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REVIEW ARTICLE

# Benefit of general anesthesia monitored by bispectral index compared with monitoring guided only by clinical parameters. Systematic review and meta-analysis

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**KEYWORDS**
General anesthesia;
Anesthetics;
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Bispectral index-monitoring

**Abstract**
*Background:* The bispectral index parameter is used to guide the titration of general anesthesia; however, many studies have shown conflicting results regarding the benefits of bispectral index monitoring. The objective of this systematic review with meta-analysis is to evaluate the clinical impact of monitoring with the bispectral index parameter.
*Methods:* The search for evidence in scientific information sources was conducted during December 2013 to January 2015, the following primary databases: Medline/PubMed, LILACS, Cochrane, CINAHL, Ovid, SCOPUS and TESES. The criteria for inclusion in the study were randomized controlled trials, comparing general anesthesia monitored, with bispectral index parameter with anesthesia guided solely by clinical parameters, and patients aged over 18 years. The criteria for exclusion were studies involving anesthesia or sedation for diagnostic procedures, and intraoperative wake-up test for surgery of the spine.
*Results:* The use of monitoring with the bispectral index has shown benefits reducing time to extubation, orientation in time and place, and discharge from both the operating room and post anesthetic care unit. The risk of nausea and vomiting after surgery was reduced by 12% in patients monitored with bispectral index. Occurred a reduction of 3% in the risk of cognitive impairment postoperatively at 3 months postoperatively and 6% reduction in the risk of postoperative delirium in patients monitored with bispectral index. Furthermore, the risk of intraoperative memory has been reduced by 1%.

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*Conclusion:* Clinically, anesthesia monitoring with the BIS can be justified because it allows advantages from reducing the recovery time after waking, mainly by reducing the administration of general anesthetics as well as the risk of adverse events.


**PALAVRAS-CHAVE**
Anestesia geral;
Anestésicos;
Inalação;
Anestesia intravenosa;
Monitoração do índice bispectral

**Benefício da anestesia geral com monitoração do índice bispectral em comparação com o monitoramento guiado apenas por parâmetros clínicos. Revisão sistemática e metanálise**

**Resumo**
*Justificativa:* O parâmetro índice bispectral (BIS) é usado para guiar a titulação da anestesia geral; no entanto, muitos estudos têm mostrado resultados conflitantes quanto aos benefícios da monitoração do BIS. O objetivo desta revisão sistemática com meta-análise foi avaliar o impacto clínico da monitoração do parâmetro BIS.
*Métodos:* A busca por evidências em fontes de informação científicas foi conduzida de dezembro de 2013 a janeiro de 2015 nas seguintes bases de dados: Medline/PubMed, LILACS, Cochrane, CINAHL, Ovid, SCOPUS e TESES. Os critérios de inclusão foram estudos randomizados e controlados, comparando anestesia geral monitorada com o parâmetro BIS com anestesia guiada apenas por parâmetros clínicos em pacientes com idade superior a 18 anos. Os critérios de exclusão foram estudos que envolveram anestesia ou sedação para procedimentos de diagnóstico e teste de despertar no intraoperatório de cirurgia da coluna vertebral.
*Resultados:* O uso de monitoração com o BIS mostrou benefícios como a redução do tempo de extubação, orientação no tempo e no espaço, alta da sala de cirurgia e da sala de recuperação pós-anestesia. O risco de náuseas e vômitos no pós-operatório foi reduzido em 12% em pacientes monitorados com o BIS. Ocorreu uma redução de 3% no risco de disfunção cognitiva em três meses do pós-operatório e 6% no risco de delírio pós-operatório em pacientes monitorados com o BIS. Além disso, o risco de despertar com memória intraoperatória foi reduzido em 1%.
*Conclusão:* Clinicamente, a monitorização com o BIS pode ser justificada, pois permite vantagens em reduzir o tempo de recuperação, principalmente reduzindo a administração de anestésicos gerais e o risco de eventos adversos.


## Introduction

Bispectral index (BIS) is a multiprocessor EEG parameter specially developed to measure the effects of anesthetics on the brain hypnotic state, making it possible to measure the depth of anesthesia. The introduction of the BIS in clinical practice is a reliable method to assess brain function and allows the titration of hypnotics on cortical activity.

Due to anesthesia may occur unpredictable responses at different times of surgery with a great variability among patients, so the exact dosage of anesthetic to be administered still remains a challenge. However, many studies have shown conflicting results regarding the advantages of BIS and if this monitoring improves recovery times and hospital discharges, as well as minimizes adverse events.

The objective of this systematic review with meta-analysis was to clinically evaluate the objective BIS monitoring parameter, compared with the clinical parameters in general anesthesia.

## Methods

The research for evidence in scientific sources of information was performed by two independent reviewers (CRDO, WMB) during the period from December 2013 to January 2015, the following primary databases: Medline/PubMed, LILACS, Cochrane, CINAHL, Ovid, SCOPUS and THESES. The search strategy was made with the following words: (Anesthesia, General OR Anesthetics, Inhalation OR Anesthetics, Intravenous) AND (Consciousness Monitors OR Monitoring, Intraoperative OR Bispectral index-monitoring technology OR Bispectral index-monitoring OR Bispectral index monitoring OR Drug Monitoring OR Awareness OR Monitoring, Physiologic OR BIS monitoring) AND Random*.

The criteria for inclusion in the study were Randomized Controlled Trials (RCTs) with level of evidence 1B/2B (Oxford Centre for Evidence-based Medicine) in English, Spanish or Portuguese languages, comparing venous or inhaled general anesthetics monitored with BIS parameter with anesthesia

**Table 1** Considered outcomes.

| |
|---|
| Time for spontaneous eye opening |
| Time for eye opening upon verbal command |
| Time to tracheal extubation |
| Time for orientation in time and place |
| Time for leaving operating room |
| Time for discharge from post anesthesia care unit (PACU) |
| Time for hospital discharge |
| Postoperative nausea and vomiting (PONV) |
| Cognitive disorders in the postoperative period (1 week after extubation) |
| Cognitive disorders in the postoperative period (3 months after extubation) |
| Postoperative delirium |
| Intraoperative memory |

guided solely by clinical parameters; patients aged over 18 years.

The criteria for exclusion were studies involving anesthesia and sedation for diagnostic procedures. Studies involving intraoperative wake-up test for surgery of the spine were excluded. Nor were objects of study the clinical trials of ketamine as venous anesthetic.

This systematic review with meta-analysis was recorded in PROSPERO database under the number CRD42015017240.

The outcomes considered are described in Table 1.

The results of the meta-analysis were obtained by the RevMan 5.2 software (Review Manager Computer program. Version 5.2 Copenhagen: The Nordic Cochrane Centre, Cochrane Collaboration© 2014).

Regarding meta-analysis, the difference was calculated in risk difference for dichotomic variables with Mantel—Haenszel (M-H) test with 95% Confidence Interval; and in mean difference with fixed effect using Inverse Variance (IV), with a 95% Confidence Interval, for continuous variables.

An $I^2$ of 0% indicates no heterogeneity among studies, values below 50% indicate a low heterogeneity, and above 50%, high heterogeneity.

When the heterogeneity was greater than 50%, a sensitivity analysis was performed, removing the studies that were out of the ''forest plot''. To achieve reduction in heterogeneity remained out of the study meta-analysis.

## Results

Initially, the search resulted in 1.747 scientific articles. After applying the inclusion and exclusion criteria were selected 17 RCT (Fig. 1).

Table 2 shows the trials selected with the respective levels of evidence, Jadad scale, number of patients randomized and analyzed, patient numbers in the intervention and control groups and PICO strategy. A total of 10,761 patients were analyzed, 5668 in the intervention group and 5093 in the control group.

Table 3 shows the 36 full-text articles excluded with reasons.

The time for spontaneous eye opening is counted from the end of the last suture, when then inhaled or intravenous anesthetic is discontinued. The monitoring with the BIS, compared exclusively with clinical parameters, showed a reduction in the time for spontaneous opening 0.62 min eye (95% CI −1.08, −0.16), with an $I^2$ = 83%. In sensitivity analysis, when removed the study Kreuer et al.[7] was removed we have an $I^2$ = 0%, with reduction of time for

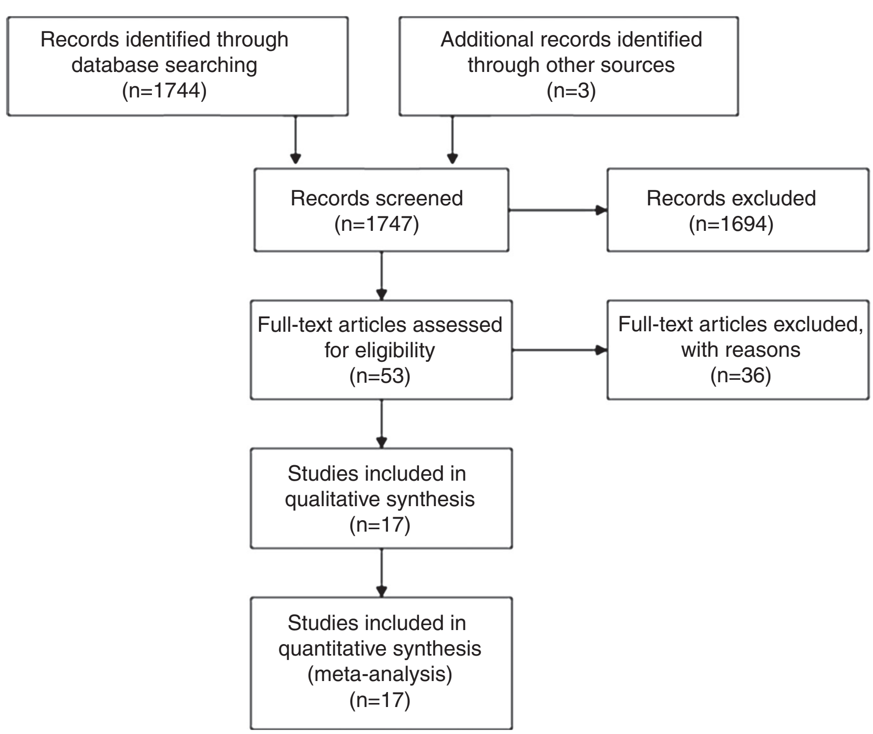


**Figure 1** Consolidated flow diagram (PRISMA Flow Diagram, 2009).

**Table 2** Selected randomized clinical trials (RCT).

| RCT | EL | J | R/A | I/C | P | I | C | O |
|---|---|---|---|---|---|---|---|---|
| Nelskylä et al. (2001)[1] | 2B | 0 | 62/62 | 32/30 | ASA I or II, between 18 and 50 years, gynecological surgery. | BIS between 50 and 60 years | ''Blinded'' monitor. Anesthesia was adjusted according to clinical parameters. | Time for spontaneous eye opening, extubation, orientation in time and place, hospital discharge and PONV. |
| Wong et al. (2002)[2] | 1B | 3 | 68/60 | 29/31 | >60 years, ASA I–III, orthopedic surgery. | BIS between 50 and 60. | ''Blinded'' monitor. Anesthesia was adjusted according to clinical parameters. | Time for spontaneous eye opening, orientation in time and place and PACU discharge. |
| Luginbühl et al. (2003)[3] | 2B | 2 | 160/160 | 80/80 | >18 years, gynecological surgery. | BIS between 45 and 55. | Anesthesia was adjusted according to clinical parameters. | Time to tracheal extubation. |
| Ahmad et al. (2003)[4] | 1B | 3 | 99/97 | 49/48 | >18 years, gynecological surgery. | BIS between 50 and 60. | Anesthesia was adjusted according to clinical parameters. | Time for hospital discharge. |
| Başar et al. (2003)[5] | 2B | 0 | 60/60 | 30/30 | >18 years, ASA I or II, abdominal surgery. | BIS between 40 and 60. | ''Blinded'' monitor. Anesthesia was adjusted according to clinical parameters. | Time of eye opening upon verbal command. |
| Puri and Murthy (2003)[6] | 2B | 2 | 30/30 | 14/16 | >18 years, myocardial revascularization or valve replacement with cardiopulmonary bypass, 18–70 years. | BIS between 45 and 55. | ''Blinded'' monitor. Anesthesia was adjusted according to clinical parameters. | Time of eye opening upon verbal command and extubation, intraoperative memory. |
| Kreuer et al. (2003)[7] | 2B | 2 | 120/120 | 40/40 | >18 years, ASA I-III, orthopedic surgery. | BIS 50 and in the last 15 min of 60. | Anesthesia was adjusted according to clinical parameters. | Time for spontaneous eye opening and extubation. |
| Myles et al. (2004)[8] | 1B | 5 | 2.503/2.463 | 1.225/1.238 | >18 years with at least one high risk factor to intraoperative awakening. | BIS between 40 and 60. | Monitor turned off. Anesthesia was adjusted according to clinical parameters. | Time for spontaneous eye opening, time for discharge from PACU and intraoperative memory. |
| Bruhn et al. (2005)[9] | 2B | 2 | 200/200 | 71/58 | >18 years, ASA I-III. | BIS of 50. In the last 15 min BIS of 60. | Anesthesia was adjusted according to clinical parameters. | Time for spontaneous eye opening and extubation, PONV and intraoperative memory. |
| Kreuer et al. (2005)[10] | 1B | 4 | 120/120 | 40/40 | >18 years, ASA I-III, orthopedic surgery. | BIS 50 and in the last 15 min change to 60. | Anesthesia was adjusted according to clinical parameters. | Time for spontaneous eye opening, extubation and time for leaving operation room. |
| Vretzakis et al. (2005)[11] | 1B | 3 | 130/121 | 36/44 | >18 years, myocardial revascularization or valve replacement with cardiopulmonary bypass, ejection fraction >45%. | BIS under 60. | Anesthesia was adjusted according to clinical parameters. | Intraoperative memory. |

**Table 2** (*Continued*)

| RCT | EL | J | R/A | I/C | P | I | C | O |
|---|---|---|---|---|---|---|---|---|
| Aimé et al. (2006)[12] | 2B | 1 | 140/125 | 34/54 | Age between 18 and 80 years, ASA I-III, urologic, orthopedic, abdominal and gynecological surgery. | BIS between 40 and 60. | ''Blinded'' monitor. Anesthesia was adjusted according to clinical parameters. | Time for spontaneous eye opening and traqueal extubation. |
| Ibraheim et al. (2008)[13] | 2B | 0 | 30/30 | 15/15 | >18 years, morbid obese, gastric band surgery. | BIS between 40 and 60. | Anesthesia was adjusted according to clinical parameters | Time of eye opening upon verbal command, time for extubation and discharge from PACU. |
| Kamal et al. (2009)[14] | 2B | 1 | 60/57 | 29/28 | >18 years, ASA I-III, abdominal surgery | BIS between 50 and 60. | ''Blinded'' monitor. Anesthesia was adjusted according to clinical parameters. | Time for spontaneous eye opening, extubation, orientation in time and place, leaving operating room, discharge from PACU and intraoperative memory. |
| Zhang et al. (2011)[15] | 1B | 5 | 5.309/5.228 | 2.919/2.309 | >18 years, total intravenous anesthesia | BIS between 40 and 60. | ''Blinded'' monitor. Anesthesia was adjusted according to clinical parameters. | Intraoperative memory. |
| Chan et al. (2013)[16] | 1B | 3 | 921/902 | 450/452 | >60 years, elective non-cardiac surgery. | BIS between 40 and 60. | Anesthesia was adjusted according to clinical parameters. | Time for spontaneous eye opening, time for discharge from PACU, cognitive dysfunction in the postoperative period (one week and three months later) and delirium. |
| Radtke et al. (2013)[17] | 1B | 3 | 1.277/1.155 | 575/580 | >60 years | BIS between 40 and 60. | ''Blinded'' monitor. Anesthesia was adjusted according to clinical parameters. | Cognitive dysfunction in the postoperative period (one week and three months later) and delirium. |

ASA, American Society of Anesthesiologists Physical Status; RCT, Randomized Clinical Trial; EL, Evidence Level; J, Jadad score; R/A, patients randomized and analyzed; I/C, intervention group/control group; P, population; I, intervention; C, control or comparison; O, outcome.

spontaneous eye opening of 0.28 min (95% CI −0.75, 0.20). However, the statistically significant difference was lost (Fig. 2).

The time for eye opening upon verbal command is counted from the end of last suture, when the inhaled or intravenous anesthetic is discontinued and the patient is asked to open his eyes. There was a reduction in time to eye opening at verbal command of 0.63 min (95% CI −1.30, 0.05), with an $I^2 = 67\%$, with no statistically significant difference (Fig. 3).

The use of BIS reduced 1.18 min in the time of tracheal extubation (95% CI −1.65, −0.70), with an $I^2 = 79\%$. In sensitivity analysis, when the study Kreuer et al.[7] was removed, the time to tracheal extubation reduced 0.87 min (95% CI −1.36, −0.38), with an $I^2 = 59\%$, maintaining, therefore, a statistically significant difference (Fig. 4).

The combination of three studies[1,2,14] demonstrated that the time for orientation in time and place reduced 3.08 min (95% CI −3.70, −2.45) with an $I^2 = 73\%$. In sensitivity analysis, when the study Nelskylä et al.[1] was removed we have a reduction of 3.76 min (95% CI −4.55, −2.97) with an $I^2 = 0\%$, maintaining, therefore, a statistically significant difference (Fig. 5).

When using the BIS, the time for the patient to be able to get out of the operating room and go to PACU reduced 2.93 min (95% CI −3.68, −2.18), with an $I^2 = 92\%$. In sensitivity analysis, when removed the study Kreuer et al.,[10] we

**Table 3** Full-text articles excluded with reasons.

| Article | Reason of exclusion |
|---|---|
| Sebel et al. (1997)[18] | Before incision tetanus stimulation was applied to the ulnar nerve. Any presence of movement, anesthesia was deepened. In the absence of movement, anesthesia was maintained. After incision any movement was considered for the deepening of anesthesia. The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Yli-Hankala et al. (1999)[19] | The data expression of the outcomes was made in medians. |
| Mi et al. (1999)[20] | Patients were monitored with BIS and outcomes were analyzed due to different anesthetic regimens. The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Nakayama et al. (2002)[21] | All patients were monitored with BIS and outcomes were analyzed due to different anesthetic regimens (only propofol or propofol and fentanyl). The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Lehmann et al. (2002)[22] | All patients were monitored with BIS and analyzed outcomes resulting from different anesthetic techniques (with manual propofol infusion vs. propofol in Target Controlled Infusion – TCI). The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Paventi et al. (2002)[23] | All patients were monitored with BIS and analyzed outcomes resulting from different anesthetic techniques (manual propofol infusion vs. propofol in TCI). The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Lehmann et al. (2003)[24] | All patients were monitored with BIS (group BIS 50 and group BIS 40). The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Yamaguchi et al. (2003)[25] | All patients were monitored with BIS and analyzed outcomes resulting from different anesthetic drugs and techniques (propofol group/iv induction and sevoflurane group with inhalational induction in adult by the vital capacity technique). The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Buyukkocak et al. (2003)[26] | All patients were monitored with BIS and outcomes were analyzed due to different anesthetic drugs, four different methods of sedation associated with topical anesthesia. The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Forestier et al. (2003)[27] | All patients were monitored with BIS and analyzed five groups with different concentrations of sufentanil. The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Schneider et al. (2003)[28] | All patients were monitored with BIS and analyzed four different anesthetic regimens. The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Schneider et al. (2003)[29] | All patients were monitored with BIS and analyzed two different anesthetic regimens. The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Liu (2004)[30] | Meta-analysis. The criteria for inclusion in the systematic review were randomized controlled trials. |
| Bauer et al. (2004)[31] | All patients were monitored with BIS and analyzed two different anesthetic regimens (TCI vs. manual propofol infusion). The BIS was used but is not described whether it was blinded. The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Bestas et al. (2004)[32] | All 50 patients (two groups of 25) were monitored with BIS and were blinded, with analysis of two different anesthetic regimes. The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Boztug et al. (2006)[33] | Article not found. |
| Puri et al. (2007)[34] | All patients were monitored with BIS, with analysis of two different types of propofol infusion. The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |

**Table 3** (*Continued*)

| Article | Reason of exclusion |
|---|---|
| Lindholm et al. (2008)[35] | The paper analyzes the degree of proficiency in handling the BIS by nurses' anesthetists. The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Avidan et al. (2008)[36] | In the control group, anesthesia was maintained with BIS ''blinded'' but with an expired fraction of 0.7–1.3 minimum alveolar concentration of inhaled anesthetic. |
| Bejjani et al. (2009)[37] | All patients were monitored with BIS with memory processing analysis. The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Delfino et al. (2009)[38] | All patients were monitored with BIS or cerebral state index, with analysis of propofol infusion with these two types of monitoring. The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Kerssens et al. (2009)[39] | Study of intraoperative memory and retrieval of words heard during the trans-operative, through memory tests postoperatively. |
| Mashour et al. (2009)[40] | Cohort study. The criteria for inclusion in the systematic review were randomized controlled trials. |
| Satisha et al. (2010)[41] | Cohort study. The criteria for inclusion in the systematic review were randomized controlled trials. |
| Meybohm et al. (2010)[42] | Protocol study. The criteria for inclusion in the systematic review were randomized controlled trials. |
| Leslie et al. (2010)[43] | Retrospective cohort study. The criteria for inclusion in the systematic review were randomized controlled trials. |
| Avidan et al. (2009)[44] | Protocol study. The criteria for inclusion in the systematic review were randomized controlled trials. |
| Ellerkmann et al. (2010)[45] | Inhalation or intravenous anesthesia, complemented by regional anesthesia (combined anesthesia). The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Yufune et al. (2011)[46] | The 38 patients were monitored with BIS and outcomes were analyzed due to different anesthetic regimens, as well as different concentrations of remifentanil. The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Liu et al. (2011)[47] | All patients were monitored with BIS and outcomes were analyzed due to different anesthetic regimens, target controlled infusion of propofol vs. closed-loop management. The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Avidan et al. (2011)[48] | The control group was adjusted for maintaining an expired fraction of 0.7–1.3 minimum alveolar concentration of inhaled anesthetic. |
| Aimé et al. (2012)[49] | The 102 patients were monitored with BIS or Entropy, in both groups, the values were blinded, and anesthesia was conducted by clinical parameters. The study goes out of focus – BIS intervention compared to the control group (consciousness guided by clinical parameters only). |
| Mashour et al. (2012)[50] | The control group was blinded, but adjusted to a minimum alveolar concentration of inhaled anesthetic by age. |
| Persec et al. (2012)[51] | The results of this study cannot be meta-analyzed as they provide no standard deviation. |
| Fritz et al. (2013)[52] | Retrospective cohort study. The criteria for inclusion in the systematic review were randomized controlled trials. |
| Villafranca et al. (2013)[53] | Retrospective cohort study. The criteria for inclusion in the systematic review were randomized controlled trials. |

BIS, bispectral index.

have a reduction of 4.89 min (95% CI −5.95, −3.83) with an $I^2 = 0\%$, maintaining, therefore, statistically significant difference (Fig. 6).

The time for patients to achieve the discharge criteria in the PACU (Aldrete-Kroulik modified index) was reduced 4.05 min (95% CI −7.23, −0.87), with $I^2 = 91\%$. In sensitivity analysis, when removed the study Ibraheim et al.,[13] we have a reduction of 22.35 min (95% CI −31.01, −13.69) with $I^2 = 20\%$, maintaining statistically significant difference (Fig. 7).

There was no statistically significant difference between the intervention and control in the evaluation of the necessary time to hospital discharge (95% CI, −22.08, 30.52) with $I^2 = 0\%$ (Fig. 8).

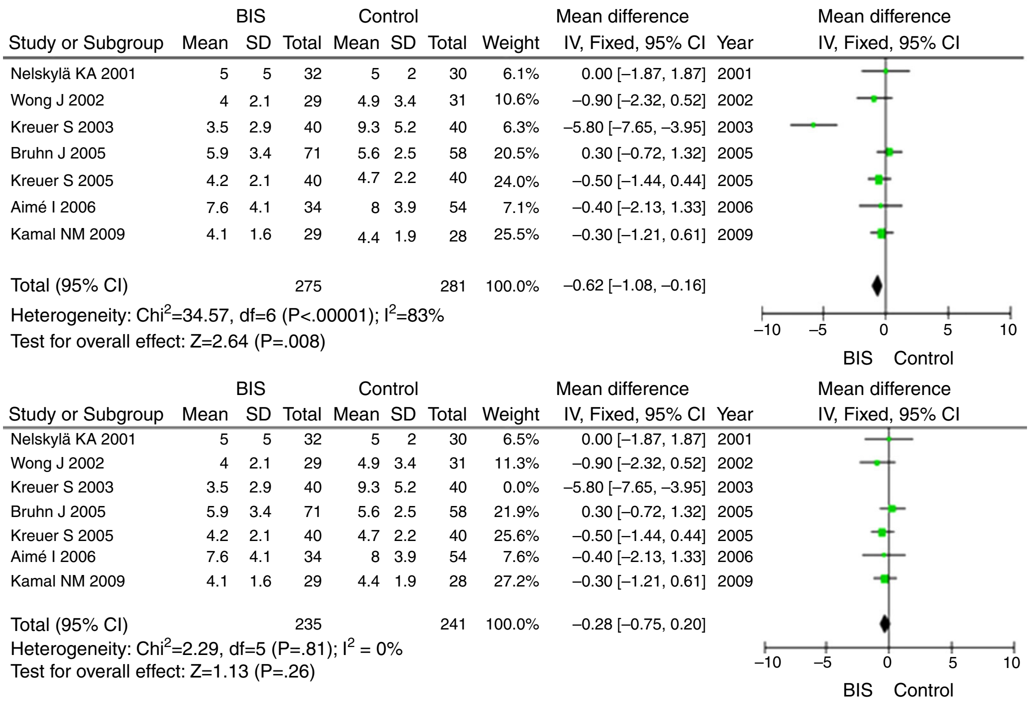


**Figure 2** Time for spontaneous eye opening (min).

The incidence of PONV was lower in anesthesia conducted with BIS, with a risk reduction of 12% (95% CI −0.22, −0.01) with $I^2 = 61\%$, which was statistically significant (Fig. 9).

There was no risk reduction of cognitive disorders in the post operatory with 1 week after extubation, in patients using BIS (95% CI, −0.06, 0.01, $I^2 = 0\%$). There was no statistically significant difference between the intervention and control (Fig. 10).

The cognitive disorders after surgery at 3 months after extubation had a risk reduction of 3% (95% CI −0.05, −0.00), and $I^2 = 52\%$, which was statistically significant (Fig. 11).

There was a 6% reduction in the risk of delirium in the post operatory in patients monitored with BIS (95% CI −0.10, −0.03) $I^2 = 11\%$, which was statistically significant (Fig. 12).

The use of BIS had a risk reduction of 1% for the intraoperative memory (Recall), a statistically significant difference (−0.01 [95% CI, −0.01, −0.00]) with $I^2 = 0\%$. The intraoperative memory is the awakening confirmed by the patient. It was not made a differentiation of studies with patients classified as low or high risk for intraoperative memory (Fig. 13).

## Discussion

The use of monitoring with the BIS showed benefits by reducing the time to extubation in 0.87 min, orientation in time and place in 3.76 min and leaving operating room in 4.89 min. Patients had a reduction in 22.35 min to reach the criteria for PACU discharge. The combined results of the studies showed that the incidence of PONV risk reduction of 12% in patients BIS monitoring.

Cognitive disorders in postoperative patients with 1 week after extubation did not show statistically significant difference. However, there was a 3% reduction in the risk of cognitive disorders in the postoperative patients

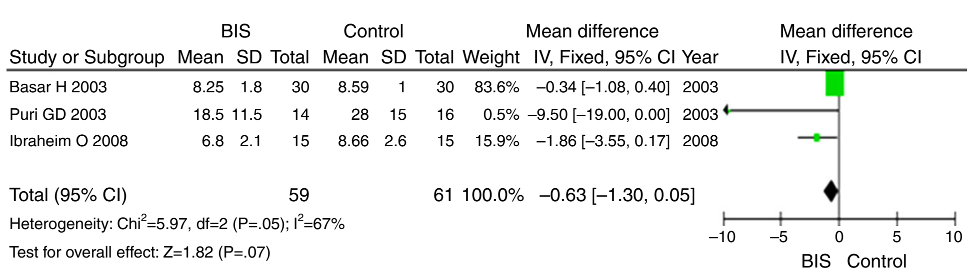


**Figure 3** Time for eye opening upon verbal command (min).

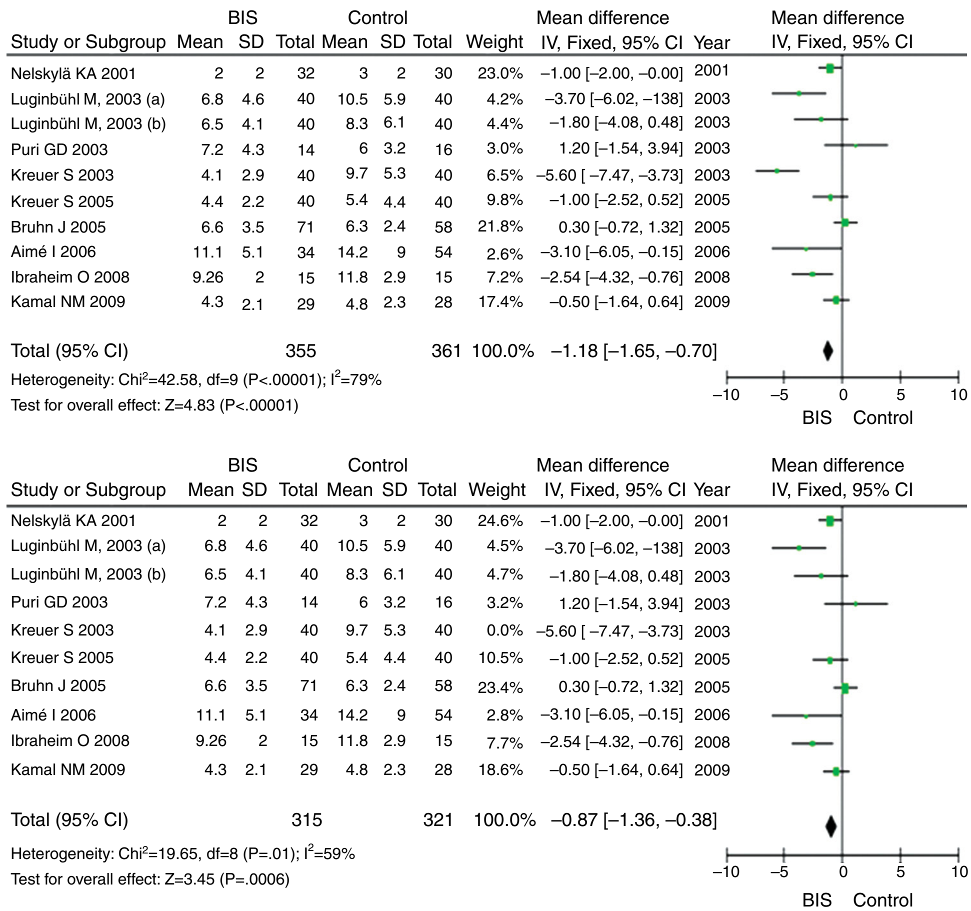


**Figure 4** Time to tracheal extubation (min). Luginbühl (2003) studied within a single outcome, two different anesthetic regimens with propofol (a) and desflurane (b).

3 months after extubation. There was a 6% reduction in the risk of delirium incidence of postoperative in patients using BIS monitoring. In addition, the memory of the intraoperative risk had a reduction of 1% after using BIS.

The 17 studies selected by the pre-established criteria showed a heterogeneity that was soon noticed. Factors related to anesthetic technique, the patient and the surgical procedure were observed. Studies that analyzed the consumption of anesthetics showed no standardized meas-

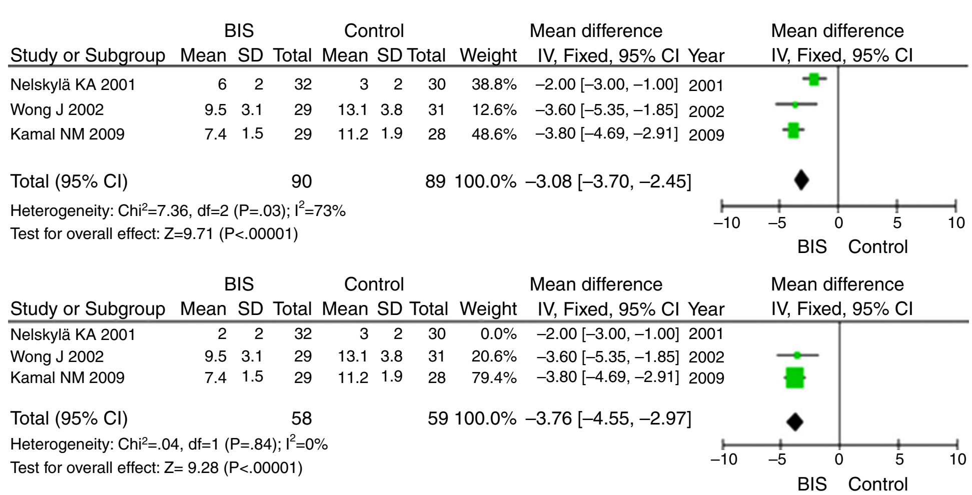


**Figure 5** Time for orientation in time and place (min).

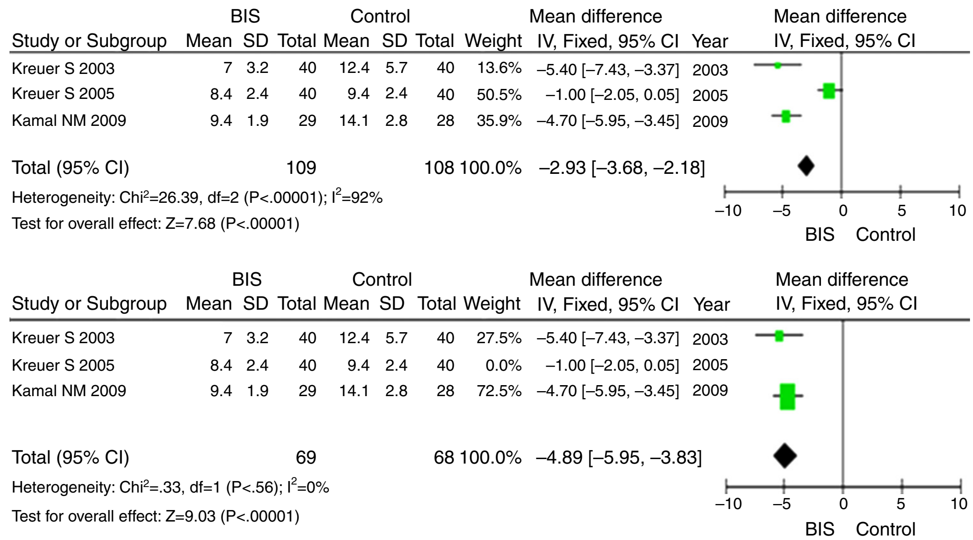


**Figure 6** Time for leaving operation room (min).

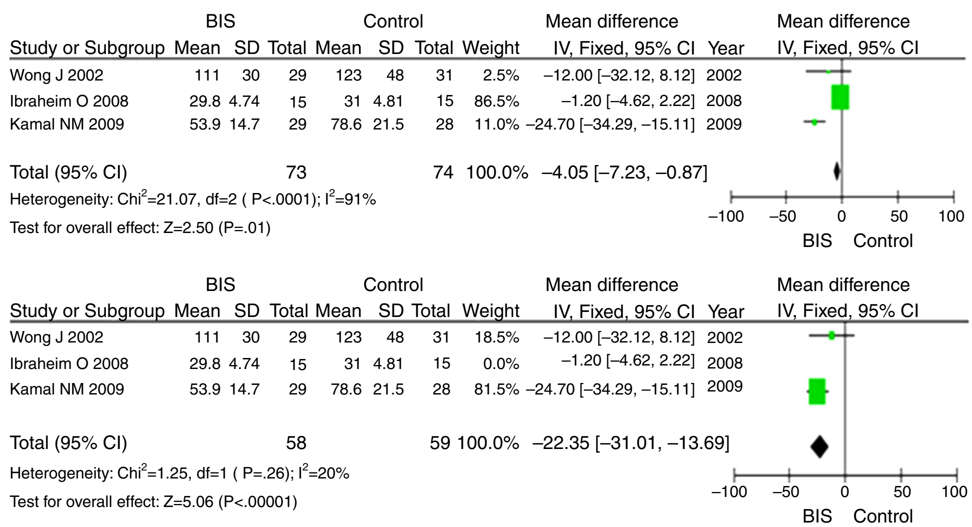


**Figure 7** Time for discharge from PACU (min).

ures that enabled the selection of at least two studies for the meta-analysis.

The study Ibraheim et al.[13] involved morbidly obese patients. Three studies were conducted exclusively with patients over 60 years of age.[2,16,17]

Puri et al.[6] and Vretzakis et al.[11] studied patients undergoing cardiac surgery with extracorporeal circulation.

Myles et al.[8] studied patients with at least one high-risk factor for awakening with intraoperative memories (high risk heart surgery, cesarean sections, hypovolemic shock, rigid bronchoscopy, cardiovascular instability and expected hypotension during surgery, lung disease in advanced stages, historical of awakening with intraoperative memories, difficult airway, high consumption of alcohol, chronic use

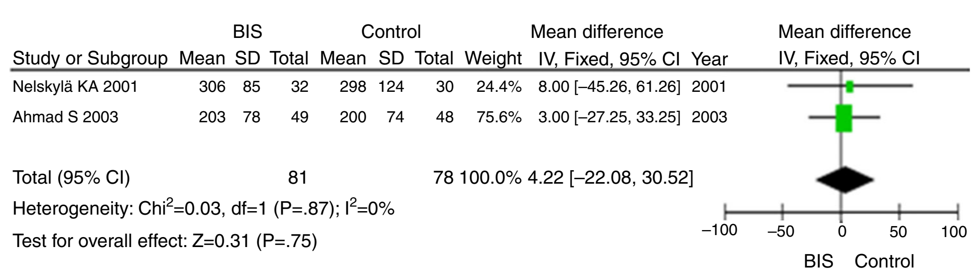


**Figure 8** Time to hospital discharge (min).

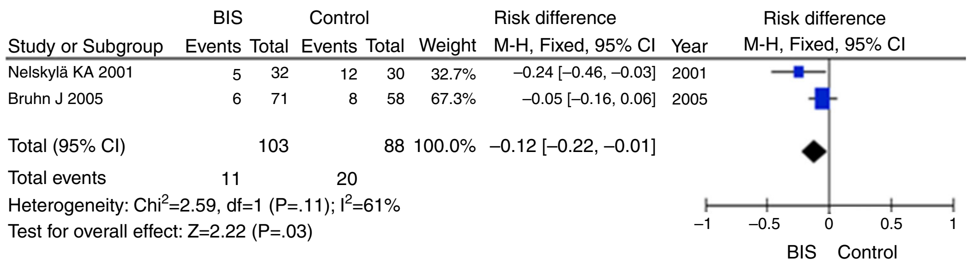


**Figure 9** Postoperative nausea and vomiting (PONV) – *n* (%).

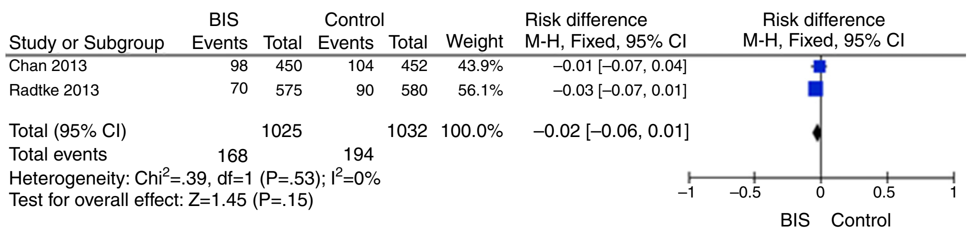


**Figure 10** Cognitive disorders in the postoperative period (1 week after extubation) – *n* (%).

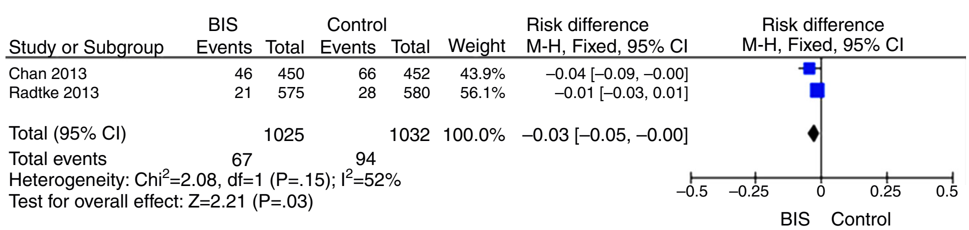


**Figure 11** Cognitive disorders in the postoperative period (3 months after extubation) – *n* (%).

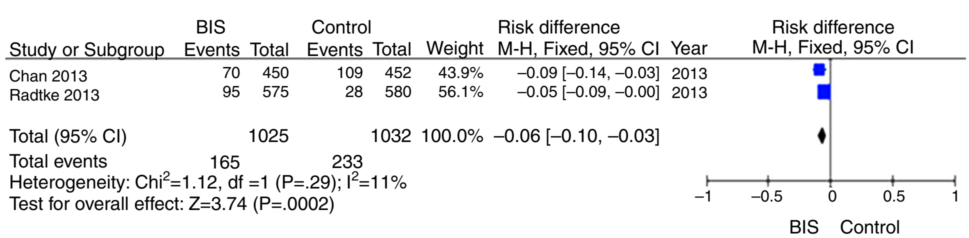


**Figure 12** Postoperative delirium – *n* (%).

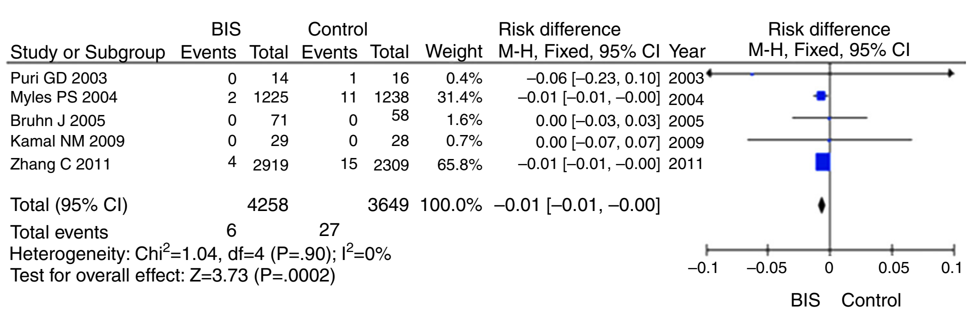


**Figure 13** Intraoperative memory – *n* (%).

of benzodiazepines or opioids and therapy with protease inhibitors).

The outcomes analyzed with continuously variable related to the time of recovery and discharge of patients were: time for spontaneous eye opening, time for eye opening upon verbal command, time for extubation, time for orientation in time and place, time for leaving operating room, time for PACU discharge and time for hospital discharge.

The outcomes of dichotomous variable, related to adverse events were PONV, cognitive disorders in the postoperative 1 week after extubation, cognitive disorders in the postoperative 3 months after extubation, postoperative delirium and intraoperative memory.

Some primary studies contributed only one outcome analyzed.[3–5,11,15]

The individualization of outcomes derived from studies involving balanced anesthesia or total intravenous anesthesia was not made.

Clinically, the cost of implementation of BIS monitoring can be justified by allowing advantages in the maintenance of ambulatory surgeries as well as in the techniques of early awakening and especially it can reduce the incidence of adverse events.

The cost of the disposable electrode is a cause of discussion about the value in use of BIS. Thus, it is important the active participation of professionals, primarily with health administrators, in developing a policy plan that optimize resources and give greater safety and comfort for the patients.

So far, there is no gold standard to span the entire spectrum of anesthetic effect on the central nervous system, and the BIS is undoubtedly the most studied, but is one of many monitors derived from EEG used nowadays. Monitoring the depth of anesthesia as new technology is in its beginning. The new boundary is the individualization of monitoring the hypnotic and its effects on the central nervous system.

## Conflicts of interest

The authors declare no conflicts of interest.

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