, severity, and duration of hypotension and its associated complications in older adults is warranted.

PREOPERATIVE BENZODIAZEPINE USE

A Historical Lens on Benzodiazepines Use and Brain Health

The Beers Criteria were initially introduced to inform practitioners of medications to use with caution in nursing home residents, and these criteria were expanded to all older adults in 1997. In 2012, the American Geriatrics Society (AGS) assumed stewardship of the Criteria, introducing rigorous, evidence-based approaches to medications. These recommendations, updated in 2023, continue to place benzodiazepines on the "potentially inappropriate" list for adults over the age of 65. In the context of neuroanesthesia, brain health, and patient safety, where cognitive preservation is paramount, this caution seems well-founded. Currently, the pervasive culture around benzodiazepines in many institutions is to avoid them preoperatively.

However, it is important to recognize the limitations of the scope of the Beers Criteria. Much of the early evidence grouped benzodiazepines together: short- and long-acting agents, outpatient and inpatient medicine, one-time dose and chronic use.

Contemporary Practice Advisories and Evidence from Recent Trials

The ASA Practice Advisory for Perioperative Care of Older Adults Scheduled for Inpatient Surgery thoughtfully addressed the impact of perioperative medications with central nervous system effects on postoperative cognitive dysfunction and outcomes. The Advisory took a measured approach: "Consider the risks and benefits of medications with potential CNS effects in older adults, as these drugs may increase the risk of postoperative delirium."[13] Notably, the Advisory did not recommend avoiding short-acting benzodiazepines like midazolam or remimazolam, recognizing recent data have not demonstrated a consistent link between their use and cognitive dysfunction/delirium in older adults.

Recently, a prospective multicenter cohort study of >5,600 patients aged 65 years and older undergoing elective noncardiac procedures in China did not show an increased risk of postoperative delirium in those who received intraoperative midazolam versus those who did not (adjusted risk ratio 1.09 (95% CI, 0.91–1.22; *P*=0.35).[14] Subgroup analyses based on age, sex, ASA class, and comorbidities revealed no population in which midazolam incurred an increased delirium risk. However, patients who received midazolam had significantly lower rates of postoperative anxiety (5.7% versus 13.4%).[14]

A multiperiod, double-blinded, cluster-randomized crossover trial to assess the impact of perioperative benzodiazepine use on delirium was conducted at 20 North American cardiac surgical centers (n=19,768; mean age, 65 years).[15] The patients underwent cardiac surgery during either restricted (n=9,827) or liberal (n=9,941) benzodiazepine use periods. Delirium occurred in 1,373 patients (14.0%) during restricted periods and 1,485 patients (14.9%) during liberal periods (adjusted odds ratio [aOR], 0.92; 95% CI, 0.84–1.01; *P*=0.07). The investigators concluded that restricting benzodiazepines during cardiac surgery did not reduce the incidence of delirium.[15]

Pragmatic Clinical Takeaways

Altogether—between the 2025 ASA Practice Advisory and recent multicenter studies—the evidence likely does not support a recommendation to avoid single-use of short-acting benzodiazepines like midazolam in the perioperative setting in older adults.

The APSF Brain Health PSPAG agrees that in older adults:

- Regular review of home medications and deprescribing when appropriate can reduce the risk of postoperative delirium.
- Preoperative doses of short- (midazolam) or ultra-short acting benzodiazepines (remimazolam) need not be proscriptively avoided if specifically trying to minimize postoperative delirium.

Table 2: Anesthesia Depth and Postoperative Delirium.

Study Type	Authors / Source	Population	Key Findings	Conclusion
Randomized clinical trial	Wildes T et al.[16] *JAMA* 2019	1232 patients (aged >60, undergoing major surgery and receiving general anesthesia)	Postoperative delirium occurred in 26.0% of the EEG-guided anesthetic group and 23.0% of the usual care group	The use of EEG-guided anesthetic administration did not prevent postoperative delirium
Multicenter randomized clinical trial	Deschamps A, et al.[17] *JAMA* 2024	1140 patients (aged >60, undergoing cardiac surgery with cardiopulmonary bypass)	Delirium during postoperative days 1 to 5 occurred in 18.15% in the EEG-guided group and 18.10% in the usual care group	EEG-guided anesthetic administration did not decrease the incidence of postoperative delirium
Multicenter randomized clinical trial Delirium subgroup was retrospectively registered. The subgroup study was conducted in China	Evered LA, et al.[18] *BJA* 2021	547 patients (aged >60, undergoing major surgery lasting 2 hr or more)	The incidence of postoperative delirium in the bispectral index (BIS) 50 group was 19% and in the BIS 35 group was 28% (*P*=0.010)	Targeting light anesthesia reduced the risk of postoperative delirium.

EEG: electroencephalography; BIS: bispectral index.

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Data on the Effects of Intraoperative EEG on Postoperative Delirium is Inconclusive

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- Cognitive screening should still be considered to incorporate into preoperative workflows.

ANESTHESIA DEPTH AND MONITORING

For many years, the impact of monitoring and maintaining anesthetic depth with electroencephalography (EEG) monitoring on postoperative cognitive decline has been debated. The results are mixed (Table 2). The ENGAGES trial (1232 patients) found no significant reduction in delirium with EEG-guided anesthesia (26.0% vs 23.0%, *P*=0.22).[16] In that trial, EEG guidance successfully reduced EEG burst suppression but failed to reduce the rate of delirium. Similarly, the ENGAGES-Canada trial (1140 patients) found delirium incidence of 18.15% vs 18.10% (EEG-guided vs usual care).[17] A sub-study of the BALANCED trial (515 patients) reported lower delirium with lighter anesthesia (BIS 50: 19% vs BIS 35: 28%, *P*=0.010),[18] but the full BALANCED trial (6644 patients) showed no overall benefit to targeting light vs deep anesthesia.[18] The lower delirium incidence with lighter anesthesia in the BALANCED subtrial may be driven by centers with high baseline delirium, including patients with high frailty and preoperative risk factors. Furthermore, the sub-study results were mostly reflective of Asian centers, potentially highlighting the need for a population-based approach to anesthetic delivery.[19]

However, the benefits of intraoperative EEG monitoring were demonstrated in a randomized clinical trial of 177 pediatric patients in which EEG-guided titration of anesthesia was compared with standard 1.0-MAC sevoflurane anesthesia. EEG-guided management of general anesthesia reduced the incidence of pediatric emergence delirium (35% vs 21%), while also resulting in faster emergence and shorter postanesthesia care unit stays.[20] While promising, these findings may not directly translate to adult populations given the differing pathophysiology and types of delirium.

The evidence from studies in adult patients suggests the use of EEG-guided anesthetic administration for the prevention of postoperative delirium did not decrease the incidence of postoperative delirium or yield significantly superior outcomes in patients receiving volatile-agent-based general anesthesia. Burst suppression can be visually identified in raw EEG recordings, yet its association with postoperative delirium remains unclear. Most studies rely on commercial monitoring technologies that estimate burst suppression using processed EEG values, which typically underestimate its extent. Some experts suggest that raw EEG-guided intraoperative drug titration may offer a more accurate and effective approach to detect and prevent burst suppression.[21] Future clinical trials are needed.

Table 3: Summary of APSF Brain Health PSPAG Recommendations.

Clinical Category	APSF Brain Health PSPAG Recommendations
Preoperative Benzodiazepine Use	Preoperative doses of short- (midazolam) or ultra-short acting benzodiazepines (remimazolam) need not be proscriptively avoided if specifically trying to minimize postoperative delirium in older adults.
Intraoperative Hypotension	Maintaining optimal intraoperative blood pressure is recommended, with proactive and individualized management strategies to minimize the occurrence, duration, and severity of hypotension and its associated complications in older adults.
Anesthesia Depth and Monitoring	Currently, the data on intraoperative EEG monitoring and the prevention of postoperative delirium in older adults is inconclusive.
Anesthesia Techniques	Selection of anesthesia techniques (GA or RA) does not significantly affect the incidence of postoperative delirium in older adults.

EEG: electroencephalography; GA: general anesthesia; RA: regional anesthesia.

The APSF Brain Health PSPAG agrees that in older adults:

1. Intraoperative EEG monitoring is a useful adjunct to tailor anesthetic depth and support precision anesthesia by individualizing care, where it may help minimize drug exposure.
2. The evidence on intraoperative EEG monitoring and prevention of postoperative delirium is inconclusive.

ANESTHESIA TECHNIQUES

Alongside depth, the choice of anesthetic (general vs regional) has been debated. A recent meta-analysis (21 trials, >1.7 million patients)[22] found that delirium was not significantly different between general anesthesia and regional anesthesia groups once confounders were controlled.[22] The RAGA trial (950 patients) found similar delirium rates with regional anesthesia without sedation (6.2%) vs general anesthesia (5.1%), a nonsignificant difference.[23] Using regional techniques alone did not reduce postoperative delirium. A recent meta-analysis encompassing 10 randomized controlled trials with a total of 3,968 elderly patients undergoing hip fracture surgery found no significant difference in the incidence of postoperative delirium between neuraxial anesthesia and general anesthesia.[24] The authors concluded choice of anesthesia technique alone does not significantly influence postoperative delirium risk in this patient population. Interestingly, a small study (n=114) of elderly patients undergoing hip fracture surgery under spinal anesthesia, reported that light propofol sedation (BIS ≥80) halved delirium incidence compared to deep sedation (19% vs 40%, *P*=0.02).[25] Avoiding excessive sedation may be a key strategy. Future work is needed to identify subgroups and confounding variables that explain conflicting results and help us learn how to selectively apply these interventions.

Current evidence indicates that there are no significant differences in the incidence of postoperative delirium or other delirium-related outcomes between the regional anesthesia and general anesthesia groups.

The APSF Brain Health PSPAG agrees that in older adults (Table 3):

1. Selection of anesthesia techniques does not significantly affect the incidence of postoperative delirium.

CONCLUSION

Current evidence suggests that intraoperative hypotension is unlikely to be a primary driver of postoperative delirium. However, maintaining optimal intraoperative blood pressure remains important to minimize related complications, particularly in older adults. The use of short-acting (e.g., midazolam) or ultra-short-acting benzodiazepines (e.g., remimazolam) in the preoperative period does not need to be categorically avoided solely to reduce the risk of postoperative delirium. The data on intraoperative EEG monitoring and delirium prevention is inconclusive. Furthermore, the choice of anesthetic technique—whether general or regional anesthesia—does not appear to significantly impact the incidence of postoperative delirium. As brain health research continues to evolve globally, it is essential to regularly update clinical guidelines based on emerging evidence, and all recommendations should be interpreted in the context of ongoing developments.

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Selection of Anesthetic Technique (GA vs RA) Does Not Affect Postoperative Delirium in Older Adults

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REFERENCES

1. Peden CJ, Miller TR, Deiner SG, et al. Improving perioperative brain health: an expert consensus review of key actions for the perioperative care team. *Br J Anaesth*. 2021;126:423–432. PMID: 33413977.
2. Partridge JSL, Crichton S, Biswell E, et al. Measuring the distress related to delirium in older surgical patients and their relatives. *Int J Geriatr Psychiatry.* 2019;34:1070–1077. PMID: 30945343.
3. Moreland NC, Scotto L, Abcejo AS. Methangkool E. Perioperative brain health: a patient safety priority all anesthesia professionals must address. *APSF Newsletter.* 2023; 38:2,34,36–38. https://www.apsf.org/news-updates/the-patient-safety-movement-foundation-and-anesthesia-patient-safety-foundation-award-the-patient-safety-curriculum-award/ Accessed August 10, 2025.
4. Aldecoa C, Bettelli G, Bilotta F, et al. Update of the European Society of Anaesthesiology and Intensive Care Medicine evidence-based and consensus-based guideline on postoperative delirium in adult patients. *Eur J Anaesthesiol.* 2024;41:81–108. PMID: 37599617.
5. Wang Y, Chen K, Ye M, Shen X. Intraoperative hypotension and postoperative delirium in elderly male patients undergoing laryngectomy: a single-center retrospective cohort study. *Braz J Anesthesiol*. 2024;75:844560. PMID: 39277101.
6. Qureshi O, Arthur ME. Recent advances in predicting, preventing, and managing postoperative delirium. *Fac Rev.* 2023;12:19. PMID: 37529149.
7. Wachtendorf LJ, Azimaraghi O, Santer P, et al. Association between intraoperative arterial hypotension and postoperative delirium after noncardiac surgery: a retrospective multicenter cohort study. *Anesth Analg*. 2022;134:822–833. PMID: 34517389.
8. Feng X, Hu J, Hua F, et al. The correlation of intraoperative hypotension and postoperative cognitive impairment: a meta-analysis of randomized controlled trials. *BMC Anesthesiol.* 2020;20:193. PMID: 32758153.
9. Hirsch J, DePalma G, Tsai TT, et al. Impact of intraoperative hypotension and blood pressure fluctuations on early postoperative delirium after non-cardiac surgery. *Br J Anaesth.* 2015;115:418–426. PMID: 25616677.
10. Yang P, Fan Y, Tang W. Correlation of intraoperative blood pressure variability and postoperative delirium in elderly hip fracture surgery. *Sci Rep.* 2025;15:15007. PMID: 40301442.
11. Zarour S, Weiss Y, Abu-Ghanim M, et al. Association between intraoperative hypotension and postoperative delirium: a retrospective cohort analysis. *Anesthesiology.* 2024;141:707–718. PMID: 38995701.
12. Marcucci M, Chan MTV, Painter TW, et al. cogPOISE-3 Trial Investigators and Study Groups. Effects of a hypotension-avoidance versus a hypertension-avoidance strategy on neurocognitive outcomes after noncardiac surgery. *Ann Intern Med.* 2025;178:909–920. PMID: 40456161.
13. Sieber F, McIsaac DI, Deiner S, et al. 2025 American Society of Anesthesiologists practice advisory for perioperative care of older adults scheduled for inpatient surgery. *Anesthesiology.* 2025;142:22–51. PMID: 39655991.
14. Li H, Liu C, Yang Y, et al. Effect of intraoperative midazolam on postoperative delirium in older surgical patients: a prospective, multicenter cohort study. *Anesthesiology*. 2025;142:268–277. PMID: 39470760.
15. Spence J, Devereaux PJ, Lee SF, et al. B-Free Investigators and the Canadian Perioperative Anesthesia Clinical Trials Group. Benzodiazepine-free cardiac anesthesia for reduction of postoperative delirium: a cluster randomized crossover trial. *JAMA Surg*. 2025;160:286–294. PMID: 39878960.
16. 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;321:473–483. PMID: 30721296.
17. 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;332:112–123. PMID: 38857019.
18. Evered LA, Chan MTV, Han R, et al. Anaesthetic depth and delirium after major surgery: a randomised clinical trial. *Br J Anaesth*. 2021;127:704–712. PMID: 34465469.
19. Miyasaka KW, Suzuki Y, Brown EN, Nagasaka Y. EEG-guided titration of sevoflurane and pediatric anesthesia emergence delirium: a randomized clinical trial. *JAMA Pediatr.* 2025;179:704–712. PMID: 40257811.
20. Whitlock EL, Gross ER, King CR, Avidan MS. Anaesthetic depth and delirium: a challenging balancing act. *Br J Anaesth*. 2021;127:667–671. PMID: 34503835.
21. Pawar N, Barreto Chang OL. Burst suppression during general anesthesia and postoperative outcomes: mini review. *Front Syst Neurosci*. 2022;15:767489. PMID: 35069132.
22. Zhu X, Yang M, Mu J, et al. The effect of general anesthesia vs. regional anesthesia on postoperative delirium—a systematic review and meta-analysis. *Front Med (Lausanne).* 2022;9:844371. PMID: 35419373.
23. Li T, Li J, Yuan L, et al. Effect of regional vs general anesthesia on incidence of postoperative delirium in older patients undergoing hip fracture surgery: the RAGA Randomized Trial. *JAMA*. 2022;327:50–58. PMID: 34928310.
24. Cheung KY, Yang TX, Chong DY, So EH. Neuraxial versus general anesthesia in elderly patients undergoing hip fracture surgery and the incidence of postoperative delirium: a systematic review and stratified meta-analysis. *BMC Anesthesiol.* 2023;23:250. PMID: 37481517.
25. Sieber FE, Zakriya KJ, Gottschalk A, et al. Sedation depth during spinal anesthesia and the development of postoperative delirium in elderly patients undergoing hip fracture repair. *Mayo Clin Proc*. 2010;85:18–26. PMID: 20042557.