In 2015, a multidisciplinary group of scientists and clinicians reported that a diagnosis of postoperative delirium independently increases the likelihood of:

- Institutionalization
- 30-day readmission
- An extended hospital stay

These outcomes are associated with an increase in approximately $3,400–$5,500 in hospital admission costs. Patients with postoperative delirium also have significantly increased odds of dying in the hospital and three to six months after surgery.

In 2015, the American Geriatrics Society issued a best practice statement concerning risk factors, diagnosis, and perioperative mitigation strategies. They recommend managing intraoperative anesthetic exposure by employing “processed electroencephalographic monitors of anesthetic depth during intravenous sedation or general anesthesia of older patients to reduce postoperative delirium.” A consensus group from Brazil and the European Society of Anaesthesiology issued similar recommendations. In 2018, The American Society of Anesthesiology Brain Health Initiative working group also recommended that anesthesia providers should “perform EEG based anesthetic management in older adults.” Subsequently, the American Society for Enhanced Recovery and Perioperative Quality Initiative recommended “clinicians consider using EEG monitoring to detect unintended burst suppression” for mitigating postoperative delirium.

In 2019, the Associazione Chirurghi Ospedalieri Italiani and the PeriOperative Italian Society recommended cerebral monitoring, including processed EEG, to “improve recovery and reduce the risk of postoperative delirium.”

This evidence package discusses the association between titrating anesthesia using processed EEG indices and a reduced risk of postoperative delirium in elderly surgical patients.

†The BIS™ system should not be used as the sole basis for diagnosis or therapy and is intended only as an adjunct in patient assessment. Reliance on the BIS™ system alone for intraoperative anesthetic management is not recommended.

‡$10,339 in charges were adjusted to $3,446 in costs using 3:1 charge to cost ratio. This ratio was chosen based on MedPAC March 2016 report to Congress, specifically “Ratios of Charges to costs are correlated with profits” Table 3-A1 on page 3 (decile 5 of 330% ratio was rounded to 300% for simplicity of calculation). http://www.medpac.gov/docs/default-source/reports/chapter-3-online-only-appendixes-hospital-inpatient-and-outpatient-services-march-2016-report--pdf

§Incremental cost of $5,521 is derived from Table 2 on p.79 ($28,223 in delirium vs. $22,702 non delirium groups).
Intraoperative EEG suppression is an independent risk factor for postoperative delirium in a general surgical population

Intraoperative electroencephalogram suppression predicts postoperative delirium
FRITZ BA, KALARICKAL PL, MAYBRIER HR, ET AL. (USA).

Among the sample:
- 89 percent experienced EEG suppression
- 42 percent experienced BIS™ index values < 20
- 26 percent diagnosed with postoperative delirium

Single-center prospective observational trial examining the relationship between intraoperative EEG suppression, as reported by the BIS™ index, and postoperative delirium. In the findings:
- Adult patients undergoing general surgery (N=727) were monitored with BIS™ index technology and divided into five groups:
  - No time in burst suppression
  - First quartile of time in burst suppression (0.1 mins – 0.6 mins)
  - Second quartile (0.7 mins – 4.4 mins)
  - Third quartile (4.5 mins – 17.4 mins)
  - Fourth quartile (> 17.4 mins)
- Patients assessed for postoperative delirium using the Confusion Assessment Method twice daily until ICU discharge unless sedated
- Increased duration of EEG suppression was independently associated with 22 percent increased odds of postoperative delirium (P=0.0002)
Higher intraoperative burst suppression ratio, and time in burst suppression, are predictors of postoperative delirium

Intraoperative burst suppression is associated with postoperative delirium following cardiac surgery: a prospective, observational study

SOEHLE M, DITTMANN A, ELLERKMANN RK, ET AL. (Germany)

Among the sample:
- 32 percent were diagnosed with postoperative delirium

Those diagnosed with postoperative delirium:
- Spent twice as long in the ICU
- Had a higher 6-month mortality rate

Single-center prospective observational trial to examine the relationship between BIS™ index values, time in burst suppression, burst suppression ratio (BSR), asymmetry, and adverse postoperative outcomes. In the findings:
- Elderly patients (>60 yo) undergoing on-pump cardiac surgery (N=87) monitored with BIS™ index technology and divided into two comparison groups:
  - No postoperative delirium
  - Postoperative delirium
- Patients assessed for postoperative delirium using the Confusion Assessment Method daily
- Postoperative delirium was associated with:
  - Higher intraoperative BSR (1.24 percent vs 0.44 percent; P=0.028)
  - More time in burst suppression (107 minutes vs 44 minutes; P=0.018)
  - Higher 6-month mortality rate (11.5 percent vs. 0 percent)
- The amount of anesthetic used and the BIS™ index values did not differ between the groups
Heightened sensitivity to volatile anesthetics is associated with higher odds of postoperative delirium

Intraoperative electroencephalogram suppression at lower volatile anesthetic concentrations predicts postoperative delirium occurring in the intensive care unit

FRITZ BA, MAYBRIER HR, AND AVIDAN MS. (USA)

Post hoc retrospective analysis of a single-center prospective observational trial examining whether patients with EEG suppression at lower end-tidal anesthetic gas concentrations are more likely to develop postoperative delirium. In the findings:

- Adult patients undergoing elective surgery (N=618) were monitored with BIS™ index technology and end-tidal anesthetic gas concentrations
- Patients assessed for postoperative delirium using the Confusion Assessment Method twice daily until ICU discharge unless sedated
- EEG suppression at lower end-tidal anesthetic gas concentrations indicate heightened sensitivity to volatile anesthetics
- Patients with heightened sensitivity to volatile anesthetics had over twice the odds of a postoperative delirium diagnosis (odds ratio (OR) 2.18)
- Duration of EEG suppression alone was not a predictor of postoperative delirium in this analysis
Using BIS™ index brain monitoring technology to provide light sedation can help reduce the relative risk of postoperative delirium by more than 50 percent

Sedation depth during spinal anesthesia and the development of postoperative delirium in elderly patients undergoing hip fracture repair

SIEBER FE, ZAKRIYA KJ, GOTTSCHALK A, ET AL. (USA)

**Figure:** Incidence of postoperative delirium among elderly patients undergoing hip fracture repair receiving light or deep sedation along with spinal anesthesia (P=0.02)

Deep sedation was associated with:

- More propofol but less midazolam
- Lower mean BIS™ index value
- 12x longer duration with a BIS™ index value < 50

Single-center randomized controlled trial comparing the risk of postoperative delirium between patients receiving deep (BIS™ index value ~ 50) and light sedation (BIS™ index value ≥80). In the findings:

- Elderly patients (≥ 65 yo) undergoing hip fracture repair with spinal anesthesia (N=114) were monitored BIS™ index technology
- Patients assessed for postoperative delirium using the Confusion Assessment Method daily starting on the second postoperative day until hospital discharge
- Postoperative delirium was identified in 39 percent of patients
- Deep sedation was associated with lower mean BIS™ index value (49.9 vs. 85.7)
- Deep sedation was associated with more than twice the odds of developing postoperative delirium (OR 2.69)
- Light sedation was associated with a 52 percent relative reduction in the risk of postoperative delirium (19 percent vs 40 percent, P=0.02)
The combination of light general anesthesia and peripheral nerve block is associated with lower incidence of postoperative delirium

Peripheral nerve block as a supplement to light or deep general anesthesia in elderly patients receiving total hip arthroplasty: a prospective randomized study

MEI B, ZHA H, LU X, ET AL. (China)

Figure: Incidence of postoperative delirium among elderly hip arthroplasty patients receiving different anesthesia protocols (*P=0.007 light general anesthesia vs. both GA groups)

Light general anesthesia and a peripheral nerve block was associated with significant reduction in incidence of postoperative delirium

Single-center randomized controlled trial evaluating the combination of general anesthesia (GA) and peripheral nerve blockage in elderly patients undergoing hip arthroplasty. In the findings:

- Elderly patients (≥ 65 yo) undergoing total hip arthroplasty (N=203) were divided into three comparison groups:
  - Deep GA plus nerve block
  - Light GA plus nerve block
  - GA alone
- Patients assessed for postoperative delirium using the Confusion Assessment Method daily for three days postoperatively
- Light general anesthesia plus peripheral nerve block vs. GA alone (17 percent vs. 40 percent, P=0.007)
- Light GA plus peripheral nerve block vs. deep GA plus peripheral nerve block (17 percent vs. 38 percent, P=0.007)
BIS™ index guided anesthetic delivery is associated with 42 percent lower odds of postoperative delirium

BIS™-guided anesthesia decreases postoperative delirium and cognitive decline
CHAN MT, CHENG BC, LEE TM, ET AL. (China)

Multicenter randomized controlled trial evaluating the association between BIS™ index guided anesthesia and the risk of postoperative cognitive dysfunction (POCD) and delirium. In the findings:

- Elderly patients (≥ 60 yo) undergoing elective major surgery (N=921) were randomized to one of two conditions:
  - Routine monitoring
  - BIS™ index guided anesthesia
- Patients assessed for postoperative delirium using the Confusion Assessment Method daily and POCD through a battery of three neuropsychological tests within the first week, at the end of week one, and 3 months postoperative
- Postoperative delirium was identified in 20 percent of patients
- BIS™ index guided anesthesia associated with:
  - Higher mean BIS™ values (53.2 vs 38.6, P<0.001)
  - 38 percent lower odds of developing POCD at 3 months (P=0.02)
  - 35 percent relative reduction in the risk of postoperative delirium (15.6 percent vs 24.1 percent, P=0.01)
  - 42 percent lower odds of developing postoperative delirium (P<0.01)
- In 1,000 elderly patients undergoing major surgery, use of BIS™ index guided anesthesia is expected to prevent 23 cases of POCD and 83 cases of postoperative delirium
Use of BIS™ index monitoring technology is associated with a reduced incidence of deep anesthesia and 30 percent reduction in the risk of postoperative delirium

Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction

RADTKE FM, FRANCK M, LENDNER J, ET AL. (Germany)

Single-center randomized controlled trial to determine the association between BIS™ index guided anesthesia and the risk of postoperative delirium. In the findings:

- Elderly patients (≥ 60 yo) undergoing elective major surgery (N=1,155) were randomized to one of two conditions:
  - Blinded monitoring; routine care to manage anesthetic delivery
  - BIS™ index guided anesthesia
- Patients assessed for postoperative delirium using the Diagnostic and Statistical Manual of Mental Disorders (DSM IV) twice daily for a week postoperative
- Postoperative delirium was identified in 18.8 percent of patients
- BIS™ index guided anesthesia was associated with:
  - 33 percent lower number of average BIS™ index values < 20 (3.7 times vs 5.6 times; P=0.04)
  - 30 percent relative reduction in postoperative delirium (16.7 percent vs 24.1 percent, P=0.036)
  - Trend towards lower risk of postoperative cognitive dysfunction at seven days (18.1 percent vs 23.9 percent, P=0.062)
- The percentage of BIS™ values < 20 was independently associated with higher odds of postoperative delirium (OR 1.027, P=0.006)

Figure: Incidence of postoperative delirium among elderly elective major surgery patients anesthetized with and without BIS™ index guidance (P=0.036)
BIS™ index-guided TIVA may be associated with less anesthetic use, quicker cognitive recovery, and less postoperative delirium

Bispectral index monitoring during anesthesia promotes early postoperative recovery of cognitive function and reduces acute delirium in elderly patients with colon carcinoma: a prospective controlled study using the Attention Network Test

ZHOU Y, LI Y, WANG K. (China)

The BIS™ index guided anesthesia was associated with recovery to preoperative levels of alerting and orienting functions by day five

Figure: Percent of elderly colon carcinoma surgery patients diagnosed with postoperative delirium using the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) (P < 0.001).

38% decrease in the incidence of delirium

38% decrease in the incidence of delirium

The BIS™ index guided anesthesia was associated with recovery to preoperative levels of alerting and orienting functions by day five

Single-center randomized controlled trial examining the effect of BIS™ monitoring-guided TIVA on drug use and postoperative cognitive impairment. In the findings:

- Elderly colon carcinoma patients (N=81) with an expected duration of surgery > two hours and hospital length of stay > seven days. They were randomized to the following arms:
  - TIVA titrated using clinical signs
  - BIS™ index-guided titration of TIVA to an index value of 40–60
- TIVA regimen included sufentanil, propofol, and vecuronium for induction, and propofol, vecuronium, and remifentanil for maintenance
- Patients assessed for postoperative delirium using the Confusion Assessment Method once daily for 5 days postoperatively
- Compared to the control group, the BIS™ monitoring technology group:
  - Had higher BIS™ index values (51 vs. 41; P < 0.001)
  - Received less propofol and remifentanil (P < 0.001)
  - Showed recovery in alerting and orienting functions to preoperative values by day 5 (which continued to be impaired in the control group)
  - Had fewer patients with postoperative delirium (17 percent vs. 27.5 percent, P < 0.001)
Processed EEG monitoring-guided anesthesia is associated with a 29 percent reduction in the risk of postoperative delirium and cognitive dysfunction

Processed electroencephalogram and evoked potential techniques for amelioration of postoperative delirium and cognitive dysfunction following non-cardiac and nonneurosurgical procedures in adults

PUNJASAWADWONG Y, CHAU-IN W, LAOPAIBOON M, ET AL

In a meta-analysis of randomized controlled trials, BIS™ index-guided anesthesia was shown to impact the incidence of postoperative delirium

29%
Reduction in the risk of postoperative delirium

17
Patients treated with BIS™ index guided anesthesia to avoid 1 case of postoperative delirium

38
Patients treated with BIS™ index guided anesthesia to avoid 1 case of postoperative cognitive dysfunction

Systematic review and meta-analysis of randomized controlled trials evaluating the effectiveness of guiding anesthesia with depth of anesthesia monitoring (processed EEG or auditory evoked potentials) to reduce the risk of postoperative delirium and postoperative cognitive dysfunction. In the findings:

- Six studies on adults (>60 yo) undergoing non-cardiac and non-neurosurgical surgery:
  - Three postoperative delirium studies with 2,197 patients total
  - Three postoperative cognitive dysfunction studies with 2,270 patients total
- Patients assessed for postoperative delirium using the Confusion Assessment Method and the Diagnostic and Statistical Manual (DSM-IV). Patients assessed for postoperative cognitive dysfunction with the Mini-Mental State Exam
- BIS™-monitoring guided anesthesia was associated with:
  - 29 percent reduction in the risk of postoperative delirium (RR 0.71; 95% CI 0.59 to 0.85)
  - 29 percent reduction in the risk of postoperative cognitive dysfunction at 12 weeks postoperative (RR 0.71; 95% CI 0.53 to 0.96)
- The authors did not find a significant reduction in postoperative cognitive dysfunction at one week postoperative
- The evidence quality was rated as moderate due to lack of blinding of the anesthesia providers and some incomplete outcome data

29%
Patients treated with BIS™ index guided anesthesia to avoid 1 case of postoperative delirium

38
Patients treated with BIS™ index guided anesthesia to avoid 1 case of postoperative cognitive dysfunction
A selection of clinical studies about BIS™ index monitoring technology and postoperative delirium


REFERENCES


