BIS™ BRAIN MONITORING SYSTEM: ADVANCED MONITORING FOR IMPROVED OUTCOMES

POSTOPERATIVE DELIRIUM

In 2015, a multidisciplinary group of scientists and clinicians discovered that a diagnosis of postoperative delirium independently increases the likelihood of institutionalization, 30-day readmission, and extended hospital stay[1], which may increase cost of care by over 8,300 USD[2]. Delirious patients experience significantly increased odds of dying in the hospital[3,4], as well as 3 to 6 months after surgery[3,4,5].

The American Geriatrics Society recently elevated the issue of postoperative delirium; in 2015, they issued a best practice statement concerning risk factors, diagnosis, and perioperative mitigation strategies[6]. The group recommends managing intraoperative exposure to anesthetic agents by employing "processed electroencephalographic monitors of anesthetic depth during intravenous sedation or general anesthesia of older patients to reduce postoperative delirium"[6], a recommendation echoed shortly after by a consensus group from Brazil[7].

Mounting evidence associating the use of processed EEG monitors with a reduced risk of postoperative delirium has contributed to this recent interest[5,8,9,10]. Sieber et al. reported over 2.5-times increased odds of postoperative delirium in elderly spinal surgery patients randomized to deep versus light BIS™ monitoring-guided anesthesia[8]. In a larger cohort of elderly general surgery patients, the BIS™ monitoring-guided anesthesia group experienced a 35% relative reduction in the risk of postoperative delirium compared to routine monitoring[9]. A subsequent study in elderly noncardiac surgery patients echoed these results with a 22% relative reduction in the risk of postoperative delirium[5]. More recently, a secondary analysis of 310 cardiac surgery patients found a 33% relative reduction in risk[10]. Taken together in a meta-analysis, these 4 studies indicate reduced odds of developing postoperative delirium by 44% when BIS™ monitoring-guided anesthesia is used[10]. The trials are summarized in the following clinical evidence package.

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Using BIS™ monitoring technology to provide light sedation can help reduce the relative risk of postoperative delirium by more than 50%

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.

Study design	Single-center randomized controlled trial (US)
Arms	Deep sedation: BIS™ monitoring-guided anesthesia titrated to a BIS™ value of approximately 50 Light sedation: BIS™ monitoring-guided anesthesia titrated to a BIS™ value of ≥ 80
Objective	Compare the risk of postoperative delirium between patients receiving deep and light sedation
N	114
Population	Elderly patients (≥ 65 years) undergoing hip fracture repair with spinal anesthesia
Delirium assessment tool or definition	Confusion Assessment Method
Timing of assessment	Daily in the morning, starting on the second postoperative day until hospital discharge
Results	▪ 39% of patients developed postoperative delirium ▪ Deep sedation was associated with – more propofol (10.2 vs 2.5 mg/kg; P<0.001) – less midazolam (1.26 vs 5.53 mg/kg; P=0.04) – lower mean BIS™ value (49.9 vs 85.7; P<0.001) – longer duration with a BIS™ value < 50 (48 vs 4 mins; P<0.001) – more than twice the odds of developing postoperative delirium (OR 2.69; P=0.04) ▪ Light sedation was associated with a 52% relative reduction in the risk of postoperative delirium (19 vs 40%; P=0.02) ▪ The number needed to treat with light sedation to prevent 1 case of postoperative delirium was 4.7 patients
Conclusions	In elderly patients undergoing hip fracture repair under spinal anesthesia, using BIS™ monitoring to titrate anesthesia to lighter levels can help reduce the risk of postoperative delirium by more than 50%

BIS™-guided anesthetic delivery is associated with 42% lower odds of postoperative delirium

BIS™-guided anesthesia decreases postoperative delirium and cognitive decline.

Chan MT, Cheng BC, Lee TM, Gin T; CODA Trial Group.

Study design	Multicenter randomized controlled trial (China) *Cognitive Dysfunction After Anesthesia* (CODA) Trial
Arms	Control: Blinded monitoring; routine care to manage anesthetic delivery Intervention: BIS™ monitoring-guided anesthesia titrated to a BIS™ value of 40 – 60
Objective	Determine the association between BIS™ monitoring-guided anesthesia and the risk of postoperative cognitive dysfunction (POCD) and delirium
N	921
Population	Elderly patients (≥ 60 years) undergoing elective major surgery ≥ 2 hours and expected to stay in the hospital ≥ 4 days
Delirium assessment tool or definition	Acute fluctuating course of inattention, AND disorganized thinking OR altered level of consciousness
Timing of assessment	Daily in the morning, starting on the second postoperative day until hospital discharge
Results	▪ 20% of patients developed postoperative delirium ▪ BIS™ monitoring-guided anesthesia was associated with – less propofol and volatile anesthetic gas use – higher mean BIS™ values (53.2 vs 38.6; P<0.001) – shorter duration with a BIS™ value < 40 (7.2 vs 22.8 mins; P<0.001) ▪ Fewer patients experienced postoperative cognitive issues in the BIS™ monitoring group – 38% lower odds of developing POCD at 3 months (P=0.02) – 35% relative reduction in the risk of postoperative delirium (15.6 vs 24.1%; P=0.01) – 42% lower odds of developing postoperative delirium (P=0.01) ▪ In 1000 elderly patients undergoing major surgery, use of BIS™ monitoring-guided anesthesia is expected to prevent 23 cases of POCD and 83 patients of postoperative delirium
Conclusions	Use of BIS™ monitoring-guided anesthesia reduced the time spent with BIS™ values < 40, subsequently reducing the risk of postoperative cognitive issues

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Use of BIS™ monitoring technology is associated with a reduced incidence of deep anesthesia and 22% lower relative 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, Krüger S, Wernecke KD, Spies CD.

Study design	Single-center randomized controlled trial (Germany)
Arms	Control: Blinded monitoring; routine care to manage anesthetic delivery Intervention: BIS™ monitoring-guided anesthesia
Objective	Determine the association between BIS™ monitoring-guided anesthesia and the risk of postoperative delirium
N	1,155
Population	Elderly patients (≥ 60 years) undergoing elective major surgery ≥ 1 hour
Delirium assessment tool or definition	Diagnostic and Statistical Manual of Mental Disorders (DSM IV)
Timing of assessment	Twice daily starting on the first postoperative day through the seventh day
Results	▪ 18.8% of patients developed postoperative delirium ▪ BIS™ monitoring-guided anesthesia was associated with a – lower number of average BIS™ values < 20 (P=0.04) – 22% relative reduction in postoperative delirium (16.7 vs 24.1%; P=0.036) – trend towards lower risk of POCD at 7 days (18.1 vs 23.9%; P=0.062) ▪ The percentage of BIS™ values < 20 was independently associated with a higher odds of postoperative delirium (1.027; P=0.006)
Conclusions	BIS™ monitoring was associated with a reduced incidence of low BIS™ values and a reduced risk of postoperative delirium

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BIS™ monitoring-guided anesthesia is associated with a 44% reduction in the odds of postoperative delirium across 4 randomized controlled trials

Postoperative delirium in a substudy of cardiothoracic surgical patients in the BAG-RECALL clinical trial.

Whitlock EL, Torres BA, Lin N, et al.

Study design	Single-center (US) randomized controlled trial Secondary analysis of 6,100- patient multicenter international *BIS or Anesthetic Gas to Reduce Explicit Recall* (BAG-RECALL) Trial
Arms	Control: Blinded BIS™ monitoring; end-tidal anesthetic concentration (ETAC) monitoring to manage anesthetic delivery to an age-adjusted minimum alveolar concentration of 0.7 – 1.3 Intervention: BIS™ monitoring-guided anesthesia titrated to a BIS™ value of 40 – 60
Objective	Determine the association between BIS™ monitoring-guided anesthesia and intraoperative awareness (the postoperative delirium endpoint was part of a prespecified single-center substudy)
N	310
Population	Cardiac and/or thoracic surgery patients at high risk for intraoperative awareness
Delirium assessment tool or definition	Confusion Assessment Method for the Intensive Care Unit
Timing of assessment	Twice daily until the tenth postoperative day or until ICU discharge
Results	▪ 23.5% of patients developed postoperative delirium ▪ BIS™ monitoring-guided anesthesia was associated with a trend towards a 33% relative reduced risk of postoperative delirium (18.8 vs 28.0%; P=0.058) ▪ When taken together, a *posthoc* meta-analysis combining the results of this study with three others[5,8,9] found that the use of BIS™ monitoring-guided anesthesia was associated with significant 44% reduction in the odds of postoperative delirium
Conclusions	Although this study did not show a significant association between BIS™ monitoring and a reduced risk of postoperative delirium compared to ETAC, a *posthoc* meta-analysis including these results showed a significant reduction in the odds of developing postoperative delirium.

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